Eduvest – Journal of Universal Studies
Volume 5 Number 6, June, 2025
p- ISSN 2775-3735- e-ISSN 2775-3727

THE EFFECT OF GOLDEN SEA CUCUMBER EXTRACT (STICHOPUS HERMANII) ADMINISTRATION ON SERUM MALONDIALDEHYDE (MDA) LEVELS IN WISTAR STRAIN WHITE RATS (RATTUS NORVEGICUS) INDUCED BY ASPIRIN

Ajeng Hanum Arditha Anggraeni[1], Nita Pranitasari[2], Wachjudi Kurnia[3], Lena Wijayaningrum[4]
Universitas Hang Tuah, Indonesia[1]
Email: ajenghanum18@gmail.com

ABSTRACT

Drug-Induced Hepatitis (DIH) is a liver function disorder caused by the use of hepatotoxic drugs, which can affect liver metabolism acutely or chronically. A new paradigm suggests that natural-based treatments, such as sea cucumbers, have potential as therapy due to their superior antibacterial bioactivity. This study aims to evaluate the effect of golden sea cucumber extract (Stichopus hermanii) on serum malondialdehyde (MDA) levels in Wistar strain white rats (Rattus norvegicus) induced by aspirin. The study was conducted using a true experimental design with a post-test only control group and random sampling method, involving four treatment groups at the Hyperbaric and Biomolecular Laboratory of Hang Tuah University, Surabaya. The results showed that administering golden sea cucumber extract (Stichopus hermanii) at a dose of 972 mg/kg BW resulted in the highest serum MDA levels in Wistar strain white rats (Rattus norvegicus) induced by aspirin (p=0.001). The study concluded that the administration of golden sea cucumber extract (Stichopus hermanii) significantly affects serum MDA levels in Wistar strain white rats (Rattus norvegicus) induced by aspirin.

KEYWORDS *golden sea cucumber extract (Stichopus Hermanii), malondialdehyde (MDA), aspirin*

INTRODUCTION

Drug-Induced Hepatitis (DIH) is a liver function disorder caused by the use of hepatotoxic drugs (Wesnawa & Kusmiati, 2020). Drug-induced hepatotoxicity poses significant clinical risks that can affect liver metabolism as an acute or chronic response to natural or synthetic compounds. Although the actual incidence rate is difficult to estimate, this condition has become a leading cause of acute liver failure (ALF) in the United States. Risk factors for DIH include female gender, older age, and increased body mass index.

As the second largest organ in the body (after the epidermis), the liver is essential for supporting life and performing metabolic functions. Damage caused by toxic chemicals, persistent metabolites, and circulatory disorders can significantly impair this organ. The metabolism of xenobiotic compounds, or foreign substances not needed by the body, in the liver leads to the formation of hydroxyl compounds that act as free radicals (Palawe et al., 2021).

A common pain reliever for mild to moderate discomfort is aspirin, a nonsteroidal anti-inflammatory drug (NSAID). Its pharmacological actions include analgesic, antipyretic, anti-inflammatory, and anticoagulant effects. Oral administration of aspirin results in efficient absorption in the small intestine, followed by hydrolysis of the active ingredients, salicylic acid and acetate, in the blood and tissues (Makiyah, 2018; Makiyah & Khumaisah, 2018; Makiyah & Tresnayanti, 2017; Merdana et al., 2019). Plasma aspirin levels can range from 3 to 10 mg/dL for therapeutic doses and 70 to 140 mg/dL for acute toxicity. Due to delayed absorption of certain formulations, levels should be checked 4 hours after ingestion and every 2 hours thereafter until peak levels are reached (Arif, 2023a).

At specific doses (75–100 mg), aspirin exhibits antitumor properties, helping prevent cancer and reducing cancer mortality risks by 40% for colorectal cancer, 60% for esophageal cancer, 30% for lung cancer, and 10% for prostate cancer. The main proposed mechanism for aspirin's inhibition of cancer progression is the direct inhibition of cyclooxygenase-2 (COX-2) activity, although other mechanisms have also been hypothesized, including oxidative stress induction and cancer cell apoptosis (Kacprzak & Pawliczak, 2015).

