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# Test the Cardioprotective Effectiveness of Turmeric Ethanol Extract (Curcuma Longa) in Doxorubicin-In-Rat Wistar (Rattus Norvegicus) Doxorubicin-Induced Males

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**Abstract:** *Cardiotoxicity is mostly due to the use of chemotherapy drugs, with the class of anthracyclines drugs being 86.8. One of the most commonly used anthracyclines is doxorubicin. Turmeric with the scientific name Curcuma longa linn is one of the medicinal plants, the main compound is curcumin is considered able to reduce the risk of heart attack. The goal of this study tested the cardioprotective effectiveness of turmeric ethanol extract (curcuma longa linn.) in doxorubicin-induced male wistar (rattus norvegicus) mice. This type of research is experimental, in the Pharmacology Laboratory of the Faculty of Pharmacy, University of North Sumatra, and November 2020. Animals experimented on male wistar rats (Rattus norvegicus) weighing 150 - 200 grams. Data analysis, if (P > 0.05), continued with One Way ANOVA, but if (P <.05) followed by the Tukey HSD Post Hoc test to see real differences between treatments. If the distributed data is abnormal then the Kruskal-Wallis test results are used. Statistical test results, serum levels of CK–MB in the normal group have significant differences (p<0.05) with the negative control treatment group and the treatment group I, but do not have a significant difference (p>0.05) with the positive control group, treatment group II and the treatment group III. Concluding that turmeric ethanol extract has the ability to lower levels of biomarkers of heart damage namely CK-MB and LDH induced with doxorubicin, gradually increasing doses of turmeric ethanol extract can reduce the incidence of heart cell damage, which is most effective at doses of EEK 500 mg / kg BB. Turmeric ethanol extract has cardioprotective effects induced with doxorubicin. Administration of turmeric ethanol extract can repair heart organ tissue induced with doxorubicin based on histological picture of the heart. It is hoped that researchers will be able to conduct research on the toxic effects of giving turmeric ethanol extract to the hearts of mice conducted subchronically.*
**Keywords:** *turmeric ethanol extract; cardioprotective; doxorubicin*

## I. Introduction

Cardiotoxicity is a condition in which the occurrence of damage to the heart and blood vessels due to toxic chemical exposure (Huang et al. 2011);(Wisman, Nasution, and Panggabean 2017). Cardiotoxicity is mostly due to the use of chemotherapy drugs (Siahaan et al. 2016), the drug anthracyclines are 86, 8% (Martha, Surianata, and Santoso 2007). One of the drugs of the anthracyclines that are often used is doxorubicin (Tacar, Sriamornsak, and Dass 2013); (Childs et al. 2002); (Thomas 2017); (Justyna 2017). The incidence of patients treated with doxorubicin and its derivatives is about 10% will experience heart complications up to 10 years after the cessation of chemotherapy (Octavia et al. 2012). Schulke's study, giving doxorubicin 4 mg/kg BB in animals tried to mice done once a wTEE for 4 weeks intraperitoneal (IP) there was an increase in heart fibrosis when compared to the control group that was not given doxorubicin (Schunke et al. 2013).

Turmeric with the scientific name Curcuma longa is one of the spice plants and is also a medicinal plant (Ariani 2017); (Sabale, Modi, and Sabale 2013). The main compound of turmeric is curcumin (Nabofa et al. 2018). Many researchers are interested in studying the safety, antioxidant properties (Wanninger et al. 2015a), anti-inflammatory, anti-cancer and its ability to lower the risk of heart attack (Hartati 2013).

Based on the description above, researchers are interested in testing the effectiveness of turmeric ethanol extract (EEK) on doxorubicin-induced experimental animals on the heart organ with the parameters measured are CK-MB (Creatine kinase-MB) and LDH (Lactate dehydrogenase) as biomarkers and perform a histopathological examination of heart tissue in trial animals. The study aimed to test the cardioprotective effectiveness of turmeric ethanol extract (Curcuma longa) in doxorubicin-induced male Wistar (Rattus norvegicus) mice.

