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The separation of Raru (Vatica pauciflora Blume) Bark Ethanol Extracts -Glucosidase inhibitor (In Vitro) using the chromatography column Ida Duma Riris1, Martina Asiati Napitupulu2 1,2Faculty of Matematics and Natural Sciences State University of Medan Indonesia Medan, North Sumatera, Indonesia ABSTRACT: The study aims to identify and characterize the alpha-Glucosidase inhibitory activity of the Raru (Vatica pauciflora Blume).

The inbitory activity was found in aqueous ethanol extracts of bark of the stem.Column Chromatography was used and found for the process of fractination. The 1st coloum of the ethanol extract fractination showed IC50 of 94.94 as an inhibitors towards the enzyme -glucosidase. The compounds of the 1st column were separated again (2nd column) and showed the IC50 of 92.49.

The 3rd chromatography column was conducted and produced one single compound on the fraction of 9-4-4-1 with the IC50 of 93.46. In every once separation of the Raru bark epidermis produced 40.2 mg single fraction. This compound will be used to explore the effect of the compound on the decreasing of the sugar level of alloxan- induced Wistar rats.

KEYWORDS: raru (Vatica pauciflora Blume); enzym -glucosidase; chromatography 1. INTRODUCTION Traditional medicines have been used in most part of the world. In Indonesia, they have been used for thousand cine, which has been Heine, 2007). It is well known that the extract of Aloevera (Bunyatpraphasara,et al); Rhyzoma (Tohitshiro,2001S), Conisium fenestratum (Anishiwaikar,2005) has been proved to affect the decreased level of blood sugar level of the alloxaninduced Wistar rats.

The test for the inhibitor of anti-diabetic ekstract n-heksan, ethyil acetat, ethanol, and water of the bark stem of the Raru plant (Vatica pauciflora Blume) showed that the inhibitor of - glucosidase of the ethanol extract of the -hexan or even water extracts using acarbose to control (Ida, 2013). Acarbose is the -glukosidase enzyme inhibitor which is competitive and reversible in the human intestine (Bischoff H, 1995).

Ida Duma Riris (2014) found that the bark stem of Raru plants isolation, separated by chromatography, and the structures were determine by NMR; COSY;HSBC; HMQC it has the methoxy bergenin which inhibits the glucosidase enzyme by in-vitro way. To obtain it from the bark stem of Raru ethanol extract it can be done by chromatography column separation.

Based on those fact above, this study was aimed to obtain the methoxy bergenin of the bark stem of Rar u plants ethanol extract using the chromatography column. This will be used to explore the effect for the alloxan -induced Wistar rats, and compare it with the use of acarbose in to reduce the sugar blood level (in-vitro). 2.

SEPARATION AND PURIFICATION METHODS Chromatography is one of the separation methods which is considered simple to use, the data can be obtain in short time, it has the highest sensitivity and separation ability compared to other separation such as destilation, edimentation, etc. The definition of chromatography is a procedure to separate solutes by a dynamic differential migration process in the system which has 2 (two) phases or more, one of them moves continuously to certain direction. Inside the processes it determined by the anlytic method.

As general rule, the chromatography tec the two phases, the still and moving phase. The moving phase take the diluted substances through a medium until they are separated from the other solutes which has been aluened in the beginning or last process. Most of the solutes are taken through a separation medium of the flow of liquid or gaseous solvent known as eluen.

The still phase can act as the absorbant, or as solvent, to produce partition between the still and moving phase. In this last process one liquid layer on the innert buffer functions as the still phase. 98 1. Thin Layer Chromatography Thin Layer Chromatography is separation method in a physico-chemical used widely to separate and identify es place is caused by the componen distribution differences in the still and moving phase, or in other words,it takes place caused by the affinity and absorbtion compound differences of the still and moving phase (Gritter, 1985). The separation layer consists of grain material (still phase), as something to support in the glass, metal flat or suitable layer.

