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Antioxidant and Cytotoxic Activity Test of Srikaya (Annona squamosa L.) Leaves and Matoa (Pometia pinnata) Leaves Extract Combination on Oral Squamous Carcinoma Cells (HSC-3)

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KEYWORDS
Srikaya leaf extract (Annona squamosa L); matoa leaf extract (Pometia pinnata); antioxidant; cytotoxicity; HSC-3 cells

ABSTRACT
Oral cancer, particularly oral squamous cell carcinoma, is a prevalent and lethal disease that often metastasizes to surrounding tissues. Traditional treatments such as surgery, radiotherapy, and chemotherapy present various side effects, necessitating the exploration of alternative therapies. This study aims to determine the antioxidant value of the combination of ethanol extracts of srikaya leaves (*Annona squamosa L*) and matoa leaves (*Pometia pinnata*) against HSC-3 cell cytotoxicity. The antioxidant test on the combination of ethanol extracts of srikaya leaves and matoa leaves using DPPH *assay* to obtain $IC_{50.}$ HSC-3 cell lines were treated with a combination of ethanol extracts of srikaya leaves (*Annona squamosa L*) and matoa leaves (*Pometia pinnata*) with concentrations of 12.5 µl/ml, 25 µl/ml, 50 µl/ml, 100 µl/ml, and 200 µl/ml for 24 hours and tested with the CCK-8 *assay* method to calculate cell viability and obtain $IC_{(50.}$The results of the antioxidant test of the combination of ethanol extracts of srikaya leaves (*Annona squamosa L*) and matoa leaves (*Pometia pinnata*) in the regression analysis results, obtained a significant value of *p-Value* = 0.033 <0.050, so it is stated that the concentration has a significant effect on inhibition. In the results of IC_{50} obtained 7.62 µl / ml shows antioxidant activity is classified as very strong which is characterized by the value of IC_{50} < 50 µl / ml. Statistical analysis using ANOVA followed by *Tukey*'s HSD *post hoc* test obtained (*p-Value* = 0.000 with a correlation value of r = 0.599) means that the treatment given does not have a significant effect on the observation results. Ethanol extracts of srikaya leaves (*Annona squamosa L*) and matoa leaves (*Pometia pinnata*) have the potential to be made as a therapy using natural ingredients on anticancer HSC-3 cancer cells.

Introduction

Cancer is a health condition characterized by abnormal cell growth. If the spread of these cells is not addressed, it can result in death. The factors that cause cancer are often related to

unhealthy lifestyles, such as smoking, obesity, and irreversible genetic factors (American Cancer Society, 2019). According to the WHO cancer is a series of diseases that can start in almost any tissue of the body. This condition occurs when abnormal cells grow without control, often invading into other organs. This process causes death and is called metastasis (WHO, 2018).

According to Globocan (2021), the number of cancer cases worldwide will increase to 19.3 million with 10 million deaths. As many as one in 5 people worldwide suffer from cancer, and statistics show that one in 8 men and one in 11 women die from this disease. Based on riskesdas data, the prevalence of cancer in Indonesia has increased from 1.4 per 1000 population in 2013 to 1.79 per 1000 population in 2018 (Badan Penelitian dan Pengembangan Keseatan Kementrian Kesehatan Republik Indonesia, 2018).

Oral cancer is a type of malignant tumor that originates from mucosal squamous epithelial cells and has a tendency to invade and metastasize to surrounding tissues. Squamous cell carcinoma most often occurs in the tongue, as much as 40% and 35% in the oral cavity (Setoaji et al., 2022). Oral squamous cell carcinoma has a fairly high mortality rate, with death in oral squamous cell carcinoma can be caused by the increasing size of the cancer in the oral cavity or metastasis to various organs (Gharat et al., 2016; Majumdar et al., 2017). Oral cancer is more common in men than women, and 90% are affected at the age of over 45 years (Mahawar et al., 2020).

There are several risk factors for oral cancer, namely local factors such as lack of oral hygiene and external factors such as smoking, alcohol, and use of betel nut. In addition, there are predisposing factors such as age, gender, and immunological nutrition (I. S. Wibowo et al., 2022). but the risk factors that are often found are smoking, betel nut, and alcohol (Shrestha et al., 2020). Common symptoms that patients experience are long-lasting mouth ulcers or there may be lumps that cause the face to look symmetrical. In cases involving the tongue, squamous cell carcinoma that has spread can make it difficult for patients to move the tongue, which has an impact on speech disorders (Setoaji et al., 2022). In 2018, the international cancer research agency GLOBOCAN (Global Cancer Observatory) recorded 177,384 deaths from oral cancer. The number of cases and deaths from oral cancer ranks first in low-income countries in the world, where the number of deaths from oral cancer is higher. In America (2020), there were 53,260 who experienced oral cancer, which is more often affected in men than women. In men, as many as 38,380 and in women, as many as 14,880, while deaths affected by oral cancer were 10,750, with men 7,760 deaths and women 2,990 deaths (Siegel et al., 2020).

Therapeutic methods for oral cancer include surgery, radiotherapy, and chemotherapy (Sari, 2021). Although efforts to cure cancer using the above methods have not produced satisfactory results due to postoperative and therapeutic side effects, alternative treatments are sought, including traditional medicine, to inhibit cell growth speed (Nurasih et al., 2021). According to (WHO), traditional medicine uses herbal medicine as the main treatment for about 80% of the population in the world today (Drasar & Khripach, 2019). This encourages the search for new sources of drugs derived from nature, one of which is herbal plants. Some of the natural ingredients that show their potential as anticancers are srikaya leaves and matoa leaves (Batubara & Prastya, 2020).

Srikaya leaf (*Annona squamosa*) is a plant in the Annonaceae family with a tree height of ± 8 meters. Srikaya leaves are single, ovate, pointed tip, 6-18 cm long, 2-6 cm wide, pinnate repetition, yellowish green, and contain flavonoids, saponins, tannins, polyphenols, and alkaloids. (Depkes RI, 2001). The content ofrikaya leaves contain bioactive ingredients that can function as anticancers, such as diterpene, acetogenin, cyclopeptides, essential oils, and tannins. Anticancer activity has been proven inrikaya leaves and seeds (Fadholly, 2023).

Matoa leaves (*Pometia pinnata*) are plants with the Sapindaceae family and contain flavonoids, alkaloids, tannins, saponins, terpenoids and coumarins (Restuinjaya et al., 2019). Matoa leaf extract contains flavonoids, tannins, triterpenoids, glycosides and saponins (Fatimah et al., 2021). Bioactivity compounds contained in matoa leaf extract have anti-cancer properties (Naidi et al., 2021).

Plants have an important role, which is explained in the Quran as clear evidence of Allah's power, and plants are used as parables to convey wisdom. Several types of plants and fruits are specifically mentioned in the Quran. The Quran also explains the functions and benefits of plants for human life, one of which is as *sifa'* (medicine) (Apriadi Fauzan, 2015). The use of plants as medicine has strong roots in the Qur'an and Hadith. Rasulullah SAW has provided examples of the use of plants for treatment through the concept of *Thibbun Nabawi*, or Prophetic medicine. Some plants, such as habbatussauda, olive, and honey, are often mentioned in the Qur'an and Hadith for their health benefits (Ahmad, 2023).