From the above facts, it becomes important to develop herbal remedies. Mangosteen peel is a shell that is discarded by consumers or can be called agricultural waste. The use of mangosteen peel for treatment in Indonesia is still not much, especially as an antipyretic analgesic. Thus, this study was designed to find out the analgesic and antipyretic effects of mangosteen peel methanol extract on male Wistar rats.

## II. Review of Literatures

Cardiotoxicity is damage that occurs in cardiac electrophysiology or heart muscle damage. The heart becomes weak and inefficient in pumping blood flow throughout the body. This condition can also occur as a result of chemotherapy treatment (Huang et al. 2011). According to Thomas (2017), systemic anticancer treatment can have a detrimental effect on the cardiovascular system (Biogen 2020). Doxorubicin can cause cardiotoxicity in long-term use, side effects on chronic use are irreversible (Han et al. 2008). From the results of research conducted by Zhou et al., (2001) try-and-test animals injected with doxorubicin resulting in higher levels of ROS.

Superoxide and hydrogen peroxide are two major components of ROS that are important in the cardiovascular system (Zhou et al. 2001). In the field of traditional medicine turmeric is familiar and widely used as an ingredient for herbal medicine. In turmeric contained curcumin compounds. The efficacy and interesting properties of chemical physics of curcumin compounds, making it used as a lead compound for the development of new drug compounds (Wanninger et al. 2015b). Curcumin can be seen closely related to the cardiovascular system through pharmacological activities, among others, cardioprotective, hypolipidemic, antihypertensive and vasodilation (Chattopadhyay et al. 2004).

## III. Research Methods

This type of research is experimental, in the Laboratory of Pharmacology Faculty of Pharmacy,University of North Sumatra, November 2020.

### 3.1 Tool

Veterinary surgery tools, laboratory glass tools, microscopes, 1 ml syringe, 3 ml syringe, oral sonde, centrifuge, test tubes, animal balance/analytical balance sheet, beaker glass, mortar, stamper, spatula, parchment paper, measuring pumpkin, kuvet, microtube, micropipette, rotarymikrotom, water handler, and object-glass.

### 3.2 Material

Turmeric Ethanol extract comes from fresh turmeric purchased at Medan Sei

Sikambing Market, Doxorubicin, NaCl, 10% formalin, chloroform, CMC-Na, liquid paraffin, toluene, and acetone, CK-MB, and LDH reagents. The experiment animal male Wistar rat (Rattus norvegicus) weighing 150 - 200 grams.

### 3.3 Preparation of Turmeric Ethanol Extract Test Ingredients

Phytochemical screening of turmeric ethanol extract, phytochemical screening is done to find out the group of compounds from alkaloids, flavonoids, glycosides, saponins, tannins, and steroids / triterpenoids (Depkes RI, 1995., Farnsworth, 1996). Solution manufacturing includes the manufacture of CMC-Na suspension 0.5% b/v and TEE (Turmeric Ethanol Extract) suspension doses of 100, 300, and 500 mg/kg weight. Cardioprotective effectiveness test procedures refer to several studies, namely El-Sayed,et al 2011; Aggarwal, el al 2009; Salam et al 2016. This test was conducted using male wistar rats as subjects.

1. Group I (Normal): Group of male wistar rats (Rattus norvegicus) is only given feed and Na

a. CMC 0.5%.

2. Group II (Negative control): Group of male Wistar rats (Rattus norvegicus) who were given doxorubicin 5 mg/kg weight on an i.p basis and drank a 0.5% Na-CMC suspension.
3. Group III (Positive control): Group of male wistar rats (Rattus norvegicus) induced doxorubicin 5 mg / kg weight 1 day 1 time on days 1, 7, 14 and 20 on an i.p+ Vitamin E 1% weight orally 1 time 1 day daily.
4. Group IV: Group of male wistar rats (Rattus norvegicus) induced doxorubicin 5 mg / kgBB 1 day 1 time on days 1, 7, 14 and 20 i.p + 100 mg / kgbb TEE orally 1 time 1 day daily.
5. Group V: Group of male wistar rats (Rattus norvegicus) induced doxorubicin 5 mg / kg weight 1 day 1 time on days 1, 7, 14 and 20 i.p + 300 mg / kgbb TEE orally 1 time 1 day daily.
6. Group VI: Group of male wistar rats (Rattus norvegicus) induced doxorubicin 5 mg / kgBB 1 day 1 time on days 1, 7, 14 and 20 i.p + 500 mg / kg weight TEE orally 1 time 1 day daily.