The good still phase is uniformity, does nor dissolve in the moving phase and the solvent. Silica gel, aluminium, cellulose is the usual still phase. The silica gel usually contains additional calcium sulfate to improve its sticky power, where this substance is used as universal adsorban for the neutral, acid and base chromatography compounds. The mix which can be separated comes in the form of solution, will be put as mark or stripe.

Once it takes place in the tighten-closed jar which contains suitable expanding solution. The separation during the process of the moving phase for detection the compounds without colour. The moving phase is the transport medium consists of one or several solvent and move inside the still phase as they have the capillary power.

Using the mixed solvent with the different polarity level can give good power of all types of compounds. In the thin layer chromatography, the moving phase selection will based on the eluotrophic row which is the row that are made using the elution ability to increase in balance with the increased polarity. Thin layer chromatography can be used primarily qualitative, quantitative, and preparatively.

Then, the second is to learn the solvent and supporting system which will be used in the chromatography column or in the High Performance Liquid Cromatografi (HPLC) (Meyer, 2004). 2. Chromatography Column jar made from glass, metal, or plastic, where underneath of the jar has a tap to control the flow of the liquid. The sorpsi material is similar with the thin layer chromatography which are silica gel, oxyde alumunium, polyamides, cellulosa, and active chacoal and sugar flour.Some of the checked media are diluted with small amount of solvent, and added into the peak column and are allowed to flow into the absorbant.

The good substances are absorbed form the solution by the absorbant perfectly in the form of narrow ribbon/tape. By allowing the solvent to flow, with or without air pressure, each is moving down by defractination and fraction which contain the same substances. The rapid movement of the substances are affected by the power of the adsorbant of the absorbant, the size of the particle and the width of the surfce, the character and polarity of the solvent, the pressure used, and the chromatography temperature system (Roth, 2000).

In order to determine the chemical structure of one compound spectroscopy UV-vis method, spectrophotometry Fourier Transform Infra Red (FT-IR), Massa Spectrometry, dan Resonance Magnetic Central Spectrometry are used. 3. METHODS OF RESEARCH Sample The stem bark of Raru (Vatica pauciflora Blume) originated from Central Tapanuli are used to be the samples.

They were chosen to be the old - brownish stem bark. Material and Instruments Chemical materials used in this research are those with pure proanalisis level and some solvent are at the technical for the extraction needs. Meanwhile, the chromatography needs the material are at the level of chromatography.

The material used are the solvent n- hexan ethanol, acetat ethyl, methanol, silica gel 60 mesh, chloroform Sea Sand B, silica SiO2, and the chloroform-acetonitril. Instruments needed are chemical glasses: erlenmeyer beaker, pipet, column and other glasses used for the sampling purification. Research Prosedure Sample Preparation (Vatica pauciflora Blume) were collected from the forest of the central Tapanuli, were cleaned and dried in the open aired room to avoid direct sun. the collection were cut into small pieces.

The Extraction of the Stem Bark of the Raru (Vatica pauciflora Blume) Extraction was conducted using the method suggested by Harbon (1987). The method is the stratified extraction using different solvent with the polarity degree, they are: n-hexan, acetat ethyl, ethanol, and water. Each extract were gathered and evaporated using the rotavapor until they become concentrated or thick. The procedure is: About 500mg -hexan solvent.

The filtrate was evaporated using the vacuum rotavapor until the n-hexan thick extracts resulted. The process of extraction continued until the colour changing of the solvent stopped. The residue was then reflucted again using the acetat ethyl until the changing colour process also stopped.

Then, the residue was filtered and the filtrates were rotate and is known as the acetat ethyl fraction. The residues from the reflucted were again going to the same process but reflucted using the ethanol, we 99 called this the ethanol fraction. When the same process was conducted using the water, and the residues were thrown away.