Islam teaches the use of herbal remedies as part of an effort to maintain health and improve the condition of the body but also emphasizes that healing is the will of Allah SWT. The utilization of plants as medicine has been an important part of the Islamic medical tradition, using a variety of plants. This teaches about the balance between human effort and faith in Allah (Ahmad, 2023). As the Prophet Muhammad said:

" فِي الْحَبَّةِ السَّوْدَاءِ شِفَاءٌ مِنْ كُلِّ دَاءٍ إِلَّا السَّامَإِنَّ"

Meaning*: "Verily in habbatus sauda there is a cure for all kinds of diseases except death" (HR Bukhari No. 5688, Muslim No. 2215).*

The content of the Hadith is that the Prophet SAW encouraged his people to utilize natural ingredients, such as habbatussauda. Habbatussauda is referred to as a healer of various diseases because it contains active compounds known to have antioxidant, anti-inflammatory, and anticancer properties. This Hadith reminds us that endeavors are very important, but the cure remains entirely in the will of Allah SWT. This teaches a balance between human effort and trust in Him, showing that Islam highly values medical science and efforts to maintain health (Amalia et al., 2022).

HSC SEL

Referring to the things that have been described, the researcher is interested in conducting research titled "Antioxidant Activity and Cytotoxicity Test of Srikaya Leaf Extract (Annona squamosa L), Matoa Leaf (Pometia pinnata) Combination Against Oral Squamous Carcinoma

Cells (HSC-3) and Its Review According to Islamic Views." This research has never been conducted at the Faculty of Medicine, YARSI University.

Based on this background, the problem in this study is whether the combination of ethanol extracts of srikaya leaves (*Annona squamosa*) and matoa leaves (*Pometia pinnata*) has antioxidant activity and cytotoxic effects on oral squamous cancer cells (HSC-3)?

The purpose of this research is to study the antioxidant activity value of the combination of extracts of srikaya leaves (*Annona squamosa* L.) and matoa leaves (*Pometia pinnata*) using ethanol solvent. In addition, this study also aims to assess the cytotoxicity effect of the ethanol extract ofrikaya leaves (*Annona squamosa* L.) against HSC-3 cancer cells and evaluate the cytotoxicity effect of the combination of extracts ofrikaya leaves and matoa leaves on the same cancer cells. Furthermore, this study seeks to determine the Islamic view on the antioxidant activity and cytotoxicity effect of the combination of extracts of srikaya leaves and matoa leaves against oral carcinoma cancer cells (HSC-3).

This research is expected to benefit the author, YARSI University, the community, and in an Islamic perspective. For the author, this research adds insight into the antioxidant activity and cytotoxic effects of srikaya leaves (Annona squamosa) and matoa leaves (Pometia pinnata) against oral squamous cancer cells (HSC-3), and improves research skills. For YARSI University, this research enriches academic insights, especially for academicians who are interested in antioxidant studies and the cytotoxic effects of these leaf extracts. For the community, this research is a source of scientific information regarding the potential of srikaya leaves and matoa leaves as antioxidant and cytotoxic agents and opens opportunities for the development of herbal therapies. From the Islamic perspective, this research is expected to support the development of herbal medicine in accordance with the principles of Sharia so that it becomes an alternative therapy that is halal and beneficial for the people.

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Research Methods

The type of research used is experimental in the laboratory by measuring the toxicity and antioxidant value of IC_{50} of each simplisia extract and the combination of both simplisia using the CCK-8 assay method. This research uses quantitative data. The type of data obtained is determined through the calculation of the percentage of inhibition and the determination of the IC_{50} value to determine the concentration at which the extract can cause 50% cell death. The higher the IC_{50}, the lower the toxicity of the extract.

The research will be conducted in several stages, namely:

a. Preparation of ethanol fractions derived from extracts of srikaya leaves (*Annona squamosa L)* and matoa leaves *(Pometia pinnata)* and their combination.
b. To see the cytotoxicity effect of ethanol fraction of srikaya leaves *(Annona Squamosa L.)* and matoa leaves *(Pometia pinnata*) combined against HSC-3 cells.

The samples used were srikaya leaves (Annona squamosa L.), and matoa leaves (Pometia pinnata) from East Jakarta, which will be extracted and combined. HSC-3 cells were obtained from the Integrated Laboratory of YARSI University, cultured, and tested for cytotoxicity against

extracts using ethanol, ethyl acetate, and water solvents. Sample Determination Method: Samples were tested for determination to ensure the authenticity of the material, then extracted with ethanol and solidified using a rotary evaporator to separate the active substance from the solvent.

This study uses statistical test analysis conducted with the Shapiro-Wilk data normality test. Antioxidant analysis using Independent Samples Test. The statistical significance of cytotoxicity data was calculated by analyzing variances using the *One Way* ANOVA test followed by *Tukey*'s HSD *post hoc* test. The results of the analysis were declared significant if <0.005. This test used the IBM *Statistical Program for Social Sciences* version 20.

Results and Discussion

Determination Test

First, the plants to be used must be determined to ensure the correct identity of the plants to be studied. Determination results conducted at the National Research and Innovation Agency (BRIN), Bogor-Cibinong, stated that the srikaya leaves used in this study were true srikaya leaves (*Annona Squamosa L*).

Research Results

Antioxidant test using DPPH method with UV-Vis Spectrophotometer

Testing the antioxidant activity of srikaya leaf and matoa leaf extracts at various concentrations was done by mixing them with 0.1 mM DPPH solution and then incubating them for 30 minutes. This incubation gives time for the sample to react with free radicals, which is marked by a color change from purple to yellow, indicating antioxidant activity. DPPH free radicals are purple because they have unpaired electrons, while the color changes to yellow when the electrons are paired. The decrease in the intensity of the purple color occurs due to the reaction of DPPH with hydrogen atoms from compounds in the sample, forming diphenyl picrylhydrazine compounds, which causes a change in color and a decrease in absorbance value with each increase in extract concentration (Hasan et al., 2022).

The antioxidant power was measured using the IC50 (Inhibition Concentration 50 Value) value, which indicates the concentration required to inhibit 50% of the free radical activity of DPPH. The smaller the IC50 value, the higher the antioxidant activity of the extract. The test results showed variations in the ability of matoa bark extracts to donate electrons to DPPH.

Table 1. Inhibition Data. On the combination of extracts of sugar apple leaves and matoa leaves

Sample	Concentration	Absorbance			Average Absorbance	%Inhibition
		Repetition 1	Repetition 2	Repetition 3		
Antioxidants	0	0.852	0.856	0.814	0.841	-
	5	0.592	0.579	0.547	0.573	31.892
	10	0.388	0.316	0.328	0.344	59.083
	15	0.178	0.144	0.132	0.151	82.023

	20	0.104	0.09	0.1	0.098	88.332
	25	0.098	0.096	0.099	0.098	88.373
Ascorbic Acid	0	0.959	0.91	0.952	0.940	-
	1	0.799	0.797	0.787	0.794	15.478
	2	0.683	0.687	0.7	0.690	26.585
	3	0.593	0.556	0.595	0.581	38.189
	4	0.459	0.438	0.464	0.454	51.756
	5	0.344	0.317	0.333	0.331	64.772

The results of the sample testing at various % inhibition values are presented in the form of a curve to illustrate the sample's antioxidant profile. The curve was created based on sample concentration and % inhibition data, with sample concentration placed on the X-axis and % inhibition on the Y-axis. The resulting antioxidant profile shows the correlation relationship between sample concentration and % inhibition value in Figure 1.

