

Syafruddil_ilyas_Rostime

by Syaruddin_ilyas Rostime

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The effect of Andaliman (*Zanthoxylum acanthopodium* DC) methanol extract on the Histology of Cervical Cancer Rat's with Staining of AgNOR

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Abstract

Andaliman (*Zanthoxylum acanthopodium* DC) is an endemic plant from Northern Sumatera Indonesia that have high antioxidant. Cervical cancer is an abnormally growing cell in the cervix and then undergoes tumour growth. The number of cervical cancer cases in Indonesia was increasing every years. The purpose of this study is to know the effect of andaliman on the histology of the cervical cancer cells of rats induced benzopyrene by staining of AgNOR. This research used 5 groups of female rats consisting of: Control negative (normal rats), Control positive (rats were induced Benzo(a)pyrene=BaP), treatment group; andaliman methanol extract (100, 200 and 400 mg/BW/0,5 ml corn oil). Based on the data there were significant difference to the histology of the rat cervical cancer cells by benzopyrene induced via staining of AgNOR on the negative control and treatment group, but was not found a significant difference on body and cervical weight of the rats, although based on the average values seem to increase both of. So, andaliman methanol extract can repair of destruction cell caused by cancer and described as being a cancer drug in the future.

I. INTRODUCTION

The potential of local plants that are beneficial to health are still many who have not been assessed and a few plants have been studied that have health benefits and one is a plant andaliman (*Zanthoxylum acanthopodium* DC.) both the fruit and leaves. Seed of andaliman has long been used by the Toba Batakness as a spice in cooking or a mixture of the cuisine of various types of food, such as goldfish "naniarsik, natinombur, and saksang". Cuisine that uses the fruit of andaliman are generally more durable [1]. Seeds of andaliman have compounds chemical class of alkaloids, flavonoids, tannins, glycosides, steroids, terpenoids [2] and also contain compounds antioxidants such as flavonoids, antioxidant activity, and inhibit carbonyl reductase, ascorbic acid (vitamin c) [3-6]. The fruit of *Zanthoxylum* have been used to treat pain, vomiting, diarrhea, ascariases, and the treatment of eczema, topical anaesthesia, the drug stomach, and itching in China [7]. The characteristic flavours andaliman is dominated by aromas of citrus, namely limonene and citronellol because due to the content of oil atsiri contained in it, which is largely a class of terpenoid, namely geranyl acetate. The other component is a β -myrcene, β -ocimene, linalool and E-1-decenal [8].

Cancer is a large group of diseases that can occur in almost any organ or tissue of the body when abnormal cells grow uncontrolled. Other terms used for cancer is a malignant tumour and neoplasm. Cervical cancer is the second leading cause of death globally and is estimated at 9.6 million deaths, or one in six deaths in the year 2018. The most common cancer in men are lung cancer, prostate, prectal, stomach and liver. While cancer is attack in women are breast, cervical, colorectal, lung, brain and thyroid. From the research that has been done

and found the increase in of cervical cancer in women case is caused by one factor the women's knowledge level of about cervical cancer and pap smear as the early detection of cervical cancer is still low [9]. About 70% of deaths due to cancer occur in low and middle income countries. one-third of deaths are caused by five (5) risks associated with behavioral factors and strict diet such as: height body of mass index, low intake of fruits and vegetables, lack of physical activity, tobacco and alcohol use [10]. One of the plants local originating from North Sumatra, andaliman has compounded that is believed to be beneficial as anti-cancer and need to be developed at the next future.

II. MATERIAL AND METHODS

This study used 30 female rat (*Ratus norvegicus*) from The Development Animal and research Center of North Sumatra and a weight of 200-250 g. Handling of experimental animals in accordance with the requirements of the applicable code of ethics. Rats were divided into 5 groups: negative control or normal was a rats normal group only given the food standard, positive control was rats cancer model and 3 treatment groups of administration andaliman extract methanol each dose and a group contained 6 rats as a replay. Animal model cancer through induction benzopyrene 50mg/Kg/BW/0,5 oil corn to the layer of cervical (positive control), then left up to 3 (three) months then growth of cancer [11]. To ensure that the cancer cells have grown then do a pap smear. After given andaliman methanol extract with a dose of 100 mg/kg/BW, 200 mg/kg/BW and 400 mg/kg/BW/0,5 ml corn oil orally for 30 days [12-14]. The research method was a completely randomized design experimental method. The parameters of this study was the weight of the body

and cervix, and the histological observation of cancer cells with the calculation of the grain AgNOR. Body Weight and cervical histology were carried out in Anatomical Pathology Laboratory and Animal house of Universitas Sumatera Utara. The histological observation of cancer cells sustaining AgNOR was done in the Anatomical Pathology Laboratory of Mangunkusumo Cipto of Hospital in Jakarta.

III. RESULT AND DISCUSSION

Based on the results of research that, benzopyrene induction could affected of histology cervical a significant but its difference on the body and cervical weight, no significant difference although the average value indicates that there were an increase in weight of rats. Based on the difference in body weight between treatment groups dose of the extract of andaliman found on the group dose 400 mg/kg/BW showed the difference in weight which is lower than the other groups (Table 1). This is shown the highest dose of andaliman methanol extract can lose weight mouse cancer although statistically was not significantly. Also based on the cervical weight data (Table 1) after administration of the andaliman methanol extract is no significant difference between treatment groups, based on the average value of the weight cervical lowest was found in the negative control group, while the weight of the cervix is the highest in the positive control group (model cervical cancer). Based on the average value of the methanol extract of the fruit of andaliman can lose weight cervical mouse models of cancer, although was not different significantly.

