Anthocyanin and recent development as functional food

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Abstract. Anthocyanins are pigments responsible to red, purple, and blue colours in some fruits and vegetables. In the previous time, anthocyanin was only used to attract insects, for pollination and seed dispersal, Nowadays, they are known to have high antioxidant activity, and great benefit for human health, especially coronary heart disease. The aim of this research was to determine the effect of anthocyanin consumption to lipid profile of elderly human. 40 persons in a factory were educated and willing to take part in the research, they were divided into 4 groups and then consumed fruit juice contained anthocyanin in 3 dosages, and one group of control that consumed drink without anthocyanin. The lipid profile of the participant was measured before and after fruit juice treatment, then the data before and after treatment were compared, and analysed by statistical analysis. The result showed, that the highest dosage of anthocyanin intake could reduce blood total cholesterol level, LDL level and triglyceride level, but did not have effect on HDL level and ratio of total cholesterol to HDL.

Keywords: anthocyanin, antioxidant, human, lipid profile, strawberry fruit

1. Introduction
Anthocyanin are pigments responsible to red, purple, and blue colours in many fruits, vegetables, flowers, grains, and some other parts of plants like grape, blueberry, and cranberry. In the previous time it was only known to attract animal, which contribute to pollination and seed dispersal, as protective agents in photosynthesis, and very useful in taxonomic studies [1]. Recently, it has known has high antioxidant activity and positive effects on human health, especially to decrease the risk of coronary heart disease, several kinds of cancer and give benefit to visual, as anthocyanin could avoid macula degradation [2].

Many researches have been done on anthocyanin from fruits and vegetables from subtropical countries, and not many from tropical country. Indonesia has many kinds of purple tropical fruits and vegetables that has not been investigated, like java plum fruit (Syzygium cumini), banana bract (Musa paradisiaca), blue marble fruit (Elaeocarpus angustifolius), java prune fruit (Kopsia pruniformis), Iler leaves (Coleus sp), eggplant (Solanum melongena), that has high antioxidant and potential as functional food [3].

Consumption of tomi-tomi fruit juice for 3 weeks could decrease total cholesterol of mice blood in all dosage, there was a correlation between dosage of fruit juice intake and total cholesterol level; the higher the dosage of fruit juice, the lower the total cholesterol. For dosage 4 the total cholesterol level was better than control+ (simvastatin, a standard prescription for decrease blood cholesterol) [4].
Furthermore, dosage 4 could also decrease the LDL and triglyceride. It could be concluded that consumption of tomi-tomi fruit juice regularly will give good effect to the lipid profile. Tomi-tomi fruit intake for dosage 4 could also decrease glucose level of mice blood, but not better than control+ (simvastatin) [4].

Furthermore, the highest dosage could decrease total cholesterol level in blood up to 10% and increase the ‘circumference of heart’ compared to control (−) group that not consumed anthocyanin extract of tomi-tomi fruit, especially for dosage 1 and 2, but for dosage 3 and 4 it decreases again, but still better than negative control (11.48±940.00μm). Furthermore, intake of anthocyanin extract from tomi-tomi fruit in dosage 1, 2 and 3 gave better ‘circumference of heart’ compared to positive control (+) that consumed ‘simvastatin’ a standard prescription for cholesterol disease. (12.227±834.5μm). For intake of anthocyanin extract in mice could improve the structure of ‘circumference of heart’ of dyslipidemia mice, therefore we would like to investigate for human. The aim of this research was to determine the effect of anthocyanin consumption to lipid profile of elderly human.

2. Materials and Methods

2.1. Materials
Several tropical purple fruit (java plum, tomi-tomi fruit, purple sweet potato, local Bali grape, kersen, strawberry fruit); reagent for total anthocyanin and antioxidant activity determination: methanol, hydrochloric acid (Merck, Germany), DPPH (1,1-diphenyl-2-pycrylhydrazil (Sigma, USA).

2.2. Apparatus
Analytical balance 2 decimal (Ohaus, TAJ 602) and 4 decimals (Ohaus pioneer, PA 214), UV-Vis spectrophotometer (Optizen, UV 2120), pH meter (Hanna Instrument 9812), mixer (Philips, HR1538), glassware.