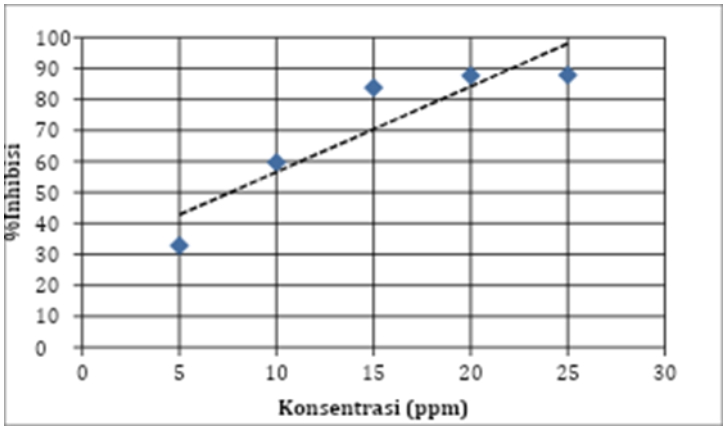

Figure 1. Regression curve of concentration with %inhibition on the combination of extracts of srikaya leaves (*Annona Squamosa L.)* and matoa leaves *(Pometia Pinnata)*.

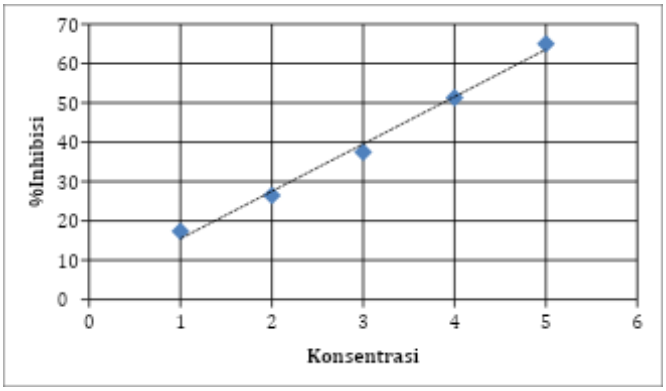

Figure 2. Ascorbic Acid

The correlation between concentration and %inhibition results in a linear regression equation with the general equation y = bx + a used to determine the IC50 value.

Table 2. IC50 result data on Samples

Sample	Regression Equation	r^2	IC_{50} (µg/mL)	Standard Deviation
Combination of Srikaya Leaf and Matoa Leaf Extracts	y = 2.7617x + 28.943	0.825	7.62	0.86
Ascorbic Acid	y = 12,020x + 3,450	0.993	3.87	0.01

Table 2 presents the IC50 results for two types of samples, namely the combination of extracts of srikaya leaf and matoa leaf, and ascorbic acid as a comparison. The IC50 value indicates the concentration required to inhibit 50% of DPPH free radical activity which reflects the strength of antioxidant activity.

Ascorbic acid has an IC50 value of 3.87 µg/mL with a standard deviation of 0.01 based on the regression equation y=12.020x+3.450 and a coefficient of determination (r^2) of 0.993. The smaller IC50 value indicates that ascorbic acid has a higher antioxidant potential compared to the combination of extracts of srikaya leaves and matoa leaves. Based on the regression equation y=2.7617x+28.943 and the coefficient of determination (r2) of 0.825, the test results show that the combination of extracts of srikaya leaves and matoa leaves has an IC50 value of 7.62 µg/mL with a standard deviation of 0.86. This value indicates a fairly high level of antioxidant activity.

Table 3. Shapiro Wilk Data Normality Test

Test Sample	*p-value*
Antioxidants	0.000
Combination of Srikaya and Matoa Extracts	0.052
Ascorbic Acid	0.913

The data normality test using the Shapiro-Wilk method was carried out to test whether the research data was normally distributed. Based on the results of the normality test:

1. Antioxidants have a p-value of 0.000, so they are not normally distributed.
2. The combination of sawo and guava bol extract has a p-value of 0.052, so it is declared normally distributed.
3. Ascorbic acid has a p-value of 0.913, so it is declared normally distributed.

Table 4, Independent sample T-test

4 Test Sample	Mean	SD
	4.4100	5.02046
	1.9350	2.72236
Equal variances assumed	Sig.(*2-tailed*)	
	0.602	

The significance value of the t-test obtained is 0.602> 0.050, so it is stated that there is **no** average difference between the treatments given to the results of the study.

Cytotoxicity Test of Combination of Srikaya Leaf (Annona Squamosa L) and Matoa Leaf (Pometia Pinnata) Extracts

Table 5. Shapiro Wilk Data Normality Test

Shapiro Wilk	*P value*	Description
Cytotoxicity	0.000	Not Normally Distributed
Combination of Srikaya and Matoa Extracts	0.052	Normally Distributed
Ascorbic Acid	0.913	Normally Distributed

The data normality test using the Shapiro-Wilk method was carried out to test whether the research data was normally distributed. Based on the results of the normality test:

1. Antioxidants have a p-value of 0.000, so they are not normally distributed.
2. The combination of sawo and guava bol extract has a p-value of 0.052, so it is declared normally distributed.
3. Ascorbic acid has a p-value of 0.913, so it is declared normally distributed.

Table 6. ANOVA Test

5 Group	N	Mean	Std. Deviation	Sig.
100 ug/ml (2:1)	4	0.8382	0.56308	0.599
50 ug/ml (2:1)	4	0.7267	0.48579	
25 ug/ml (2:1)	4	0.7208	0.48364	
12.5 ug/ml (2:1)	4	0.7532	0.50315	
200 ug/ml (1)	4	0.6354	0.42426	
100 ug/ml (1)	4	0.9124	0.60861	
50 ug/ml (1)	4	0.7908	0.52830	
25 ug/ml (1)	4	0.7431	0.49714	
12.5 ug/ml (1)	4	0.7214	0.48204	
No Treatment	4	0.6231	0.41611	
Solvent Control	4	0.9610	0.64123	
DMSO 10%	4	0.8972	0.60055	

The average differences between the treatment groups at various concentrations of the combination of matoa and srikaya leaf extracts compared to the control group were analyzed using the ANOVA test. The analysis results showed a significance value of 0.599, which is greater than the significance limit of 0.05. Based on the results of the cytotoxicity test, it can be concluded that there is no difference between the treatment groups.

Table 7. Tuckey's Post Hoc HSD Test

(I) Group	(J) Group	Mean Difference (I-J)	Sig.	95% Confidence Interval for Mean		Description
				Lower Bound	Lower Bound	
	100 ug/ml (2:1)	0.11155	0.756	-0.6084	0.8315	**
	50 ug/ml (2:1)	0.11737	0.743	-0.6026	0.8374	**