### 3.4 Making Heart Tissue Preparations

The preparation of heart tissue by the procedure outlined by Miranda-Osorio, (2016). The organ is fixated with a 10% formalin solution for 3-4 hours, then with acetone 3 times, cleaning (cleaning) using toluent 3 times (1-2 hours each), embedding (immersion) samples in liquid paraffin at a temperature of 60-70 ° C as much as 3 times (each for 2 hours), then printing paraffin blocks. The cutting stage of paraffin blocks is done using microtomes, sheets with a thickness of 5 μm. Placed in a water handler at 30 °C temperature, packaged on the object-glass, and heated in the oven for 2-3 minutes. The resulting sheet is observed under a light microscope with a magnification of 10x40, observed the number of necrosis and normal cells (Salam, 2016).

### 3.5 Operational Definition

**Table 1.** Operational Definitions

| No | Variable | Definition | Measuring instruments | Measuring results | Scale |
|---|---|---|---|---|---|
| **1.** | Turmeric ethanol extract (variable free) | Turmeric extraction results using a 96% ethanol solvent by maceration are given for 21 days at doses of 100, 300, and 500 mg / kg weight in subjects. | Scales | Concentration (%) | Ratio |
| **2.** | CK-MB and LDH (parameter) | Markers used to detect cardiotoxicity | Spektrofotometer | Measure (U/L) | Ratio |
| **3.** | Vitamin E | Positive controls used as comparisons and cardioprotective standards | | Vitamin E | Ratio |
| **4.** | CMC- Na 0,5% | Cellulose derivatives that serve as negative controls and solvents in the manufacture of TEE suspensions | Activity | Measure (U/L) | Ratio |
| **5.** | Damage to heart tissue (variable bound) | The circumstances resulting from the administration of doxorubicin are characterized by necrosis. | Light microscope | Myositolysis/vacuoleization of myocardial necrosis. Normal cell bleeding interstitial fibrosis and its distribution | Nominal |
| **6.** | Doxorubicin | Anthracycical antibiotics used to induce cardiotoxicity. | Activity | Measure (U/L) | Rasio |

### 3.6 Data Analysis

The data were analyzed with Shapiro-Wilk to see the normality of the data. If the data is normally distributed ($P > 0.05$), proceed with One Way ANOVA to determine the average difference between the groups. If ($P < 0.05$) continued with the Tukey HSD Post Hoc test to see a noticeable difference between treatments. But if the distributed data is not normal then the Kruskal-Wallis test is used.

## IV. Discussion

### 4.1 Cardioprotective Effectiveness of Turmeric Ethanol Extract against CK Serum Size

Turmeric ethanol extract (EEK) was given orally from day one in treatment groups I, II, and III. The positive control group was given vitamin e 1% BB daily orally. Administration of doxorubicin is done intraperitoneally as much as 5 mg/kg weight on days 1, 7, 14, and 20. Previous research on doxorubicin doses of 5 mg / kg weight given gradually until obtained accumulative doses can cause cardiotoxic (El-Sayed et al. 2011). The effectiveness of the examination can be seen in the table below:

**Table 2.** Serum Size CK – MB

| Treatment Group | CK-MB ± SD (U/L) |
|---|---|
| Normal Group | 310,33 ± 5,00 |
| Negative Group (Induction of Doxorubicin 20 mg/kg weight + Na-CMC 0.5%) | 946,12 ± 7,25 |

| | |
|---|---|
| Positive control group (Induction of Doxorubicin 20 mg/kg weight + Vitamin E 1% weight) | 442,23 ± 3,19 |
| Treatment Group I ; Tikus Induced *Doxorubicin* 20 mg/kg weight + TEE 100 mg/kg weight | 755,22 ± 11,20 |
| Treatment Group II ; Tikus Induced *Doxorubicin* 20 mg/kg weight + TEE 300 mg/kg weight | 410,02 ± 2,11 |
| Treatment Group III ; Tikus Induced *Doxorubicin* 20 mg/kg weight + TEE 500 mg/kg weight | 358,32 ± 32,52 |