The process of purification of the extracts was held with the same method in the previous study of the isolation the - glucosidase inhibitor enzyme Riris (2014). The Test of Anti-diabetic Extracts Using the Mechanism of the -Glukosidase Inhibitor enzyme (In Vitro) (Sugiwati, 2009). The production of the Solution of Phosphate Dapar 0,1 M About 13,61 grams of Natrium phosphated single base was weighed and diluted into 500 ml of distilled water (solution A). 17,43 grams Natrium phosphated dual base was weighed and diluted into 500 ml of distilled water (solution B).

39 ml of solution A and 61 ml of the solution B were taken and and weaken up to 200 ml of distilled water, and pH (7.0) was also determined The Production of the Solution of

Phosphate Dapar 0,01 M About 5 ml of the phosphate Dapar solution 0,1 M (pH of 7.0) was added with 45 ml of distilled water, and the pH (7.0) was cheked The Production of the Solution of p-nitrophenyl- -D-glucopiranosa 0,5 M About 3.1

mg of p-nitrohenyl- -D-glucopyranosid was weighed carefully and diluted in the 20 ml of the phosphate dapar solution (pH of 7.0). The Production of the Solution of Natrium Karbonat 0,2 M About 2.12 gr of natrium carbonate was weighed and diluted into 100 ml of distilled water. The Production of Enzyme Solution -glucosidase was weighed and diluted into 1 ml Phosphate dapar 0.01 M and the solution was The production of the Test Solution The Solution with Enzyme (S1) 00 ppm), and was p- -D-glucopyranosid 0.5

mM was added and inkubated in the water steamer at - added. The absorbant was read at the length of wave 400nm using the spectrophotometer UV-Vis. 4. RESULT AND DISCUSSION The extraction was conduted by reflux up to the result is clear in colour, evaporated to get it thick using the solvent of n-hexana, acetate ethyl, ethanol, and water. The soaking were (0.62; 5.86; 7.61; 1.95) % in a row. The result of soaking was counted towards a 1 kg dried simplisia.

The extraction result showed that the highest soaking is 7.61% is due to the fact that ethanol is a good solvent for the flavonoid compounds (Harborn,1987). Ethanol with its boiling degree of 790C is easy to evaporate which is good process. The Test of Anti-diabetic Towards the Extracts The result of the anti- -glukosidase enzyme inhibitor (in-vitro) on the reflux result extracts (the extracts of n-hexana, acetate ethyl, ethanol, and water) with the concentration of the solution test of 50 ppm in a row (28.98%; 60.83%; 91.08%; dan 78.34).

The result of the activity test of the anti-diabetic towards the most active -glucosidase enzyme. Determination of the Solvent used in Chromatography Column 1 of the Ethanol Extracts. The analysis of KLT was conducted on the ethanol extracts using the still phase of silica gel plate SiO2 and moving phase of n-hexana-acetate ethyl (1:1); chloroform-methanol (10:1); chloroform-methanol (5:1). The purpose of the KLT analysis is to explore the sketch pattern for the chromatography column analysis.

To make the sketch revealing is the sulphate serum reactant followed by the heating of the KLT plate to get the sketch revealing. 100 a b c still phase : Silica gel moving phase : a. n-hexana-acetate ethyl (1:1) b. chloroform-methanol (10:1) c. chloroform-methanol (5:1) Figure 1. KLT Chromatograp (Vatica pauciflora Blume). n-hexana-acetate ethyl (1:1) compounds were not eluated and separated well.

The moving phase chromatogram of chlorofom-methanol (10:1) were not separated

visionably, and the chloroform-methanol (5:1) has proved to be eluated well. The Fractionation of the Ethanol Extract with the Chromatography Column 1. nts (Vatica pauciflora Blume) was fractinated using the column chromatography still phase silica gel of 60 mesh (0.063 mm 0.200 mm) and the moving phase (SiO2, with the solvent of chloroform-MeOH = 30:1; 1:1; 30:1; 25:1; 28:1; 27:1).