	25 ug/ml (2:1)	0.08498	0.813	-0.6350	0.8050	**
	12.5 ug/ml (2:1)	0.20280	0.572	-0.5172	0.9228	**
	200 ug/ml (1)	-0.07417	0.836	-0.7942	0.6458	**
	100 ug/ml (1)	0.04740	0.895	-0.6726	0.7674	**
	50 ug/ml (1)	0.09515	0.791	-0.6248	0.8151	**
	25 ug/ml (1)	0.11680	0.745	-0.6032	0.8368	**
	12.5 ug/ml (1)	0.21515	0.549	-0.5048	0.9351	**
	No Treatment	-0.12282	0.732	-0.8428	0.5972	**
200 ug/ml (2:1)	Solvent Control	-0.05893	0.869	-0.7789	0.6611	**
	DMSO 10%	0.81430*	0.028	0.0943	10.5343	*
	200 ug/ml (2:1)	-0.11155	0.756	-0.8315	0.6084	**
	50 ug/ml (2:1)	0.00582	0.987	-0.7142	0.7258	**
	25 ug/ml (2:1)	-0.02657	0.941	-0.7466	0.6934	**
	12.5 ug/ml (2:1)	0.09125	0.799	-0.6287	0.8112	**
	200 ug/ml (1)	-0.18573	0.605	-0.9057	0.5343	**
	100 ug/ml (1)	-0.06415	0.858	-0.7841	0.6558	**
	50 ug/ml (1)	-0.01640	0.963	-0.7364	0.7036	**
	25 ug/ml (1)	0.00525	0.988	-0.7147	0.7252	**
100 ug/ml (2:1)	12.5 ug/ml (1)	0.10360	0.773	-0.6164	0.8236	**
	No Treatment	-0.23437	0.514	-0.9544	0.4856	**
	Solvent Control	-0.17048	0.635	-0.8905	0.5495	**
	DMSO 10%	0.70275	0.055	-0.0172	10.4227	**
	200 ug/ml (2:1)	-0.11737	0.743	-0.8374	0.6026	**
	100 ug/ml (2:1)	-0.00582	0.987	-0.7258	0.7142	**
	25 ug/ml (2:1)	-0.03240	0.928	-0.7524	0.6876	**
	12.5 ug/ml (2:1)	0.08543	0.812	-0.6346	0.8054	**
	200 ug/ml (1)	-0.19155	0.594	-0.9115	0.5284	**
	100 ug/ml (1)	-0.06998	0.845	-0.7900	0.6500	**
	50 ug/ml (1)	-0.02222	0.951	-0.7422	0.6978	**
	25 ug/ml (1)	-0.00058	0.999	-0.7206	0.7194	**
	12.5 ug/ml (1)	0.09777	0.785	-0.6222	0.8178	**
	No Treatment	-0.24020	0.504	-0.9602	0.4798	**
50 ug/ml (2:1)	Solvent Control	-0.17630	0.623	-0.8963	0.5437	**
	DMSO 10%	0.69692	0.057	-0.0231	10.4169	**
25 ug/ml (2:1)	200 ug/ml (2:1)	-0.08498	0.813	-0.8050	0.6350	**
	100 ug/ml (2:1)	0.02657	0.941	-0.6934	0.7466	**
	50 ug/ml (2:1)	0.03240	0.928	-0.6876	0.7524	**
	12.5 ug/ml (2:1)	0.11783	0.742	-0.6022	0.8378	**
	200 ug/ml (1)	-0.15915	0.657	-0.8791	0.5608	**
	100 ug/ml (1)	-0.03758	0.916	-0.7576	0.6824	**
	50 ug/ml (1)	0.01017	0.977	-0.7098	0.7302	**
	25 ug/ml (1)	0.03182	0.929	-0.6882	0.7518	**
	12.5 ug/ml (1)	0.13017	0.717	-0.5898	0.8502	**
	No Treatment	-0.20780	0.563	-0.9278	0.5122	**
	Solvent Control	-0.14390	0.688	-0.8639	0.5761	**
	DMSO 10%	0.72932*	0.047	0.0093	10.4493	*
12.5 ug/ml (2:1)	200 ug/ml (2:1)	-0.20280	0.572	-0.9228	0.5172	**
	100 ug/ml (2:1)	-0.09125	0.799	-0.8112	0.6287	**
200 ug/ml (1)	50 ug/ml (2:1)	-0.08543	0.812	-0.8054	0.6346	**
	25 ug/ml (2:1)	-0.11783	0.742	-0.8378	0.6022	**
	200 ug/ml (1)	-0.27698	0.441	-0.9970	0.4430	**
	100 ug/ml (1)	-0.15540	0.665	-0.8754	0.5646	**

	50 ug/ml (1)	-0.10765	0.764	-0.8276	0.6123	**
	25 ug/ml (1)	-0.08600	0.810	-0.8060	0.6340	**
	12.5 ug/ml (1)	0.01235	0.972	-0.7076	0.7323	**
	No Treatment	-0.32563	0.366	-10.0456	0.3944	**
	Solvent Control	-0.26173	0.467	-0.9817	0.4583	**
	DMSO 10%	0.61150	0.094	-0.1085	10.3315	**
	200 ug/ml (2:1)	0.07417	0.836	-0.6458	0.7942	**
	100 ug/ml (2:1)	0.18573	0.605	-0.5343	0.9057	**
	50 ug/ml (2:1)	0.19155	0.594	-0.5284	0.9115	**
	25 ug/ml (2:1)	0.15915	0.657	-0.5608	0.8791	**
	12.5 ug/ml (2:1)	0.27698	0.441	-0.4430	0.9970	**
	100 ug/ml (1)	0.12157	0.735	-0.5984	0.8416	**
	50 ug/ml (1)	0.16932	0.637	-0.5507	0.8893	**
	25 ug/ml (1)	0.19097	0.595	-0.5290	0.9110	**
	12.5 ug/ml (1)	0.28932	0.421	-0.4307	10.0093	**
	No Treatment	-0.04865	0.892	-0.7686	0.6713	**
	Solvent Control	0.01525	0.966	-0.7047	0.7352	**
	DMSO 10%	0.88847*	0.017	0.1685	10.6085	*
100 ug/ml (1)	200 ug/ml (2:1)	-0.04740	0.895	-0.7674	0.6726	**
	100 ug/ml (2:1)	0.06415	0.858	-0.6558	0.7841	**
	50 ug/ml (2:1)	0.06998	0.845	-0.6500	0.7900	**
	25 ug/ml (2:1)	0.03758	0.916	-0.6824	0.7576	**
	12.5 ug/ml (2:1)	0.15540	0.665	-0.5646	0.8754	**
	200 ug/ml (1)	-0.12157	0.735	-0.8416	0.5984	**
	50 ug/ml (1)	0.04775	0.894	-0.6722	0.7677	**
	25 ug/ml (1)	0.06940	0.846	-0.6506	0.7894	**
	12.5 ug/ml (1)	0.16775	0.640	-0.5522	0.8877	**
	No Treatment	-0.17022	0.635	-0.8902	0.5498	**
	Solvent Control	-0.10633	0.767	-0.8263	0.6137	**
	DMSO 10%	0.76690*	0.037	0.0469	10.4869	*
50 ug/ml (1)	200 ug/ml (2:1)	-0.09515	0.791	-0.8151	0.6248	**
	100 ug/ml (2:1)	0.01640	0.963	-0.7036	0.7364	**
	50 ug/ml (2:1)	0.02222	0.951	-0.6978	0.7422	**
	25 ug/ml (2:1)	-0.01017	0.977	-0.7302	0.7098	**
	12.5 ug/ml (2:1)	0.10765	0.764	-0.6123	0.8276	**
	200 ug/ml (1)	-0.16932	0.637	-0.8893	0.5507	**
	100 ug/ml (1)	-0.04775	0.894	-0.7677	0.6722	**
	25 ug/ml (1)	0.02165	0.952	-0.6983	0.7416	**
	12.5 ug/ml (1)	0.12000	0.738	-0.6000	0.8400	**
	No Treatment	-0.21797	0.544	-0.9380	0.5020	**
	Solvent Control	-0.15408	0.668	-0.8741	0.5659	**
	DMSO 10%	0.71915	0.050	-0.0008	10.4391	**
25 ug/ml (1)	200 ug/ml (2:1)	-0.11680	0.745	-0.8368	0.6032	**
	100 ug/ml (2:1)	-0.00525	0.988	-0.7252	0.7147	**
	50 ug/ml (2:1)	0.00058	0.999	-0.7194	0.7206	**
	25 ug/ml (2:1)	-0.03182	0.929	-0.7518	0.6882	**
	12.5 ug/ml (2:1)	0.08600	0.810	-0.6340	0.8060	**
	200 ug/ml (1)	-0.19097	0.595	-0.9110	0.5290	**
	100 ug/ml (1)	-0.06940	0.846	-0.7894	0.6506	**
	50 ug/ml (1)	-0.02165	0.952	-0.7416	0.6983	**
	12.5 ug/ml (1)	0.09835	0.784	-0.6216	0.8183	**
	No Treatment	-0.23962	0.505	-0.9596	0.4804	**