The results for the serum value of CK–MB of the normal group were estimated at 310.33 ± 5.00 U/L. The negative group induced only doxorubicin had the highest serum size of CK-MB which is believed to be 996.12 ± 7.25 U/L. This is due to the formation of free radicals from doxorubicin so that the occurrence of increased oxidative stress is believed to be the forerunner of cardiotoxic occurrence (Minotti et al. 1998). While the treatment group I TEE 100 mg/kg bb + doxorubicin has the largest serum size of CK-MB which is 755.22 ± 11.20 U / L. And the treatment group III TEE 500 mg / kg weight + doxorubicin has the smallest serum size of CK - MB which is 379.32 ± 34.57 U / L which is close to the normal group. This suggests that a TEE of 500 mg/kg weight can decrease the size of doxorubicin-induced CK–MB. Based on the results of statistical tests, serum CK–MB size in the normal group had significant differences ($p<0.05$) with the negative control treatment group and treatment group I, but did not have significant differences ($p>0.05$) with the positive control group, treatment group II and treatment group III. The serum size of the CK–MB negative control group had significant differences ($p<0.05$) with the normal group, positive control treatment, treatment group I, treatment group II, and treatment group III. The serum size of the CK–MB positive control group had significant differences ($p<0.05$) with the negative control treatment group and the treatment group I and had no significant differences ($p>0.05$) with the normal control group, the control group treatment II and group treatment III. The serum size of the CK–MB treatment group I had a significant difference ($p<0.05$) with the normal group, the positive control group with a 1% BB vitamin e comparison, the treatment group II and the treatment group III. The serum size of CK–MB treatment group II had significant differences ($p<0.05$) with negative groups and treatment group I and had no significant differences ($p>0.05$) with the normal group, positive control group and treatment group III. Serum size CK–MB in treatment group III had significant differences ($p<0.05$) with negative groups and treatment group I and had no significant differences ($p>0.05$) with the normal group, positive control group and treatment group II.

**b. Cardioprotective Cardioprotective Effectiveness of Turmeric Ethanol Extract against LDH Size in Male Wistar Rats in Doxorubicin Induction**

Based on the results of the examination conducted, obtained results in the normal group of serum size values LDH differed significantly with the negative group induced doxorubicin, the treatment group I TEE 100 mg / kg weight + doxorubicin accumulative dose 20 mg / kg weight. The normal group's LDH size did not differ much from the treatment group III TEE 500 mg/kg weight + doxorubicin accumulative dose 20 mg/kgBB, the positive control group doxorubicin accumulative dose 20 mg/kg weight + vitamin E 1% weight and treatment group II doxorubicin accumulative dose 20 mg/kg weight + TEE 300 mg/kg weight. The increase in the size of LDH in the negative group could also be due to the small size of endogenous antioxidants in the heart resulting in the myocardium being

very sensitive to damage caused by free radicals resulting from doxorubicin. (Olson et al. 1988). The results of the examination can be seen in the table and figure below (table 4.3).

**Table 3.** Phytochemical Screening Results of Mangosteen Peel Methanol Extract

| **Fitokimia** | **Reactor** | **Result** |
|---|---|---|
| Alkaloid | Bouchardart | + |
| | Mayer | + |
| | Dragondroff | - |
| | Wagner | + |
| Saponin | Aquadest + Alcohol 96% | - |
| Flavonoid | FeCl3 5% | + |
| | Mg $_{(s)}$ + HCl $_{(p)}$ | - |
| | NaOH 10% | - |
| | H2SO4 (p) | - |
| Tanin | FeCl3 1% | + |
| Steroids and Terpenoids | Salkowsky | - |
| | Liberman Bouchard | + |

From the table data above, it can be seen that mangosteen peel methanol extract contains several phytochemical compounds including Alkaloids, Saponins, Flavonoids, Tannins, as well as Steroids and Terpenoids.