The chromatogram of the KLT fractination can be seen at figure 2. a b 101 c d e f g Figure 2. The Chromatogram of KLT as result of the Fractination Column I combined result of the fractination were based on the same Rf up to 14 fractination (they are: VpEt-1 up to VpEt- 14). The KLT chromatogram for the 14 fractions can be drawn in Figure 3). 102 a b Still phase : Silika gel Moving phase : a.

n-hexana-acetate ethyl (1:1) b. chloroform-methanol (10:1) Figure 3. The chromatogram of KLT for the Combined Fractions of the Column 1 The Test of the Activity of the Anti-diabetic on the Fractination Results The anti-diabetic test of the fractination result of the column 1 (VpEt-1~VpEt-14) using the method of -glukosidase enzyme inhibitor.

The result showed that the fraction VpEt 9 was the most active fraction to inhibit the enzyme as it has the highest value of inhibition percentage (94.94%). The test of -glukosidase towards the result of chromatography fractination column 1 can be summarised at the table 1. Table 1. -Glukosidase Chromatography Column 1 Sample with Enzyme (S1) without Enzyme (S0) Average (with enzyme) (X S1) Average (without enzyme) (XS0) (X S1 - X S0) % Inhibition I II I II Control 0,828 0,833 0,8305 0,0000 Blanc 0,088 0,110 0,0000 0,0990 0,7315 VpEt 1 0,148 0,139 0,030 0,035 0,1435 0,0325 0,1110 84,8257 VpEt 2 0,723 0,733 0,067 0,077 0,7280 0,0720 0,6560 10,3213 VpEt 3 0,159 0,153 0,043 0,045 0,1560 0,0440 0,1120 84,6890 VpEt 4 0,633 0,624 0,035 0,043 0,6285 0,0390 0,5895 19,4122 VpEt 5 0,486 0,467 0,081 0,080 0,4765 0,0805 0,3960 45,8647 VpEt 6 0,751 0,753 0,067 0,070 0,7520 0,0685 0,6835 6,5619 VpEt 7 0,691 0,690 0,074 0,079 0,6905 0,0765 0,6140 16,0629 VpEt 8 0,122 0,119 0,049 0,043 0,1205 0,0460 0,0745 89,8154 VpEt 9 0,066 0,067 0,028 0,031 0,0665 0,0295 0,0370 94,9419 VpEt 10 0,080 0,084 0,025 0,029 0,0820 0,0270 0,0550 92,4812 VpEt 11 0,093 0,091 0,030 0,030 0,0920 0,0300 0,0620 91,5243 VpEt 12 0,118 0,103 0,029 0,029 0,1105 0,0290 0,0815 88,8585 VpEt 13 0,066 0,063 0,024 0,023 0,0645 0,0235 0,0410 94,3951 VpEt 14 0,690 0,717 0,063 0,056 0,7035 0,0595 0,6440 11,9617 The Determination of the Solvent System on the Chromatography Column 2.

To determine the solvent on column 2 at the thin layer chromatography, the combined fraction chromatography column 1 is the 9th fraction: Moving phase : a. chloroform-methanol (10:1) b. chloroform-methanol (10:1) Still phase : Silica gel GF254 103 a b Figure 4. The Thin Layer Chromatography of the solvent Column 2 VpEt-9

Determination The thin layer chromatography VpEt-9 result was then tested using the chromatography column again: Still phase : SiO2 Moving phase : a. chloroform-methanol (20:1) b. chloroform-methanol (10:1) the result of the chromatography column was 110 fractionations.

When the thin layer chromatography was held again the result can be summarised in the following figure: A B C Figure 5. The thin layer of chromatogram fraction of the chromatography column 2 104 Moving phase : a. chloroform-methanol (5:1) b. chloroform-methanol (5:1) c. chloroform-methanol (5:1) Still phase : Silica gel GF254 The Fractination of Fraction VpEt-9 The fractinaion of fraction Vp-Et-9 with the chromatogram column (SiO2; CHCl3-MeOH= 20:1~10:1) poroduced 110 fractions, and was simplified by combining based on the same Rf to become 6 fractions (VpEt-9-1 ~VpEt-9-6).