2.3. Methods
2.3.1. Anthocyanin determination. Anthocyanin determination was done by pH differential method [5]. Fruits were extracted with methanol-HCL 1%, and diluted with buffer pH=1 and pH=4.5, then the absorbance were measured on 510 nm and 700 nm. The results were calculated with:

\[ A_510 - A_700 \]  

then the total anthocyanin was calculated with Lambert Beer, with molar extinction of cyanidin 3-glucoside=29.600.

2.3.2. Antioxidant determination. Antioxidant determination was done with DPPH as free radical [5]. 2 mL DPPH 0.1mM (diluted in methanol) was added with 0.1 mL fruit extract, then added with methanol up to 3 mL, and kept stand for 30 minutes, then the absorbance was measure at \( \lambda = 517 \) nm. Blank was made with the same procedure, but without fruit extract. The antioxidant activity was calculated by compare absorbance of sample and absorbance of blank.

\[ \text{Antioxidants activities (%) = } \left( \frac{1 - \frac{A_{\text{sample}}}{A_{\text{blank}}}}{} \right) \times 100\% \]

2.3.3. In vivo test of strawberry fruit on human. 40 persons of a factory in Salatiga were educated before participate in the research, indeed they were interested to take part in the research, and sign their agreement. The lipid profile of them were measured before and after treatment of strawberry juice. They were divided into 4 groups: 3 groups consumed fruit juice rich in anthocyanin every day for 3 weeks, in three different dosages, one group of control (without anthocyanin) with similar color, taste and sweetness of syrup.

After treatment, the people were collected together in a room for discussion and evaluation. In general, they said they feel fresh and healthier after consumption of fruit juice for several days. Some
people said their sight were better and they can see writing in white board better than before. The data of lipid profile of the participant before and after treatment were compared and calculated by statistical analysis.

3. Result and Discussion

3.1. Anthocyanin Content and the Antioxidant Activity in some purple fruit in Indonesia

Table 1. Anthocyanin content of some purple fruit and vegetables in Indonesia(mg/g) [4].

| Sample          | Anthocyanin Content (mg/g) | Average Anthocyanin Content(mg/g) | Average Anthocyanin Content(mg/100g) |
|-----------------|----------------------------|----------------------------------|-------------------------------------|
|                 | Rep 1 | Rep 2 | Rep 3 | Rep 4 |                           |                                   |                                     |
| Java plum       | 5.527 | 7.857 | 8.1607 | 8.6944 | 7.56±1.40                 | 755.98±139.87                  |
| ‘Tomi-tomi’     | 4.878 | 3.441 | 3.9867 | 3.9699 | 4.07±0.60                 | 406.89±59.59                   |
| Purple Sweet potato | 1.340 | 1.177 | 1.5387 | 2.6421 | 1.67±0.66                 | 167.45±66.18                   |
| Kersen’         | -1.084 | 0.270 | 0.6309 | 0.4358 | 0.06±0.78                 | 6.32±77.89                     |
| Bali grape      | 1.962 | 1.047 | 1.1459 | 1.4939 | 1.41±0.41                 | 141.22±41.36                   |

Table 1 showed anthocyanin content of some tropical purple fruit, the highest was java plum, followed by tomi-tomi, purple sweet potato, Bali grape, and kersen. The anthocyanin content of kersen was very low, might be the red color was caused by carotenoid, not anthocyanin.

Table 2. Antioxidant activity of some purple fruit and vegetables in Indonesia (%).

| Sample          | Antioxidant activity (%) | Average Antioxidant activity (%) |
|-----------------|--------------------------|----------------------------------|
|                 | Rep 1 | Rep 2 | Rep 3 | Rep 4 |                           |                                   |
| Java plum       | 103.13 | 106.97 | 91.00 | 98.45 | 99.89                    |                                   |
| Tomi-tomi       | 85.75  | 92.32  | 82.09 | 92.91 | 88.27                    |                                   |
| Kersen          | 48.27  | 62.45  | 48.55 | 74.91 | 58.54                    |                                   |
| Purple Sweet potato | 86.45 | 89.26  | 80.36 | 90.00 | 86.52                    |                                   |
| Bali grape      | 83.30  | 81.77  | 71.10 | 83.55 | 79.93                    |                                   |

Table 2. showed that the highest antioxidant activity was java plum, followed by tomi-tomi, purple sweet potato, Bali grape, and kersen. It was same with the anthocyanin content. Then the fruit be used for the following step, in vivo test with mice and human.