	Solvent Control	-0.17573	0.624	-0.8957	0.5443	**
	DMSO 10%	0.69750	0.057	-0.0225	10.4175	**
12.5 ug/ml (1)	200 ug/ml (2:1)	-0.21515	0.549	-0.9351	0.5048	**
	100 ug/ml (2:1)	-0.10360	0.773	-0.8236	0.6164	**
	50 ug/ml (2:1)	-0.09777	0.785	-0.8178	0.6222	**
	25 ug/ml (2:1)	-0.13017	0.717	-0.8502	0.5898	**
	12.5 ug/ml (2:1)	-0.01235	0.972	-0.7323	0.7076	**
	200 ug/ml (1)	-0.28932	0.421	-10.0093	0.4307	**
	100 ug/ml (1)	-0.16775	0.640	-0.8877	0.5522	**
	50 ug/ml (1)	-0.12000	0.738	-0.8400	0.6000	**
	25 ug/ml (1)	-0.09835	0.784	-0.8183	0.6216	**
	No Treatment	-0.33797	0.348	-10.0580	0.3820	**
	Solvent Control	-0.27408	0.446	-0.9941	0.4459	**
	DMSO 10%	0.59915	0.100	-0.1208	10.3191	**
No Treatment	200 ug/ml (2:1)	0.12282	0.732	-0.5972	0.8428	**
	100 ug/ml (2:1)	0.23437	0.514	-0.4856	0.9544	**
	50 ug/ml (2:1)	0.24020	0.504	-0.4798	0.9602	**
	25 ug/ml (2:1)	0.20780	0.563	-0.5122	0.9278	**
	12.5 ug/ml (2:1)	0.32563	0.366	-0.3944	10.0456	**
	200 ug/ml (1)	0.04865	0.892	-0.6713	0.7686	**
	100 ug/ml (1)	0.17022	0.635	-0.5498	0.8902	**
	50 ug/ml (1)	0.21797	0.544	-0.5020	0.9380	**
	25 ug/ml (1)	0.23962	0.505	-0.4804	0.9596	**
	12.5 ug/ml (1)	0.33797	0.348	-0.3820	10.0580	**
	Solvent Control	0.06390	0.858	-0.6561	0.7839	**
	DMSO 10%	0.93712*	0.012	0.2171	10.6571	*
Solvent Control	200 ug/ml (2:1)	0.05893	0.869	-0.6611	0.7789	**
	100 ug/ml (2:1)	0.17048	0.635	-0.5495	0.8905	**
	50 ug/ml (2:1)	0.17630	0.623	-0.5437	0.8963	**
	25 ug/ml (2:1)	0.14390	0.688	-0.5761	0.8639	**
	12.5 ug/ml (2:1)	0.26173	0.467	-0.4583	0.9817	**
	200 ug/ml (1)	-0.01525	0.966	-0.7352	0.7047	**
	100 ug/ml (1)	0.10633	0.767	-0.6137	0.8263	**
	50 ug/ml (1)	0.15408	0.668	-0.5659	0.8741	**
	25 ug/ml (1)	0.17573	0.624	-0.5443	0.8957	**
	12.5 ug/ml (1)	0.27408	0.446	-0.4459	0.9941	**
	No Treatment	-0.06390	0.858	-0.7839	0.6561	**
	DMSO 10%	0.87323*	0.019	0.1532	10.5932	**
DMSO 10%	200 ug/ml (2:1)	-0.81430*	0.028	-10.5343	-0.0943	**
	100 ug/ml (2:1)	-0.70275	0.055	-10.4227	0.0172	**
	50 ug/ml (2:1)	-0.69692	0.057	-10.4169	0.0231	**
	25 ug/ml (2:1)	-0.72932*	0.047	-10.4493	-0.0093	*
	12.5 ug/ml (2:1)	-0.61150	0.094	-10.3315	0.1085	**
	200 ug/ml (1)	-0.88847*	0.017	-10.6085	-0.1685	*
	100 ug/ml (1)	-0.76690*	0.037	-10.4869	-0.0469	*
	50 ug/ml (1)	-0.71915	0.050	-10.4391	0.0008	**
	25 ug/ml (1)	-0.69750	0.057	-10.4175	0.0225	**
	12.5 ug/ml (1)	-0.59915	0.100	-10.3191	0.1208	**
	No Treatment	-0.93712*	0.012	-10.6571	-0.2171	*
	Solvent Control	-0.87323*	0.019	-10.5932	-0.1532	*

Notes: *= Significantly Different; **=Not Significantly Different

The results of the analysis showed that most of the treatment groups showed no difference. This can be seen from the significance value which is greater than 0.05, indicating that the average difference between groups is not statistically related. From the analysis, the Sig. value of 0.756 indicates that there is no difference between the concentration groups of 200 µg/mL (2:1) and 100 µg/mL (2:1), while the Sig. value of 0.813 indicates that there is no difference between the concentrations of 25 µg/mL (2:1) and 12.5 µg/mL (2:1). However, there are certain groups that show a difference. The 10% DMSO group showed differences compared to several other treatment groups, with a Sig. value of 0.028 at a concentration of 200 µg/mL (2:1) and Sig. of 0.012 in the untreated group. In addition, differences were also found between the solvent control group and the 200 µg/mL concentration (1) with a Sig. value of 0.019.

Discussion

Antioxidant Activity of Combination of Extracts of Srikaya Leaf (Annona Squamosa L.) and Matoa Leaf (Pometia Pinnata)

The test results showed that the combination of extracts of srikaya leaves (Annona squamosa L.) and matoa leaves (Pometia pinnata) had significant antioxidant activity, with % inhibition increasing from 31.89% at 5 µg/mL to 88.37% at 25 µg/mL. Measurement using the DPPH method shows a purple to yellow color change, indicating neutralization of free radicals by antioxidant compounds (Werdiningsih & zahro, 2020; A. E. Wibowo et al., 2023).

The IC50 value of the combined extracts was 7.62 µg/mL, indicating high antioxidant activity, although still below ascorbic acid (IC50 = 3.87 µg/mL). The coefficient of determination (r^2) of 0.825 indicates a strong correlation between concentration and % inhibition, in line with studies that mention the role of flavonoids, polyphenols, and catechins in neutralizing free radicals. Factors such as extraction method and synergy of active compounds contribute to these results, supporting the potential of the combination of extracts as a source of natural antioxidants. Further development opportunities include pharmaceutical and functional food applications, although additional research is needed to explore their effectiveness and stability on an industrial scale.