The KLT chromatogram KLT for the chromatography fractination result column 2 can be summarised in the following figure: Moving phase : chloroform-methanol (5:1) Still phase : Silica gel GF254 Figure 5. The Combined-Thin Layer Chromatography Fraction 9 -Glukosidase enzyme and the result is the followings: Table 2. The result of the -Glucosidase Enzyme of The Extracts Chromatography Column 2 Sample With Enzyme (S1) Without Enzyme (S0) Average with Enzyme (X S1) Average without Enzyme (XS0) (X S1 - X S0) % Inhibition I II I II control 0,420 0,456 0,4380 0,0000 Blanc 0,027 0,023 0,0000 0,0250 0,4130 VpEt-9-1 0,751 0,753 0,067 0,070 0,7520 0,0685 0,6835 6,5619 VpEt-9-2 0,690 0,717 0,063 0,056 0,7035 0,0595 0,6440 11,9617 VpEt-9-3 0,152 0,166 0,051 0,047 0,1590 0,0490 0,1100 73,3656 VpEt-9-4 0,061 0,065 0,030 0,034 0,0630 0,0320 0,0310 92,4939 VpEt-9-5 0,070 0,080 0,039 0,043 0,0750 0,0410 0,0340 91,7676 VpEt-9-6 0,108 0,112 0,042 0,038 0,1100 0,0400 0,0700 83,0508 a. Solvent determination for column 3 The fraction 9.4 of the KLT is used to obtain a good solvent system column 3 is: 105 A b Figure 6.

The chromatogram of KLT for the Combined Fractions of the Column 3. Thin Layer Chromatogram VpEt-9-4 Still and Moving phases: a. SiO2, Chloroform-methanol-water (7:3:1) b. SiO2, Chloroform-methanol-water (10:3:1) Fractination of the Fraction VpEt-9.4 The fractination result of the VpEt-9-4 using the chromatography column (SiO2: CHCl3-MeOH-water = 10:3:1) produced 5 fractions (VpEt-9-4-1 ~ 9-4-5).

The KLT chromatogram ca be summarised in the Figure 7: Moving phase : chloroform-methanol-water (10:3:1) Still phase : Silica gel GF254 Figure 7. The Thin Layer Chromatography Fraction VpEt- 9-4 -glucosidase enzyme and the result showed tha the fraction 9-4-4 gave the highest value which is 93,46 %. 106 Table 3. The Test Result of the Extract -Glukosidaseof the Crhomatography Column 3.

Sample with Enzyme (S1) without Enzyme (S0) Average with Enzyme (X S1) Average without Enzyme (XS0) (X S1 - X S0) % Inhibition I II I II Controll 0,435 0,451 0,4430 0,0000 Blanc 0,029 0,031 0,0000 0,0300 0,4130 VpEt-9-4-1 0,178 0,170 0,030 0,030 0,1740 0,0300 0,1440 65,1332 VpEt-9-4-2 0,094 0,088 0,035 0,035 0,0910 0,0350 0,0560 86,4407 VpEt-9-4-3 0,064 0,059 0,024 0,030 0,0615 0,0270 0,0345 91,6465 VpEt-9-4-4 0,056 0,066 0,035 0,033 0,0610 0,0340 0,0270 93,4625 VpEt-9-4-5 0,068 0,070 0,038 0,037 0,0690 0,0375 0,0315 92,3729 Purification of Fraction 9-4-4 The purificaion of fraction VpEt-9-4-4 was held using the preparative KLT (chloroform-methanol-water = 10:3:1) and it was then known as the purified isolate 9-4-4-1 metoksi bergenin (Riris, 2014). 5.

CONCLUSION - through the separation method to obtain the metoksi bergenin (in-vitro), which has proved to have the highest inhibitor power towards cosidase enzyme compared to other compounds found in the ethanol extracts. - can be used to obtain the metoksi bergenin compounds. Suggestion -induced wistar rats can be lowered (in-vivo), as the beginning reseacrh of developing the anti-diabetic drugs. REFERENCES [1] Biscchoff H. 1995.

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