3.2. Effect of Consumption of Anthocyanin Contained fruit juice to Human Lipid Profile

The participants were 20 patients with hypertension and diabetes mellitus, that are risk factors for coronary heart disease. These patients were divided into 4 groups each of 5 people. Groups A, B, C, D consumed a glass of anthocyanin fruit juice daily for 3 weeks, with different dosages. The dosages of anthocyanin content were showed in Table 3. Group A was placebo, that had no anthocyanin content. Before and after treatment, the participants' blood lipid profile was examined. The results were analysed statistically and compared.

The anthocyanin content of the fruit juice was also analysed. The level of fruit juice given is based on the results of previous studies on animals, which showed positive results and also adjusted to the prevalence and threshold of acceptance of the taste of the fruit used.
The anthocyanin content of the fruit juice was as follow: A= Control= did not have anthocyanin content, B=75.95 mg anthocyanin/100 g fruit, C=137.95 mg anthocyanin/100 g fruit, D=213.90 mg anthocyanin/100 g fruit.

**Table 3. Anthocyanin content of fruit juice for every dosage.**

| Date  | Fruit | Anthocyanin Content (mg/100 g BB) |
|-------|-------|----------------------------------|
|       |       | Dosage B | Dosage C | Dosage D |
| 1 May | Strawberry | 74.4     | 148.8    | 223.2    |
| 2 May | Strawberry | 74.4     | 148.8    | 223.2    |
| 3 May | Strawberry | 74.4     | 148.8    | 223.2    |
| 4 May | Grape    | 13.67    | 27.34    | 41.01    |
| 5 May | Strawberry | 74.4     | 148.8    | 223.2    |
| 7 May | Strawberry | 74.4     | 124.14   | 198.4    |
| 8 May | Strawberry | 74.4     | 124.14   | 198.4    |
| 9 May | Strawberry | 74.4     | 124.14   | 198.4    |
| 11 May| Strawberry | 74.4     | 124.14   | 198.4    |
| 12 May| Strawberry | 74.4     | 124.14   | 198.4    |
| 14 May| Strawberry | 74.4     | 124.14   | 198.4    |
| 15 May| Strawberry | 74.4     | 124.14   | 198.4    |
| 16 May| Strawberry | 74.4     | 124.14   | 198.4    |
| 17 May| Strawberry | 74.4     | 124.14   | 198.4    |
| 18 May| Strawberry | 74.4     | 124.14   | 198.4    |
| 19 May| Strawberry | 74.4     | 124.14   | 198.4    |
| 21 May| Strawberry | 74.4     | 124.14   | 198.4    |
| 22 May| Strawberry | 74.4     | 124.14   | 198.4    |
| Average|        | 71.03    | 124.14   | 195.17   |

Dosage of strawberry:
- Dosage B: normal (4 box of fruit)
- Dosage C: 2x normal (8 box of fruit)
- Dosage D: 3x normal (12 box of fruit)

Dosage of grape:
- Dosage B: normal (350 gr)
- Dosage C: 2x normal (700 gr)
- Dosage D: 3x normal (1050 gr)

3.2.1. Lipid profile of participant before treatment of fruit juice contained anthocyanin. Results of lipid profile of the participants before and after treatment with fruit juices containing anthocyanins are shown in Fig. 1 (Cholesterol total), Fig. 2 (LDL Level), Fig. 3 (HDL Level), Fig. 4 (Triglyceride Level), and Fig. 5 (Ratio of total cholesterol/HDL level before and after treatment).
Figure 1. Total cholesterol before and after treatment (1=control, without anthocyanin, A; 2=anthocyanin dosage B; 3=anthocyanin dosage C; 4=anthocyanin dosage D).