Oxidative stress is known as the imbalance between the production of oxidant species (reactive oxygen (ROS) and nitrogen species (RNS), such as superoxide (O2–), hydrogen peroxide (H2O2), hypochlorite (ClO–), hydroxyl radicals (OH–), nitric oxide (NO), and peroxynitrite (ONOO–)) and the endogenous antioxidant defense in cells. Antioxidant compounds include urate, glutathione, ubiquinone, and thioredoxin, as well as proteins such as ferritin, transferrin, lactoferrin, and caeruloplasmin, which act as antioxidants by binding transition metals that can initiate oxidative reactions. Important antioxidant enzymes for respiratory protection include superoxide dismutase (SOD) and glutathione peroxidase (GPx). SOD converts superoxide into hydrogen peroxide, while GP eliminates hydrogen peroxide and lipid hydroperoxides. This GPx mechanism involves glutathione (GSH), which acts as a co-substrate and is oxidized into glutathione disulfide (GSSG) (Kacprzak & Pawliczak, 2015).

Globally, Indonesia exports more sea cucumbers than any other country. The genus Holothuria is home to the majority of sea cucumber species, followed by Stichopus. To neutralize free radicals, these compounds are converted into GSH in the body after catalyzing superoxide and H2O2. As a source of extracellular glutathione, the body can benefit from consuming golden sea cucumbers (Golden Stichopus variegatus), which are rich in amino acids and contain more protein per gram than most plants and animals. Antioxidant tests using the DPPH method have shown that sea cucumber extracts have the highest antioxidant capacity, according to research by Cahyati et al. (2018). However, this depends on determining the maximum wavelength and stability time for antioxidant measurements, which can yield results close to the comparative value of antioxidant capacity, indicating potential inaccuracies in samples (Dohude & Ramaliah, 2022; Ginting et al., 2019; Janamulia, 2019; Mulawarmanti, 2019; Rahmawati, 2019).

A new social paradigm suggests that conventional treatments made from natural materials are both safe and effective. Therefore, understanding the appropriate dosage of conventional drugs is crucial. Assessing the potential for acute toxicity is one of the first steps in determining the safety of a drug or traditional herb (Makiyah & Khumaisah, 2018).

Sea cucumbers, as natural components, offer promising treatments due to their superior antibacterial bioactivity compared to conventional antibiotics. Stichopus hermanii has the ability to suppress the growth of both gram-positive and gram-negative bacteria. Phytochemical screening results show that Stichopus hermanii extract contains bioactive components such as alkaloids, flavonoids, saponins, and triterpenoids. These components exhibit antibacterial properties (Monika et al., 2021). Flavonoids, identified by dissolving the extract in methanol with magnesium and HCl, are often used for their antioxidant properties due to their ability to scavenge free radicals.

Additionally, Hossain et al. (2022) reported that the antioxidant activity of phenolic compounds in sea cucumbers is primarily associated with their phenolic properties. Antioxidants can prevent or slow oxidative stress in cells, playing an essential role in managing cardiovascular diseases, cancer, and inflammatory diseases. Natural antioxidants in food are gaining popularity due to the potential carcinogenic effects of synthetic antioxidants (Hossain et al., 2022).

Carletti et al. (2022) demonstrated that sea cucumber extracts (H. forskali, H. arguinensis, and H. mammata), rich in polyphenols, particularly hydroethanol extracts, exhibit anti-inflammatory activity through COX-2 inhibition and osteogenic activity in zebrafish (Danio rerio). Phenolic-rich Holothuria atra extracts were effective against 7,12-dimethylbenz[a]anthracene (DMBA)-induced hepatorenal dysfunction by reducing liver malondialdehyde (MDA) levels and increasing antioxidant enzyme activity (Carletti et al., 2022).