**Table 4.** Serum Size LDH

| **Treatment Group** | **LDH ± SD (U/L)** |
|---|---|
| Normal Group | 522,11 ± 5,52 |
| Negative Group (Induction *Doxorubicin* 20 mg/kg weight+ Na-CMC 0,5%) | 2766,21 ± 2,16 |
| Positive control group ( Induksi *Doxorubicin* 20 mg/kg weight + Vitamin E 1% weight) | 651,78 ± 2,07 |
| Treatment Group I ; Tikus Induced *Doxorubicin* 20 mg/kg weight + TEE 100 mg/kg weight | 1345,10 ± 75,01 |
| Treatment Group II ; Tikus Induced Doxorubicin 20 mg/kg weight + TEE 300 mg/kg weight | 847,46 ± 2,80 |
| Treatment Group III ; Tikus Induced Doxorubicin 20 mg/kg weight + TEE 500 mg/kg weight | 731,21 ± 2,08 |

Judging from the results of serum LDH studies in tables and figures on the previous page, it is known that the results for serum LDH values of the normal group were estimated at 522.11 ±

5.52 U/L. The negative group induced only doxorubicin had the highest serum LDH size of 2766.21 ± 2.16 U/L. The increase in the size of LDH resulting from oxidative stress states affecting $Ca^{2+}$ homeostasis occurred directly through the induction of mitochondrial transition permeability with changes in calcium transport in mitochondria. Because these changes eventually cause damage to even death to heart cells followed by the release of several biomarkers into the circulation (Schimmel, et al., 2004). While the treatment group I TEE 100 mg/kg bb + doxorubicin has the largest serum LDH size of 1345.10 ± 75.01 U / L. And the treatment group III has the smallest serum size of LDH which is 731.21 ± 2.08 U / L which is close to the normal group. Just like the serum size of CK –MB, serum size

LDH also shows that TEE 500 mg / kg weight can reduce the size of LDH induced doxorubicin. This shows that curcumin compounds contained in turmeric rhizomes can prevent free radical damage caused by doxorubicin starting from the smallest dose of 100 mg / kg weight. Based on the results of statistical tests conducted, serum LDH size in the normal group had significant differences ($p<0.05$) with the negative control treatment group and treatment group I, but did not have significant differences ($p>0.05$) with the positive control group, treatment group II and treatment group III. The serum size of the negative control group LDH had significant differences ($p<0.05$) with the normal group, positive control treatment, treatment group I, treatment group II, and treatment group III. The serum size of the LDH positive control group had significant differences ($p<0.05$) with the negative control treatment group and treatment group I and had no significant differences ($p>0.05$) with the normal control group, the negative control group treatment II and group III.

Serum LDH treatment group I had significant differences ($p<0.05$) with the normal group, the positive control group with a 1% BB vitamin e comparison, the treatment group II and the treatment group III. The serum size of the LDH treatment group II had significant differences ($p<0.05$) with the negative group and the treatment group I and had no significant differences ($p>0.05$) with the normal group, the control group positive, and group treatment III. Serum LDH size in treatment group III had significant differences ($p <0.05$) with negative groups and treatment group I and had no significant differences ($p>0.05$) with normal groups, positive control groups, and treatment group II.

Thus, this study showed that turmeric ethanol extract has been shown to decrease serum size from CK-MB and LDH. The antioxidant ability derived from turmeric rhizomes is believed to be a neutralizing free radical compound, forming enzymes that inhibit oxidative reactions such as cytochrome P-450, stopping the formation of chelating which is the oxidation process of the metal ions so that no oxidation reactions occur again (Hartati 2013). So it was concluded that turmeric ethanol extract (TEE) has cardioprotective effectiveness for the heart of male wistar mice induced with doxorubicin.