Figure 2. LDL level before and after treatment (1=control, without anthocyanin, A; 2=anthocyanin dosage B; 3=anthocyanin dosage C; 4=anthocyanin dosage D).

Figure 3. HDL level before and after treatment (1=control, without anthocyanin, A; 2=anthocyanin dosage B; 3=anthocyanin dosage C; 4=anthocyanin dosage D).

Figure 4. Triglyceride level before and after treatment (1=control, without anthocyanin, A; 2=anthocyanin dosage B; 3=anthocyanin dosage C; 4=anthocyanin dosage D).
Figure 5. Ratio of total cholesterol/HDL level before and after treatment (1=control, without anthocyanin, A; 2=anthocyanin dosage B; 3=anthocyanin dosage C; 4=anthocyanin dosage D).

Table 4. Homogeneity test of sample.

|       | Levene Statistic | df1 | df2 | Sig.  |
|-------|------------------|-----|-----|-------|
| LDL-2 | 2.736            | 3   | 16  | 0.078 |
| HDL-2 | 2.571            | 3   | 16  | 0.090 |
| TRIG-2| 0.324            | 3   | 16  | 0.808 |
| Ratio-2| 2.043          | 3   | 16  | 0.148 |

Table 4, on homogeneity test, showed that the distribution of sample data was normal (p>0.05). Therefore, the data could be analysed using statistical parametric tests. The parametric test used was ANOVA because the number of treatment groups was more than 3 groups. The results of Table 5 showed that after drinking tropical fruit juice contained anthocyanin, there were no significant differences between groups (p>0.05) in the four blood lipid profiles.

Table 5. ANOVA test between groups after treatment with fruit juice.

|       | Sum of Squares | df  | Mean Square | F     | Sig.  |
|-------|----------------|-----|-------------|-------|-------|
| LDL-2 | Between Groups | 7419.350 | 3   | 2473.117 | 2.982 | 0.063 |
|       | Within Groups  | 13267.600 | 16  | 829.225  |       |       |
|       | Total          | 20686.950 | 19  |          |       |       |
| HDL-2 | Between Groups | 1354.550  | 3   | 451.517  | 3.035 | 0.060 |
|       | Within Groups  | 2380.400  | 16  | 148.775  |       |       |
|       | Total          | 3734.950  | 19  |          |       |       |
| TRIG-2| Between Groups | 22111.350 | 3   | 7370.450 | 1.941 | 0.164 |
|       | Within Groups  | 60745.600 | 16  | 3796.600 |       |       |
|       | Total          | 82856.950 | 19  |          |       |       |
| Ratio-2| Between Groups | 7.780     | 3   | 2.593    | 2.718 | 0.079 |
|       | Within Groups  | 15.268    | 16  | 0.954    |       |       |
|       | Total          | 23.048    | 19  |          |       |       |
Table 6. Correlation test between groups of treatment.

|               | koles2 | LDL-2 | HDL-2 | TRIG-2 | Ratio-2 |
|---------------|--------|-------|-------|--------|---------|
| **Pearson Correlation** | 1      | 0.979** | 0.514* | 0.043  | 0.057   |
| **Koles2 Sig. (2-tailed)** | 0.000  | 0.021  | 0.858  | 0.811  |
| **N** | 20     | 20     | 20     | 20     | 20      |
| **Pearson Correlation** | 0.979** | 1      | 0.440  | -0.016 | 0.103   |
| **LDL-2 Sig. (2-tailed)** | 0.000  | 0.052  | 0.946  | 0.665  |
| **N** | 20     | 20     | 20     | 20     | 20      |
| **Pearson Correlation** | 0.514* | 0.440  | 1      | -0.622* | -0.781**|
| **HDL-2 Sig. (2-tailed)** | 0.021  | 0.052  | 0.003  | 0.000  |
| **N** | 20     | 20     | 20     | 20     | 20      |
| **Pearson Correlation** | 0.043  | -0.016 | -0.622** | 1      | 0.778** |
| **TRIG-2 Sig. (2-tailed)** | 0.858  | 0.946  | 0.003  | 0.000  |
| **N** | 20     | 20     | 20     | 20     | 20      |
| **Pearson Correlation** | 0.057  | 0.103  | -0.781** | 0.778** | 1      |
| **Ratio-2 Sig. (2-tailed)** | 0.811  | 0.665  | 0.000  | 0.000  |
| **N** | 20     | 20     | 20     | 20     | 20      |