Two recent studies help contextualize this research. First, Arif (2023) investigated the hepatotoxic potential of aspirin and emphasized its role in inducing oxidative stress via reactive oxygen species (ROS) generation, particularly malondialdehyde (MDA) as a biomarker of lipid peroxidation. However, the study lacked any attempt to mitigate this effect using natural antioxidants. Second, Monika et al. (2021) explored the phytochemical composition of Stichopus hermanii, highlighting its antibacterial and antioxidant activities through in vitro assays, but did not evaluate its in vivo hepatoprotective potential or its effect on MDA levels under drug-induced oxidative stress. This research addresses the gap by experimentally evaluating the protective effect of golden sea cucumber (Stichopus hermanii) extract on MDA levels in aspirin-induced Wistar rats, thereby integrating both pharmacological toxicology and natural antioxidant application. The objective of this study is to determine whether Stichopus hermanii extract can reduce oxidative liver damage induced by aspirin as measured by serum MDA levels. The findings are expected to contribute to alternative hepatoprotective therapies, support the development of antioxidant-based interventions for drug-induced hepatotoxicity, and validate the functional use of marine biota in biomedical science.

RESEARCH METHOD

This study employed a true experimental design with a post-test only control group, involving male Wistar strain white rats randomly selected as subjects. Four treatment groups were established: negative control (no aspirin), positive control (aspirin 250 mg/kg BW for 11 days), treatment group 1 (golden sea cucumber extract 486 mg/kg BW for 23 days with aspirin starting on day 13), and treatment group 2 (extract 972 mg/kg BW with similar treatment). The population consisted of healthy white rats aged 3-4 months, weighing 150-200 grams, with a minimum sample size of 6 rats per group.

The study variables included the independent variable (Stichopus hermanii extract), the dependent variable (serum malondialdehyde/MDA levels), and controlled variables (rat type and condition). Measurements were conducted using spectrophotometry at a wavelength of 532 nm. The study was carried out at the Hyperbaric and Biomolecular Laboratory, Faculty of Medicine, Hang Tuah University, Surabaya, from May to December 2024.

The procedure began with a 7-day adaptation period for the rats, followed by 23 days of treatment according to the groups, and ended with intracardial blood collection to measure serum MDA levels. The sea cucumber extract was prepared using the maceration method with 80% ethanol, while the aspirin solution was prepared with 1% Na-CMC. Data were analyzed using SPSS with normality tests (Shapiro-Wilk) and homogeneity tests before statistical analysis (ANOVA or Kruskal-Wallis).

The tools and materials included Wistar rats, a spectrophotometer, a water bath, 1% Na-CMC solution, and chemicals such as thiobarbituric acid. The tested animals were euthanized and sent to an incinerator after the study.

RESULT AND DISCUSSION

This experimental research uses *experimental post-test only control group design* By analyzing the effect of golden sea cucumber extract (*Stichopus hermanii*) on serum MDA levels of white rats (*Rattus novergicus*). This research was conducted at the Integrated Hyperbaric and Biomolecular Laboratory, Faculty of Medicine, Hang Tuah University, Surabaya.

Table 1. Average and Standard Deviation of serum malondialdehyde (MDA) levels

Treatment	**Malondialdehida (MDA) (mmol/ml)**	**Std. Deviation**	**Min**	**Max**
Negative Control (-)	203,9	86,51	95	313,5
Positive Control	672,67	352	419	1330,5
Treatment Group 1 486mg/kg BB	497,54	187,6	240	793
Treatment Group 2 972mg/kg BB	826,56	479,78	316,5	1836,5

Source: Data processed

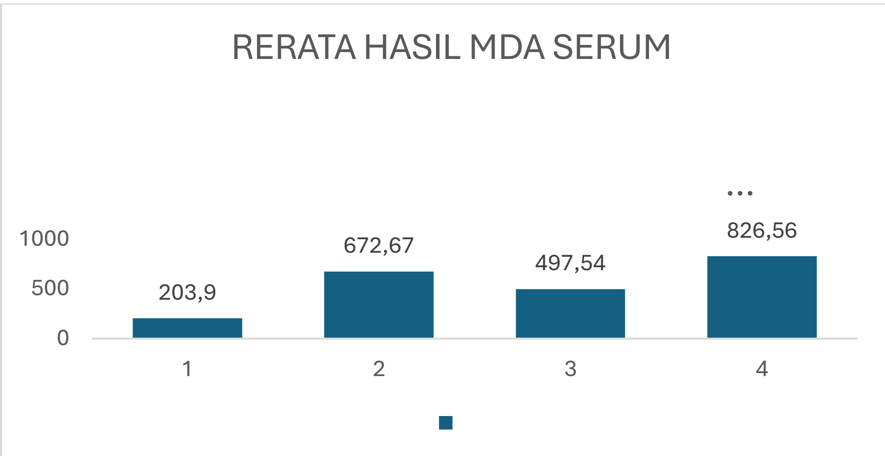

Figure 1. Serum Malondialdehyde (MDA)