Cytotoxicity Test of a combination of extracts ofrikaya leaves (Annona Squamosa L.) and Matoa leaves (Pometia Pinnata)

Based on the cytotoxicity test, the combination of srikaya leaf and matoa leaf extracts showed varying effects depending on the concentration. Most treatments were not significantly different from the control, except at a concentration of 200 µg/mL (2:1) with $p = 0.028$, which showed a significant difference compared to the untreated control. Lower concentrations, such as 12.5 µg/mL (2:1) and 12.5 µg/mL (1:1), showed no significant difference.

The cytotoxic effect at 200 µg/mL, both 2:1 and 1:1 ratios, was not significantly different to the test cells ($p > 0.05$), while at lower concentrations, cytotoxicity decreased. The solvent control (DMSO 10%) gave a more significant effect than several treatment groups, especially at a concentration of 200 µg/mL (1:1) (Rahmawati et al., 2024).

These results indicate that the combination of extracts has cytotoxic potential at high concentrations, but the effect decreases at low concentrations, possibly due to dilution of the active compounds. Therefore, the selection of the optimal concentration is an important factor to obtain the maximum cytotoxic effect.

Extracts of Srikaya Leaf (*Annona Squamosa L*) and Matoa Leaf (*Pometia Pinnata*) in Islamic Perspective

Islam teaches the utilization of nature, including plants, to meet needs and maintain health. Allah SWT provides various useful plants as food and medicine, and makes them a sign of His greatness for humans who want to think and explore their potential (Anwar O.H, 2016).

هُوَ الَّذِي جَعَلَ لَكُمُ الْأَرْضَ ذَلُولًا فَامْشُوا فِي مَنَاكِبِهَا وَكُلُوا مِنْ رِزْقِهِ وَإِلَيْهِ النُّشُورُ

Meaning*: "It is He who has made the earth easy for you, so walk in all its paths and eat of His sustenance. And it is only to Him that you (return after) being resurrected."* (QS. Al-Mulk [67]: 15)

The content of the above verse according to Tafsir Ibn Kathir, this verse shows that Allah SWT created the earth with everything in it, including plants, for the benefit of humans. Humans are commanded to utilize what is on earth wisely, including plants that have medicinal properties. In this context, the utilization of extracts of srikaya leaves and matoa leaves as herbal medicinal ingredients is one form of practicing Islamic teachings in maintaining health and utilizing nature in accordance with Allah's provisions (Ibn Katsir, 2003).

Srikaya (*Annona squamosa*) leaves have long been recognized in traditional medicine and modern scientific research for their antioxidant and anticancer properties. Some studies show that the extract ofrikaya leaves has *acetogenin* compounds that are believed to be efficacious for inhibiting the growth of cancer cells. It also has anti-inflammatory properties that can help reduce inflammation in the body. Islam strongly invites its people to seek good treatment, Rasulullah SAW said: (Anwar O.H, 2016).

شِفاءً له أنْزَلَ إلَّا داءً اللَّهُ أنْزَلَ ما

Meaning*: "Allah does not send down a disease unless He also sends down its cure."* (HR. Bukhari No. 5678)

This hadith shows that every disease that Allah has revealed has a cure. Therefore, making an effort to seek treatment is part of the religious commandment. In the context of using srikaya leaves, Muslims can see it as a form of Allah's grace that provides healing properties through plants. The use of sugar apple leaves, which are rich in antioxidants, is in accordance with Islamic guidance to utilize what is on earth for the benefit of His creatures (Faudi, 2018).

Matoa leaves (*Pometia pinnata*) also have properties that have been recognized in various studies. Matoa leaf extract is known to contain high phenolic compounds and flavonoids, which function as antioxidants. These antioxidants are important in protecting the body from oxidative

damage that can be the cause of various chronic diseases such as cancer and degenerative diseases. Islam explains the use of plants to maintain health is a form of worship, because the body is a trust that must be maintained (Amalia et al., 2022). In medicine, it is important to consume halal and tayyib (good) food, including plants that provide health benefits. Plants such as fruits, vegetables, and spices that are halal and tayyib not only meet the requirements of halalness in Islam but also contain nutrients and bioactive compounds, such as antioxidants that can protect the body from free radical damage (Ali, M *et al*, 2024) as Allah SWT says:

يَا أَيُّهَا النَّاسُ كُلُوا مِمَّا فِي الْأَرْضِ حَلَالًا طَيِّبًا وَلَا تَتَّبِعُوا خُطُوَاتِ الشَّيْطَانِ إِنَّهُ لَكُمْ عَدُوٌّ مُبِينٌ

Meaning: *"O people! Eat of that which is lawful and good which is found on the earth, and follow not the steps of the devil. Indeed, the devil is a real enemy to you."* (QS. Al-Baqarah [2] : 168)

Referring to Tafsir Al-Muyassar, it explains that this verse is an order to choose the halal and good from what Allah provides on earth, including plants. The utilization of matoa leaves in herbal medicine can be seen as an application of this teaching, which is to utilize what is good from the earth for health and well-being. The antioxidant compounds in matoa leaves that can reduce oxidative stress in the body are highly relevant to the principles of health in Islam (Al-Muyassar, 2003).

Islam strongly guides its people to seek knowledge and conduct research to understand the benefits of Allah's creation. The utilization of extracts of srikaya leaves and matoa leaves as herbal medicine ingredients is in line with Islamic teachings which encourage the search for knowledge for the good of the people as stated in the following Qur'an: (Susanti, M *et* al, 2021)

أَفَلَا يَنظُرُونَ إِلَى الْإِبِلِ كَيْفَ خُلِقَتْ

Meaning: *"Then do they not consider the camel how it was created?"* (QS. Al-Ghashiyah [88]: 17)

According to Tafsir As-Sa'di, this verse contains an order to pay attention and study Allah's creation. Islam not only emphasizes ritual worship, but also encourages its followers to pay attention to nature and understand the knowledge contained in it. By conducting research on plants such as sugar apple and matoa, people can understand the medical benefits that Allah provides through His creation, which can then be utilized for the good of mankind (Nasir, A. H. *et al*, 2005).

Overall, the utilization of srikaya leaf and matoa leaf extracts in herbal medicine is in accordance with Islamic teachings that encourage His creatures to utilize Allah's creation for good. Every plant has benefits that can be taken, and Islam guides its people to use everything wisely and not excessively. As a form of gratitude, Muslims are commanded to protect and utilize nature in accordance with the guidance of the sharia, as well as make good treatment efforts in accordance with what the Prophet Muhammad taught.

Test of Antioxidant Activity and Cytotoxicity of Srikaya Leaf Extract, Matoa Leaf, and Their Combination against Oral Carcinoma Cells (HSC-3) According to Islamic Views

The tested samples have very strong antioxidant activity, with the regression analysis results showing a significant value of 0.000 < 0.050, indicating that concentration has an effect on inhibition. The coefficient of determination (r^2) was close to 1, indicating a linear correlation between concentration and % inhibition. The IC50 value of 7.62 µg/mL indicates very strong antioxidant activity (IC50 < 50 µg/mL).

One Way ANOVA test and post hoc HSD Tukey showed no significant effect on the observation results (p = 0.000, r = 0.599). The combination of extracts of srikaya leaves (Annona squamosa L.) and matoa leaves (Pometia pinnata) has the potential to test the cytotoxicity effect on HSC-3 cancer cells, although the concentration used does not have a significant effect on the test cells.

Islam teaches that health is a trust that must be maintained. Efforts to seek treatment, including from efficacious plants, are part of Allah's command. Various plants have been created as sources of antioxidants and cytotoxic substances that have the potential to inhibit the growth of cancer cells (Susanti et al., 2021).