Table 1 The average of body and cervix weight rats K(-): Negative control group (normal rats), K(+): positive control (rats cancer model BaP 50 mg/KgBB/0,5 ml com oil), P1: extract methanol of andaliman 100 mg/KgBB, P2: 200 mg/KgBB, P3: 400 mg/KgBB.

Alkaloids and saponins are commonly used in prescription medicines. Alkaloids are toxic, while saponins used to lower the body fluids tension of and can make the blood cell haemolysis [4]. Almost all of the alkaloids found in nature have the liveliness of physiological, there is a very toxic and some are very benefited in the treatment of [15-16]. The ethanol extract of the fruit Zanthoxylum piperitum DC have the effect as anti-obesity in mice by blocking adipogenesis through the regulation of genes involved in the pathway of adipogenesis [17]. The possibility of the loss weight and cervical of caused by compound substances alkaloids and steroids high in the fruit extract of andaliman.

Based on the statistical analysis using the Kruskal-Wallis test on cervical cancer cells with

staining of AgNOR induced benzoapyren there were a significant differences of $p < 0.000$. Then done Mann-Whitney test to see the difference between the two groups. There was significant difference between the negative control group with a dose of andaliman 400 mg/kg (P3) it is assumed that the extract of methanol buah andaliman can repair the cells of the rat cervical cancer, especially at the highest dose (400 mg/kg/BW). It shows that the highest dose of the methanol extract of the fruit of andaliman the potential to repair tissue of cervical cancer stained with AgNOR or almost the same with the negative control group (K-) (Table 2 and figure 1).

Sustaining AgNOR is a diagnostic tool that is highly recommended to see the change of morphological characteristics of the tissue that can distinguish benign tumours or malignant tumours in breast cancer. AgNOR is staining NOR associated with proteins, in accordance with the type of cysts [18]. Based on the number of grains of AgNOR per cyst can be a marker of the onset of cell proliferation in the lesions of the cyst aggressive that have the potential malignancy [19] and directly increased the grain AgNOR progressively comparable with the increasing proliferation activity of the cells: cervix normal and inflammation of the cervix without dysplasia [20]. Counting grains of AgNOR very helpful as a marker of cell proliferation, which can help the diagnosis through a pap smear to determine the stages of cervical lesions [21-22], and breast cancer [23-24] as well as the correlation between the high number of average grain AgNOR with HPV positive [25]. Staining of AgNOR is also used to see the changes from benign tumors to pre cancer and malignant tumors [26].

Extract family Zanthoxylum can reduce and potentially inhibit microorganisms and cancer

Group	Body Weight (g)			Cervix Weight (g)
	Before	After	Difference of BW	
K-	200,50 ± 7,01	247,33 ± 16,77	46,83	0,37 ± 0,16
K+	207,33 ± 11,43	266,00 ± 10,19	58,67	1,60 ± 1,21
P1	221,00 ± 25,89	276,67 ± 19,48	55,67	1,00 ± 0,99
P2	228,83 ± 17,03	277,17 ± 28,18	48,34	0,78 ± 0,72
P3	233,33 ± 27,75	275,67 ± 19,02	42,34	0,38 ± 0,13

cells [27]. Family Zanthoxylum in silver colouring can be the agent of anti-cancer economic value in the future. Family Zanthoxylum can reduce inflammatory processes in the endothelial cells and repair the lesions of the cells will become cancerous [28]. Based on the it is suspected that the content of andaliman which is a family zanthoxylum can improve lesion cells and prevent the growth of cancer cells.

Group	Mean Rank	Kruskal Wallis	Mann-Whitney			
			K-	K+	P1	P2
K-	4,10	0,00		0,009 ^a	0,009 ^a	0,142
K+	22,60		0,028 ^a		0,009 ^a	0,009 ^a
P1	18,40	0,00				0,009 ^a
P2	13,00					
P3	6,90					

Table 2 Table 2 Analisis Kruskal Wallis dan Mann-whitney with sustaining AgNOR K(-): Negative control group (normal rats). K(+): positive control (rats cancer model BaP 50 mg/KgBB/0.5 ml com oil). P1: extract methanol of andaliman 100 mg/KgBB. P2: 200 mg/KgBB. P3: 400 mg/KgBB. Numbers followed by superscript are different on the same line shows appearing the difference significant, $p=0.000$ ($p<0.05$).

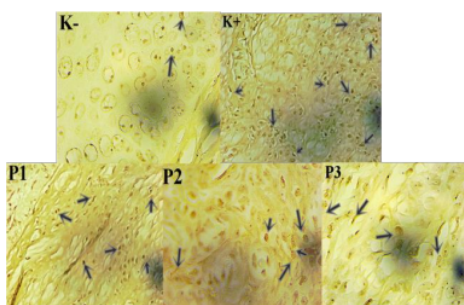


Figure 1 The histology of the cancer cells of the cervix of rats on the staining of AgNOR induced by benzo(a)pyrene. K(-): Negative control group (normal rats). K(+): positive control (rats cancer model BaP 50 mg/KgBB/0.5 ml com oil). P1: extract methanol of andaliman 100 mg/KgBB. P2: 200 mg/KgBB. P3: 400 mg/KgBB.

IV. CONCLUSION

Andaliman extract can repair the damage cervix cells of rats induced by benzopyrene and the provision of andaliman as antioxidants are one way to improve it. Andaliman can be recommended as drug to repair the destruction of cervix cells caused by cancer. However, the dose andaliman needs to be analysed. in further research.

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