Information:

Control group (-)	: White rats (*Rattus novergicus*) are given standard drinking and feed.
Control group (+)	: White rats (*Rattus novergicus*) were induced with aspirin at a dose of 250 mg/kg BB for 11 days
Treatment group 1	: White rats (*Rattus novergicus*) were given golden sea cucumber extract (*Stichopus hermanii*) at a dose of 486mg/kg BB for 23 days and aspirin at a dose of 250 mg/kg BB for 11 days starting on the 13th day of sea cucumber administration.
Treatment group 2	: White rats (*Rattus novergicus*) were given golden sea cucumber extract (*Stichopus hermanii*) at a dose of 972mg/kg BB for 23 days and aspirin at a dose of 250 mg/kg BB for 11 days starting on the 13th day of sea cucumber administration.

Source: Data processed

Based on table 1 Average levels *MalondialDehid* (MDA) serum in white rats of the wistar strain (*Rattus norvegicus*) who were aspirin-induced in the negative group with a sample of 7 white rats of the Wistar strain (*Rattus norvegicus*) has an average value of 203.9 (mmol/ml) ±86.51. The positive group with a sample of 7 white rats of the wistar strain (*Rattus norvegicus*) has an average value of 672.67 (mmol/ml) ±352. In treatment group 1 with golden sea cucumber extract (*Stichopus hermanii)* with a dose of 486mg/kg BB with an average value of 497.54 (mmol/ml) ±187.6. In treatment group 1 with golden sea cucumber extract (*Stichopus hermanii)* with a dose of 972mg/kg BB with an average value of 826.56 (mmol/ml) ±479.78.

Serum Malondialdehyde (MDA) Level Normality Test Results

Table 2. Normality Test

Group		**Shapiro-Wilk**		
		Statistic	df	Mr.
	K (-)	0.892	7	0.286*
up to MDA	K (+)	0.781	7	0.026
	Kp1	0.968	7	0.880*
	Kp2	0.875	8	0.168*

Source: Data processed

Based on table 2, it shows that the results of the normality test using the *Shapiro-Wilk* In the positive control $p<0.05$ (0.026) which means that the treatment in the positive group was not nomally distributed. The condition to proceed to the ANOVA test parametric test is that all groups of normally distributed data are normal. So the next test used is the Kruskal Wallis test.

Kruskall Wallis Test Up Malondialdehyde (MDA) Serum

Table 3. Kruskal Wallis Test Results

Treatment	**N**	**Mean Rank**	**P value**
Negative Control (-)	7	4,43	0.001*
Positive Control	7	18,29	
Treatment Group 1	7	15,50	
Treatment Group 2	8	20,94	

Source: Data processed

Based on table 3, it is shown that the results of the Kruskal Wallis test have a significant value of p=0.001 (p<0.05) with the conclusion that H0 is rejected and H1 is accepted, which means that there is a significant and significant difference in the administration of golden sea cucumber extract (*Stichopus hermanii*) on serum malondialdehyde (MDA) levels in white rats of the Wistar strain (*Rattus norvegicus*) aspirin-induced.

Mann-Whitney U Test Up Malondialdehyde (MDA) Serum

Table 4. Mann-Whitney U Results

Treatment	Negative Control (-)	Positive Control (+)	Treatment Group 1	Treatment Group 2
Negative Control (-)	-	0,002*	0,006*	0,001*
Positive Control (+)	-	-	0,655	0,563
Treatment Group 1	-	-	-	0,093
Treatment Group 2	-	-	-	-

Source: Data processed

Based on table 4, it was shown that there was a significant difference between 2 treatments in the negative group against the positive group (p=0.002), treatment group 1 with a dose of 486mg/kg BB (p=0.006), and treatment group 2 with a dose of 972mg/kg BB (p=0.001).