إِنَّ فِي خَلْقِ السَّمَاوَاتِ وَالْأَرْضِ وَاخْتِلَافِ اللَّيْلِ وَالنَّهَارِ وَالْفُلْكِ الَّتِي تَجْرِي فِي الْبَحْرِ بِمَا يَنفَعُ النَّاسَ وَمَا أَنزَلَ اللَّهُ مِنَ السَّمَاءِ مِنْ مَّاءٍ فَأَحْيَا بِهِ الْأَرْضَ بَعْدَ مَوْتِهَا وَبَثَّ فِيهَا مِن كُلِّ دَابَّةٍ وَتَصْرِيفِ الرِّيَاحِ وَالسَّحَابِ الْمُسَخَّرِ بَيْنَ السَّمَاءِ وَالْأَرْضِ لَآيَاتٍ لِّقَوْمٍ يَعْقِلُونَ

Meaning: *"Surely in the creation of the heavens and the earth, the alternation of night and day, the ships that sail the seas carrying what is beneficial to mankind, and what Allah sends down from the heavens in the form of water, and with it He gives life to the earth after it is dry, and He scatters on the earth every kind of animal, and the winds and the clouds that are controlled between the heavens and the earth; indeed, there are signs (of Allah's greatness) for those who understand."* (QS. Al-Baqarah [2] : 164)

Referring to Tafsir Ibn Kathir, this verse shows that all of Allah's creations in the heavens and the earth have benefits and are signs for those who think. Humans are encouraged to use the mind that has been given by Allah to study and utilize the surrounding nature, including in the field of medicine. The utilization of plant extracts such as srikaya leaves and matoa leaves that have antioxidant and cytotoxic content is one form of application of Islamic teachings to seek healing through nature that Allah has provided (Ibn Katsir, 2003).

Antioxidants are compounds that fight free radicals in the body, which are one of the main causes of many degenerative diseases, including cancer. Free radicals can damage cells and DNA, which if not controlled, can lead to the growth of cancer cells. Islam teaches the importance of maintaining the balance of the body and avoiding damage as Allah SWT says below: (Siddiqui, S *et al*, 2015).

مَنْ قَتَلَ نَفْسًا بِغَيْرِ نَفْسٍ أَوْ فَسَادٍ فِي الْأَرْضِ فَكَأَنَّمَا قَتَلَ النَّاسَ جَمِيعًا وَمَنْ أَحْيَاهَا فَكَأَنَّمَا أَحْيَا النَّاسَ جَمِيعًا وَمَنْ أَحْيَا النَّاسَ جَمِيعًا.

Meaning: *"Whoever kills one person for the sake of killing another or for causing mischief on earth, it is as if he has killed all of mankind. And whoever preserves the life of one person, it is as if he has preserved the life of all mankind."* (QS. Al-Maidah [5]: 32)

According to Tafsir Al-Muyassar, this verse shows the importance of preserving life and health as part of carrying out Allah's commands. In the context of antioxidants, these compounds can help maintain the balance of the body by fighting free radicals, so that health can be maintained. By using plants that contain antioxidants such as srikaya and matoa leaves, a Muslim can endeavor to maintain the balance of the body as a form of obedience to Allah. (Al-Muyassar, 2003).

HSC-3 carcinoma oral cancer cells are a type of malignant tumor that originates from mucosal squamous epithelial cells and has a tendency to invade and metastasize to surrounding tissues (Setoaji I. et al, 2022). In Islam, all diseases including cancer are part of the decree of Allah SWT. Cancer disease is seen not only as a disaster, but also as a test that contains wisdom and lessons. Therefore, the cytotoxicity effect of the leaf extract will be tested. Cytotoxicity is the ability of a substance to kill harmful cells, such as cancer cells. In medicine, cytotoxicity tests are conducted to assess the effectiveness of an extract or compound in inhibiting or killing cancer cells. Islam does not prohibit the use of therapies that aim to kill cells that damage the body, as long as it is done in a halal way and does not harm overall health. As Rasulullah SAW said: (Zainuddin, M.N, 2018).

وَجَلَّ عَزَّ اللَّهِ بِإِذْنِ بَرِئَ الدَّاءِ دَوَاءُ أُصِيبَ فَإِذَا دَوَاءٌ دَاءٍ لِكُلِّ

Meaning: *"Every disease has a cure. If the medicine matches the disease, it will be cured with Allah's permission."* (HR Muslim No. 2204)

This hadith invites Muslims to make an effort to seek treatment for every disease that exists. The utilization of srikaya and matoa leaf extracts for cancer treatment, with their high content of cytotoxic compounds, is in line with this recommendation. Scientific research shows that compounds in srikaya and matoa leaf extracts have the potential to inhibit the growth of cancer cells, which can be an alternative treatment for Muslims (Zainuddin, M.N, 2018).

Islam encourages its followers to continue to explore knowledge and develop knowledge that can provide benefits for life. The utilization of srikaya leaves and matoa leaves in cancer treatment through antioxidant and cytotoxicity research is one form of application of this teaching. By conducting research, humans can find hidden benefits in Allah's creation that are not only beneficial for individuals but also for mankind as a whole as Allah SWT says: (Susanti, M *et* al, 2021)

يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ

Meaning: "*Allah will elevate those who believe among you and those who are given knowledge by several degrees."* (QS. Al-Mujadilah [58]: 11)

The content of the above verse, according to Tafsir Ibn Kathir, this verse shows that Allah gives a high degree to those who have knowledge and faith. The development of science in the health sector, such as the utilization of plant extracts for cancer treatment, is a concrete form of this command. Islam not only encourages worship in the form of rituals but also in the form of research and development of knowledge that benefits the people (Ibn Kathir, 2003).

Based on these explanations and descriptions, it can be concluded that medical science and Islamic religion in the utilization of extracts of srikaya leaves and matoa leaves in the test of antioxidant activity and cytotoxicity against oral carcinoma cells (HSC-3) is a form of effort in accordance with Islamic teachings. By using science to find treatment solutions, Muslims can utilize Allah's creation wisely and carry out His orders to maintain health and make efforts for healing. Islam and medical science have the same goal of preserving life, treating disease, and utilizing nature in accordance with the teachings of Sharia.

Conclusion

The conclusion that can be drawn from the research "Antioxidant Activity and Cytotoxicity Test of Srikaya Leaf Extract, Matoa Leaf, and Their Combination against Oral Carcinoma Cells (HSC-3) Review According to Islamic Views" In the antioxidant test of the combination of ethanol extracts of srikaya leaves (*Annona Squamosa L*) and matoa leaves (*Pometia Pinnata*) the results of regression analysis, obtained a significant value of 0.000 <0.050, so it is stated that concentration has a significant effect on inhibition. The data of the coefficient of determination ($r^{2)}$ value in both samples is close to 1, the closer the coefficient of determination ($r^{2)}$ value is to 1, the more linear the correlation between concentration and % inhibition. In the IC_{50} results obtained 7.62 µl/ml shows antioxidant activity is classified as very strong which is characterized by IC_{50} values <50 µl/ml. The *Independent sample T test* statistical *test* used in this study showed the results obtained were 0.602> 0.050, so it was stated that there was no average difference between the treatments given to the results of the study. *The One Way* ANOVA Statistical Test followed by *Tukey*'s HSD *post hoc* test used in this study showed the results of no effect, the significance value obtained was (*p-Value* = 0.000 with a correlation value of r = 0.599) meaning that the treatment given did not have a significant effect on the observation results. Islam views plants as Allah's creation that is full of benefits, both for survival, health, and as a means of contemplating His greatness. The Qur'an mentions many plants as evidence of Allah's power, such as in the process of growing grains and fruits from fertile soil through rain as explained in Surah Al- An'am verse 99. In addition to being a source of food, plants also have medical properties that are recognized in Islam, one of the plants that can be used is the leaves of srikaya and matoa which have active compounds as anticancer. Islam encourages its people to utilize nature wisely and explore the benefits of Allah's creation as a form of gratitude and an effort to maintain health.