**c. Cardioprotective Effectiveness of Turmeric Ethanol Extract to the Picture of Cardiac Histology in Male Wistar Rats induced Doxorubicin**

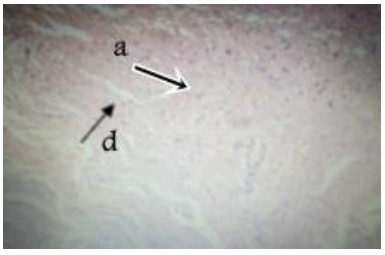


***Figure 1.*** *Normal Group + Na-CMC 0,5%*

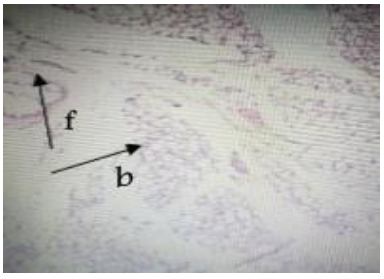


***Figure 2.*** *Negative Group doxorubicin 20 mg/kg weight + Na – CMC 0,5%*

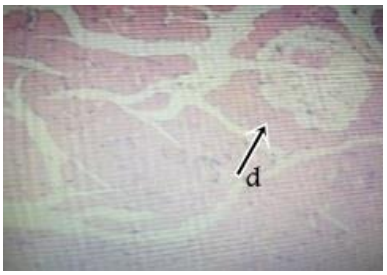


***Figure 3.*** *Positive Group doxorubicin 20 mg/kg weight + vitamin E 1% weight*

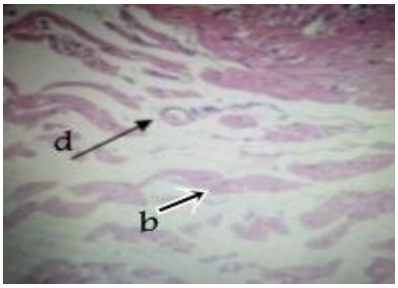


***Figure 4.*** *Treatment Group I doxorubicin 20 mg/kg weight + TEE 100 mg/kg weight*

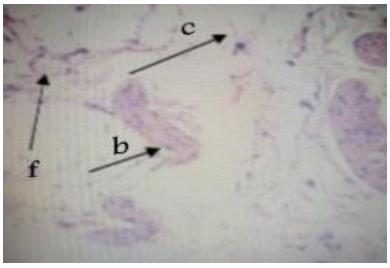


***Figure 5.*** *Treatment Group II doxorubicin 20 mg/kg weight + TEE 300 mg/kg weight*

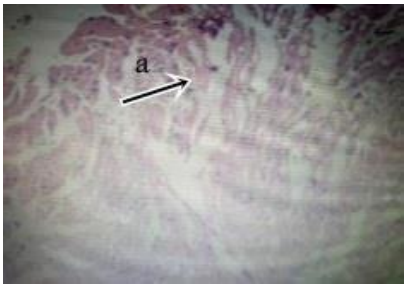


***Figure 6.*** *Treatment Group III doxorubicin 20 mg/kg weight + TEE 500 mg/kg weight*

Information:
a: Normal myocytes
b: Bleeding
c: cariolysis
d : myofibril normal
e : picnosis
f: fragmentation this study

**Table 5.** Histological Size of Male Wistar Mouse Heart Cells

| Treatment Group | Bleeding | Kariolisis | Piknosis | Fragmentation |
|---|---|---|---|---|
| Normal Group | - | - | - | - |
| Negative Group (Induction *D oxorubicin* + Na-CMC 0,5%) | +++ | +++ | +++ | +++ |
| Positive control group (Induction *Doxorubicin* + Vitamin E 1% weight) | - | - | - | + |
| Treatment Group I ; Tikus Induced *Doxorubicin* + TEE 100 mg/kg weight | ++ | ++ | ++ | ++ |
| Treatment Group II ; Tikus Induced *Doxorubicin* + TEE 300 mg/kg weight | - | + | + | ++ |
| Treatment Group III ; Tikus Induced *Doxorubicin* + TEE 500 mg/kg weight | - | - | - | + |

Information:
(+++): Serious damage
(+): minor damage
(++): moderate damage
(-): There was no damage