Interpretation of Mann-Whitney U Test Results of the Negative Control Group with the Positive Group

Table 5. Interpretation of Group Results K(-) with K(+)

	MDA
Mann-Whitney U	0,000
Wilcoxon W	28,000
With	-3,130
Asymp. Sig. (2-tailed)	0,002
Exact Sig. [2*(1-tailed Sig.)]	.001b

Source: Data processed

Based on table 5, the results of the Mann-Whitney U Test between the (-) group and the (+) group obtained a value of p=0.002 (p<0.05), it can be concluded that there is a significant difference.

Interpretation of Mann-Whitney U Test Results of Negative Control Group with Treatment Group 1

Table 6. Interpretation of Group K(-) Results with KP1

	MDA
Mann-Whitney U	3,000
Wilcoxon W	31,000
With	-2,747
Asymp. Sig. (2-tailed)	0,006
Exact Sig. [2*(1-tailed Sig.)]	.004b

Source: Data processed

Based on table 6 of the results of the Mann-Whitney U Test between the group (-) and the Treatment 1 group (KP1), the value of p=0.006 (p<0.05) can be concluded that there is a significant difference.

Interpretation of Mann-Whitney U Test Results for Negative Control Group with Treatment Group 2

Table 7. Interpretation of K(-) Group Results with KP2

	MDA
Mann-Whitney U	0,000
Wilcoxon W	28,000
With	-3,240
Asymp. Sig. (2-tailed)	0,001
Exact Sig. [2*(1-tailed Sig.)]	.000b

Source: Data processed

Based on table 7, the results of the Mann-Whitney U Test between the (-) group and the Treatment 2 group (KP2) found a value of p=0.001 (p<0.05), it can be concluded that there is a significant difference.

Interpretation of Mann-Whitney U Test Results of Positive Control Group with Treatment Group 1

Table 1. Interpretation of K(+) Group Results with KP1

	MDA
Mann-Whitney U	21,000
Wilcoxon W	49,000
With	-0,447
Asymp. Sig. (2-tailed)	0,655
Exact Sig. [2*(1-tailed Sig.)]	.710b

Source: Data processed

Based on table 8, the results of the Mann-Whitney U test between the (-) group (-) and the Treatment 1 group (KP1) found a value of p=0.655 (p>0.05), it can be concluded that there is no significant difference between the two groups.

Interpretation of Mann-Whitney U Test Results of Positive Control Group with Treatment Group 2

Table 2. Interpretation of K(+) Group Results with KP2

	MDA
Mann-Whitney U	23,000
Wilcoxon W	51,000
With	-0,579
Asymp. Sig. (2-tailed)	0,563
Exact Sig. [2*(1-tailed Sig.)]	.613b

Source: Data processed

Based on table 9, the results of the Mann-Whitney U test between the (-) group (-) and the Treatment 2 group (KP2) found a value of p=0.563 (p>0.05), it can be concluded that there is no significant difference between the two groups

Interpretation of the Results of the Mann-Whitney U Test for Treatment Group 1 with Treatment Group 2

Table 3. Interpretation of KP1 and KP2 Group Results

	MDA
Mann-Whitney U	13,500
Wilcoxon W	41,500
With	-1,680
Asymp. Sig. (2-tailed)	0,093
Exact Sig. [2*(1-tailed Sig.)]	.094b

Source: Data processed

Based on table 10, the results of the Mann-Whitney U test between treatment group 1 and treatment group 2 (KP2) found a value of p=0.093 (p>0.05), it can be concluded that there is no significant difference between the two groups.

Based on the results of the study on serum MDA levels in *Rattus novergicus,* The criteria that met the inclusion were 29 experimental animals. This is because, during the study there were 3 experimental animals that were included in the criteria *drop out* namely 1 from the negative control group (-), 1 from the positive (+) control group, and 1 from the 1 treatment group. This death is most likely caused by stress. Based on Mutiarahmi, Hartady and Lesmana, (2021), deaths in experimental animals are caused by several environmental factors, such as:

1. Inadequate circulation aspects can cause particulate contaminants such as allergens and pathogens in the air, so sufficient ventilation is needed to provide good air quality and oxygen supply.
2. Temperatures that are above normal can cause dehydration in experimental animals, potentially causing death.
3. Lighting can affect the physiological, morphological, and behavioral aspects of various animals. Potential causes of stress from light include photoperiod, light intensity and improper spectral quality of light.
4. Cleaning the husk less than 2 times a week can potentially cause disease-causing microorganisms in animals to develop.