References

American Cancer Society. (2019). *Cancer Facts & Figures*. Atlanta. https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2019.html

Badan Penelitian dan Pengembangan Keseatan Kementrian Kesehatan Republik Indonesia. (2018). *Laporan Nasional Riskesdas 2018*. Kementerian Kesehatan Republik Indonesia.

Batubara, I., & Prastya, M. E. (2020). Potential Use of Indonesian Medicinal Plants for Cosmetic and Oral Health: A Review. *Jurnal Kimia Valensi*, *6*(1), 120–124. https://doi.org/10.15408/jkv.v6i1.16252

Depkes RI. (2001). *Inventaris Tanaman Obat Indonesia Jilid 2*. Badan Penelitian dan Pengembangan Kesehatan.

Drasar, P. B., & Khripach, V. A. (2019). Growing Importance of Natural Products Research. *Molecules*, *25*(1), 6. https://doi.org/10.3390/molecules25010006

Evifania, R. D., Apridamayanti, P., & Sari, R. (2020). Uji parameter spesifik dan nonspesifik simplisia daun senggani (Melastoma malabathricum L.). *Jurnal Cerebellum*, *5*(4A), 17. https://doi.org/10.26418/jc.v6i1.43348

Fadholly, A. (2023). Daun dan Biji Srikaya (Annona squamosa L.) dan Potensinya sebagai Antikanker. *Jurnal Veteriner Dan Biomedis*, *1*(1), 45–50. https://doi.org/https://doi.org/10.29244/jvetbiomed.1.1.45-50

Fatimah, I., Purwiandono, G., Hidayat, H., Sagadevan, S., Ghazali, S. A. I. S. M., Oh, W.-C., & Doong, R.-A. (2021). Flower-like SnO2 Nanoparticle Biofabrication Using Pometia pinnata Leaf Extract and Study on Its Photocatalytic and Antibacterial Activities. *Nanomaterials*, *11*(11), 3012. https://doi.org/10.3390/nano11113012

Gharat, S. A., Momin, M. M., & Bhavsar, C. (2016). Oral squamous cell carcinoma: current treatment strategies and nanotechnology-based approaches for prevention and therapy. *Critical ReviewsTM in Therapeutic Drug Carrier Systems*, *33*(4).

Hasan, H., Ain Thomas, N., Hiola, F., Nuzul Ramadhani, F., & Ibrahim, A. S. (2022). Skrining Fitokimia dan Uji Aktivitas Antioksidan Kulit Batang Matoa (Pometia pinnata) Dengan Metode 1,1-Diphenyl-2 picrylhidrazyl (DPPH). *Indonesian Journal of Pharmaceutical Education*, *2*(1), 67–73. https://doi.org/10.37311/ijpe.v2i1.10995

Mahawar, P., Reddy, S., Bhasin, M., Kakkad, A., & Yadav, A. (2020). Oral Squamous Cell Carcinoma Case Series: A Saga of Reactions Against Risk Factors. *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, *19*(7), 55–60.

Majumdar, B., Patil, S., Sarode, S. C., Sarode, G. S., & Rao, R. S. (2017). Clinico-pathological prognosticators in oral squamous cell carcinoma. *Translational Research in Oral Oncology*, *2*. https://doi.org/10.1177/2057178X17738912

Naidi, S. N., Khan, F., Tan, A. L., Harunsani, M. H., Kim, Y.-M., & Khan, M. M. (2021). Photoantioxidant and antibiofilm studies of green synthesized Sn-doped CeO2 nanoparticles using aqueous leaf extracts of Pometia pinnata. *New Journal of Chemistry*, *45*(17), 7816–7829. https://doi.org/10.1039/D1NJ00416F

Rahmawati, J. E., Wati, A., & Handayani, S. (2024). Uji Aktivitas Sitotoksik Ekstrak Daun Matoa (Pometia pinnata) dengan Metode BSLT (Brine Shrimp Lethality Test). *Makassar Pharmaceutical Science Journal (MPSJ)*, *2*(1), 99–112.

Restuinjaya, L. A., Simaremare, E. S., & Pratiwi, R. D. (2019). Optimization of Tween 80 and Span 60 on Cream Ethanol Extract the Leaves Matoa (Pometia Pinnata) as an Antioxidant.

Journal of Advances in Pharmacy Practices, *1*(2), 11–21. https://doi.org/https://doi.org/10.5281/zenodo.3247411

Setoaji, I., Priyanto, W., & Hardianto, A. (2022). Karakteristik Karsinoma Sel Skuamosa Rongga Mulut di RSUP Dr. Hasan Sadikin Bandung. *Jurnal Kedokteran Dan Kesehatan: Publikasi Ilmiah Fakultas Kedokteran Universitas Sriwijaya*, *9*(1), 97–102.

Shrestha, A. D., Vedsted, P., Kallestrup, P., & Neupane, D. (2020). Prevalence and incidence of oral cancer in low- and middle-income countries: A scoping review. *European Journal of Cancer Care*, *29*(2). https://doi.org/10.1111/ecc.13207

Siegel, R. L., Miller, K. D., Goding Sauer, A., Fedewa, S. A., Butterly, L. F., Anderson, J. C., Cercek, A., Smith, R. A., & Jemal, A. (2020). Colorectal cancer statistics, 2020. *CA: A Cancer Journal for Clinicians*, *70*(3), 145–164. https://doi.org/10.3322/caac.21601

Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: A Cancer Journal for Clinicians*, *71*(3), 209–249. https://doi.org/10.3322/caac.21660

Werdiningsih, W., & zahro, A. (2020). Penetapan Kadar Flavonoid dan Fenol dari Daun Srikaya (Annona squamosal L) serta Aktivitas sebagai Antioksidan. *Jurnal Wiyata: Penelitian Sains & Kesehatan*, *7*(2), 156–170. https://doi.org/ttp://dx.doi.org/10.56710/wiyata.v7i2.416

WHO. (2018). Cancer. *World Health Organization*. https://www.who.int/health-topics/cancer/#:~:text=Cancer

Wibowo, A. E., Octa Ujiantari, N. S., & Susidarti, R. A. (2023). DPPH Scavenging Activity, Reducing Power, and Metal Chelating Capacity of Compound 1-(2,5-dihydroxyphenyl)-3-pyridine-2-yl-propenone. *Journal of Food and Pharmaceutical Sciences*, 936–945. https://doi.org/10.22146/jfps.7317

Wibowo, I. S., Priyanto, W., & Hardianto, A. (2022). Karakteristik Karsinoma Sel Skuamosa Rongga Mulut di RSUP Dr. Hasan Sadikin Bandung Periode Januari-Desember 2019. *Jurnal Kedokteran Dan Kesehatan: Publikasi Ilmiah Fakultas Kedokteran Universitas Sriwijaya*, *9*(1), 97–102.