**d. Antipyretic Effects**

Judging from the table above shows that the normal group does not experience damage to the tissues of the heart where myocytes appear normal and the boundary between cells with each other is visible and the myofibril heart muscle fibers appear normal. In the treatment iii group there appeared to be no bleeding, caryolysis, picnosis, and fragmentation that occurred only moderate damage. In contrast to the results of the examination in the negative group that only induced doxorubicin is visible bleeding, damage to some core cells, namely the occurrence of picnoosis or cell damage characterized by shrinkage and color tends to be darker, then continues to cariolysis i.e. the cell looks very pale and colorless, where this condition the cell nucleus has lost shape and then fragmentation and damage to the heart muscle. In the positive control group can be seen the cell only experienced mild fragmentation this is due to the administration of vitamin E which reduces the occurrence of cell damage. Treatment group I showed administration of turmeric ethanol extract at a dose of 100 mg/kgBB in doxorubicin-induced mice showed the cells had moderate damage.

Treatment group II showed the administration of turmeric ethanol extract with a dose of 300 mg / kg weight + doxorubicin cells still experienced moderate fragmentation of damage but caryolysis and picnosis suffered mild damage. The treatment iii groups with a dose of 500 mg / kg weight + doxorubicin showed that the cells recovered and only mild fragmentation occurred. It can be seen that giving turmeric ethanol extract can prevent heart cell damage in doxorubicin- induced mice, with increased doses of administration there is a decrease in damage to heart cells. The study identified the cardio protective ability of turmeric to doxorubicin-induced cardio toxicity in mice. The yellow crystal compound contained in turmeric, curcumin, has traditionally been used medically because it is considered to have cardio protective or chemo preventive effects against various cancers (Imbaby et al. 2014). The mechanism of cardiotoxicity caused by the administration of doxorubicin is clearly known from this study (Chakraborty,

Bhattacharjee, and Kamath 2017).Decreased levels of the enzymes CK-MB and LDH due to the administration of doxorubicin confirm that the administration of curcuma long a has cardio protective effects derived from curcumin compounds (Mohamad et al. 2009);(Wattanapitayakul et al. 2005).

Various studies show that giving turmeric can improve antioxidant abilities and thus can prevent damage to the heart, especially due to the action of curcumin antioxidant compounds. Turmeric ethanol extract prevents doxorubicin-induced histological changes in the tissues of the mouse heart organ, where turmeric ethanol extract can restore endogenous antioxidant activity or as an antioxidant/ both (Yang, 2013). In line with the research that has been done by El Sayed et al (2011), It was concluded that the extract was given curcuma longa was able to decrease the size of the enzymes CK-MB and LDH induced by doxorubicin and the improvement of the tissues of the mouse heart organ..

The antioxidant properties of turmeric rhizomes can reduce cardiotoxicity that occurs due to the use of doxorubicin which is very closely related to oxidative stress, so that with a certain size of turmeric ethanol extract can improve the integrity of myocardials and reduce the occurrence of cardiac toxicity (Duan et al. 2012). Referring to research conducted by Barui, turmeric can be considered a candidate that has strong potential and is beneficial in the combination of treatment with doxorubicin to limit free radical-mediated organ injury (Barui et al. 2014).

From various current research data, it can be concluded that giving turmeric extract with doxorubicin can provide cardioprotective effects to acute toxicity to the heart organ through repair of heart enzymes, modulating pathways that trigger cardiac apoptosis such as decreased GSH size, increased calcium, and excessive production of free radicals. (Childs et al. 2002), and finally normalize antioxidant enzymes. Therefore, this study is expected to be able to recommend turmeric-based supplements so that they can be used in combination treatment with doxorubicin to protect damage to the heart without reducing the expected clinical effects of doxorubicin, also expected to improve the quality of life of patients (El–Sayed et al., 2011).

## V. Conclusion

Turmeric ethanol extract has the ability to decrease the size of heart damage biomarkers CK-MB and LDH. induced with doxorubicin; Administration of turmeric ethanol extract gradually increases can reduce the incidence of heart cell damage, which is most effective at a tee dose of 500 mg / kg weight; Turmeric ethanol extract has cardioprotective effects induced with doxorubicin; Administration of turmeric ethanol extract can repair heart organ tissue induced with doxorubicin based on a picture of cardiac histology.

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