The results showed that the concentration level of golden sea cucumber extract

(*Stichopus hermanii*) 972mg/kg BB had the highest serum malondialdehyde (MDA) level in white rats of the wistar strain (*Rattus norvegicus*) aspirin-induced. High levels of malondialdehyde (MDA) in the blood cause damage, both micro and macrovascular. Malondialdehyde (MDA) is a lipid peroxidation product that is toxic to cells in the body. MDA is used as a biomarker of oxidative stress in a variety of health problems and an end product of the breakdown of arachidonic acid. Once formed, MDAs can be enzymatic or react on cellular proteins or DNA resulting in biomolecular damage. Early research suggests that possible biochemical pathways for MDA metabolism involve oxidation by mitochondrial aldehyde dehydrogenase followed by decarboxylation to produce acetaldehyde, which is oxidized by aldehyde dehydrogenase to acetate and subsequently to CO2 and H2O (Ayala et al., 2014).

The results showed that there was an effect of giving golden sea cucumber extract (*Stichopus hermanii*) on serum malondialdehyde (MDA) levels in white rats of the Wistar strain (*Rattus norvegicus*) induced aspirin ($p=0.001$). Golden sea cucumber (*Stichopus hermanii*) is a marine resource that can scavenge free radicals and has a hepatoprotective effect on the liver (Windari, 2019). Antioxidant activity of methanol extract *Stichopus hermanii* with the DPPH method has an IC50 value of 65.08 ppm which shows that the extract has strong antioxidant activity because the IC50 value is lower than 200 ppm (Rasyid, 2012). Previous studies have shown that diabetes (STZ induction of 50 mg/kg bb in rats) in a 14-day study period can significantly increase MDA levels in the liver ($p<0.05$), but MDA levels in rat blood serum did not differ significantly ($p<0.05$) between the normal group and the diabetes group (Windari, 2019).

Research conducted by Monika (2021) on the results of randement of extracts *Stichopus hermanii* with a methanol solvent of 0.038% has the potential to be utilized. This proves that the higher the percentage value of the extract, the higher the potential of the extract that can be used. Phytochemical screening is one of the tests used to determine the compounds in a sample. Each reagent used in each compound is different. Results of phytochemical screening on extracts *Stichopus hermanii*. Based on the results of phytochemical screening tests, the extract *Stichopus hermanii* Positive contains active compounds that include alkaloids, flavonoids, saponins and triterpenoids. Compounds obtained from phytochemical screening have the potential to be antibacterial (Monika, 2021)

According to Damaiyanti (2015), saponin compounds have antibacterial activity with a working system that damages the cytoplasmic membrane and kills cells (Damaiyanti, 2015). Golden sea cucumbers contain alkaloids that are used for antibacterial activities (Akerina & Janer, 2019), explaining that some marine organisms that contain Triterpenoids have biological activities such as antibacterial, antifungal and anticancer. Flavonoids are compounds that are often used for actoxidant activity because of their ability to capture free radicals. Flavonoids found in senggani leaves with n-Hexane solvent have antioxidant activity that is beneficial in the prevention of cancer (Akerina & Janer, 2019).

Flavonoids in serum MDA extracts could not decrease significantly with aspirin induction indicating that there are other compounds that act as a major barrier for oxidation reactions. The flavonoid content is still low. However, it will increase at high concentrations and optimal photosynthesis (Mahmudah & Agrifa Ali Imran, 2024). The role of flavonoids as antioxidants is to capture unstable free radicals by donating one electron. Flavonoids can also inhibit or stabilize ROS by eliminating oxidizing species of xenobiotic compounds. In the process of inhibiting ROS formation, flavonoids activate endogenous enzyme signaling pathways such as SOD, Cat, and GPx causing hydrogen peroxide (H2O2) and hydroxyl radicals (OH) is not formed (Husna et al., 2022)

CONCLUSION

The study revealed that administering golden sea cucumber extract (Stichopus hermanii) at doses of 486 mg/kg BW and 972 mg/kg BW significantly increased serum malondialdehyde (MDA) levels in Wistar strain white rats (Rattus norvegicus) induced by aspirin, with the highest MDA levels observed at the 972 mg/kg BW dose. Statistical analysis confirmed a significant effect of the golden sea cucumber extract on serum MDA levels (p=0.001). Further research is recommended to evaluate the effective and toxic doses of the extract and to identify the phytochemical compounds responsible for the biological activity of golden sea cucumber.

REFERENCES

Akerina, F. O., & Janer, S. (2019). *Analisis Fitokimia Dan Toksisitas Serta Aktivitas Antioksidan Beberapa Jenis Teripang Di Desa Kakara, Halmahera Utara. Jurnal Agribisnis Perikanan, 12(2):188-196. D.*

Ayala, A., Munoz, M. F., & Arguelles, S. (2014). *Lipid Peroxidation: Production, Metabolism, And Signaling Mechanism Of Malondaldehyde And 4-Hydroxy-2-Nonenal [Review]. Oxid. Med. Cell. Longev. 20, 1-31.*

Cahyati, M., Rahmawati, P. A. A., Kusuma, N., & Adam, S. A. (2018). Pemanfaatan Antioksidan (Glutathione) Teripang Emas Laut (Golden Stichoupus Variegatus) Berbasis Nanoteknologi Dalam Apoptosis Sel Skuamosa Kanker Mulut. *E-Prodenta Journal Of Dentistry*, *02*(02). Https://Doi.Org/10.21776/Ub.Eprodenta.2018.002.02.2

Carletti, A., Cardoso, C., Lobo-Arteaga, J., Sales, S., Juliao, D., Ferreira, I., Chainho, P., Dionísio, M. A., Gaudêncio, M. J., Afonso, C., Lourenço, H., Cancela, M. L., Bandarra, N. M., & Gavaia, P. J. (2022). Antioxidant And Anti-Inflammatory Extracts From Sea Cucumbers And Tunicates Induce A Pro-Osteogenic Effect In Zebrafish Larvae. *Frontiers In Nutrition*, *9*. Https://Doi.Org/10.3389/Fnut.2022.888360

Damaiyanti, D. W. (2015). *Karakterisasi Esktrak Air Teripang Emas (Stichopus Hermanii). Jurnal Kedokteran Gigi, 9(1):74-81.*

Dohude, G. A., & Ramaliah, R. (2022). Tingkat Pengetahuan Dokter Gigi Mengenai Deteksi Dini Karsinoma Sel Skuamosa Rongga Mulut. *Padjadjaran Journal Of Dental Researchers And Students*, *6*(2).

Ginting, R., Betty, B., & Michelle, M. (2019). Karakteristik Karsinoma Sel Skuamosa Rongga Mulut. *Jurnal Ilmiah Pannmed (Pharmacist, Analyst, Nurse, Nutrition, Midwivery, Environment, Dentist)*, *10*(1). Https://Doi.Org/10.36911/Pannmed.V10i1.193

Hossain, A., Dave, D., & Shahidi, F. (2022). Antioxidant Potential Of Sea Cucumbers And Their Beneficial Effects On Human Health. In *Marine Drugs* (Vol. 20, Issue 8). Https://Doi.Org/10.3390/Md20080521

Husna, P. A. U., Kairupan, C. F., & Lintong, P. M. (2022). Tinjauan Mengenai Manfaat

Flavonoid Pada Tumbuhan Obat Sebagai Antioksidan Dan Antiinflamasi. *Ebiomedik*, *10*(1), 76–83.

Janamulia, A. (2019). Potensi Bioaktif Teripang Emas (Stichopus Hermanii) Terhadap Penyembuhan Luka Rongga Mulut. *Literature Review*.

Kacprzak, D., & Pawliczak, R. (2015). Does Aspirin-Induced Oxidative Stress Cause Asthma Exacerbation? In *Archives Of Medical Science* (Vol. 11, Issue 3). Https://Doi.Org/10.5114/Aoms.2014.41960

Mahmudah, Atul, & Agrifa Ali Imran, S. (2024). Standarisasi Dan Uji Aktivitas Antikolesterol Ekstrak Etanol Daun Labu Kuning (Cucurbita Moschata Duch.). *Jurnal Mandala Pharmacon Indonesia (Jmpi)*, *10*(1), 111–121.

Makiyah, A. (2018). Gambaran Histopatologi Hepar Tikus Putih Strain Wistar Setelah Pemberian Ekstrak Etanol Umbi Iles-Iles (Amorphophallus Variabilis Bl.) Berbagai Dosis. *Lentera: Jurnal Ilmiah Kesehatan Dan …*.

Makiyah, A., & Khumaisah, L. L. (2018). Studi Gambaran Histopatologi Hepar Tikus Putih Strain Wistar Yang Diinduksi Aspirin Pascapemberian Ekstrak Etanol Umbi Iles-Iles (Amorphophallus Variabilis Bl.) Selama 7 Hari. *Majalah Kedokteran Bandung*, *50*(2). Https://Doi.Org/10.15395/Mkb.V50n2.1323

Makiyah, A., & Tresnayanti, S. (2017). Uji Toksisitas Akut Yang Diukur Dengan Penentuan Ld50 Ekstrak Etanol Umbi Iles-Iles (Amorphophallus Variabilis Bl.) Pada Tikus Putih Strain Wistar. *Majalah Kedokteran Bandung*, *49*(3). Https://Doi.Org/10.15395/Mkb.V49n3.1130

Merdana, I. M., Kardena, I. M., Budiasa, K., & Gunawan, I. M. D. (2019). Histopatologi Hepar Tikus Putih Setelah Pemberian Ekstrak Sarang Semut Yang Diinduksi Paracetamol Dosis Toksik. *Buletin Veteriner Udayana*, *21*.

Monika, R. (2021). Potensi Ekstrak Teripang Stichopus Hermanii, Semper 1868 (Holothuroidea : Stichopodidae) Sebagai Penghasil Senyawa Antibakteri Terhadap Streptococcus Mutans Clarke, 1924 (Bacilli : Streptococcaceae). *Journal Of Marine Research*.

Monika, R., Pringgenies, D., & Setyati, W. A. (2021). Potensi Ekstrak Teripang Stichopus Hermanii, Semper 1868 (Holothuroidea: Stichopodidae) Sebagai Penghasil Senyawa Antibakteri Terhadap Streptococcus Mutans Clarke, 1924 (Bacilli: Streptococcaceae). *Journal Of Marine Research*, *10*(3), 421–427.

Mulawarmanti, D. (2019). Biota Laut Sebagai Alternative Bahan Obat (Pemanfaatan Teripang Emas Sebagai Terapi Ajuvan Di Kedokteran Gigi). *Prosiding Seminakel*.

Palawe, C. Y., Kairupan, C. F., & Lintong, P. M. (2021). Efek Hepatoprotektif Tanaman Obat. *Medical Scope Journal*, *3*(1). Https://Doi.Org/10.35790/Msj.V3i1.33542

Rahmawati, P. A. A. (2019). Pemanfaatan Antioksidan (Glutathione) Teripang Emas Laut (Stichopus Hermanni) Berbasis Nanoteknologi Dalam Apoptosis Sel Skuamosa Kanker Mulut. *Universitas Brawijaya*.

Rasyid, A. (2012). *Identifikasi Senyawa Metabolit Sekunder Serta Uji Aktivitas Antibakteri Dan Antioksidan Ekstrak Metanol Teripang (Stichopus Hermanii). Jitkt. 4, 360- 368*.

Wesnawa, M. A. D. P., & Kusmiati, T. (2020). Drug Induced Hepatitis Pada Tuberkulosis Paru Dengan Multisite Tuberkulosis Ekstraparu. *Jurnal Respirasi*, *5*(2).

Https://Doi.Org/10.20473/Jr.V5-I.2.2019.34-40

Windari, H. A. S. (2019). *Antioxidant Activity Of Spirulina Platensis And Sea Cucumber Stichopus Hermanii In Streptozotocininduced Diabetic Rats. Tropical Life Sciences Research. 30, 119-129*.