**. Correlation was significant at the 0.01 level (2-tailed)
*
. Correlation was significant at the 0.05 level (2-tailed).

Table 6 about correlation test to determine the relationship between increasing of anthocyanin dosage and decreasing of blood lipid between treatment groups. The results showed that the blood lipid profile in the treatment groups was strongly correlated between total cholesterol and LDL (p=0.000; r=0.979 α<0.001) and HDL (p=0.021 r=0.514); triglycerides with a ratio of total cholesterol/HDL (p=0.000 r=0.778) and weak correlation between total cholesterol and triglycerides (p=0.858 r=0.043) and the ratio of total cholesterol/HDL (p=0.811 r=0.057). And the negative correlation between triglycerides and LDL (p=0.946 r=-0.016) and HDL (p=0.003 r=-0.622 α<0.001) and HDL with total/HDL cholesterol ratio (p=0.000 r=-0.781 α<0.001).

Table 7. Statistical test on paired t before and after treatment of fruit juice.

|               | Paired Differences |         |         |              |         |       |       |
|---------------|--------------------|---------|---------|--------------|---------|-------|-------|
|               |                    | Mean    | Std. Deviation | Std. Error Mean | 95% Confidence Interval of the Difference | t    | df    | Sig. (2-tailed) |
|               |                    |         |            |              |       | Lower | Upper |
| Pair 1        | koles2-Kol1        | 2.45000 | 17.80442 | 3.98119      | -5.88273 | 10.78273 | 0.615 | 19    | 0.546 |
| Pair 2        | LDL02-LDL01       | 23.40000 | 37.10781 | 8.29756      | 6.03301   | 40.76699 | 2.820 | 19    | 0.011 |
| Pair 3        | HDL02-HDL01       | -1.45000 | 4.85012 | 1.08452      | -3.71993  | 0.81993  | -     | 19    | 0.197 |
| Pair 4        | TRIG02-TRIG01     | -3.85000 | 45.93849 | 10.27216     | -25.34987 | 17.64987 | -     | 19    | 0.712 |
| Pair 5        | Ratio02-Ratio01   | 0.24000  | 0.47727  | 0.10672      | 0.01663   | 0.46337  | 2.249 | 19    | 0.037 |

Table 7 about statistical test on paired t before and after treatment of fruit juice.
In table 7, paired t-test between blood lipid profile before and after drinking juice, it could be seen that the participants who consumed highest dosage of fruit juice could decrease of LDL in blood \((p=0.011)\) and ratio of total cholesterol/HDL \((p=0.037)\) was significant; whereas total cholesterol \((p=0.546)\), HDL \((p=0.197)\) and triglyceride \((p=0.712)\) were not significant.

The results of the research showed that after treatment with fruit juice for 3 weeks, group D who consumed anthocyanin 213.90 mg/100 g of fruit, had the best result, with total cholesterol 18.6 mg/dL and decrease LDL 14.2 mg/dL, HDL 3.2 mg/dL, and triglyceride 24.4 mg/dL, and ratio of total cholesterol/HDL 0.14, as the highest decrease compared to other groups. If antioxidant be consumed too much, it will become prooxidant, that give bad effect for health. However, the highest dosage of strawberry juice in this research was estimated not too high, because it is from natural source, that usually do not give effect as prooxidant.

It was supported by the similar research of Sutirta-Yasa and Jawi [6] on purple sweet potato, that consumed water extract containing anthocyanin for 3 months in rabbit, could avoid increasing of MDA (Malondialdehyde), increase total antioxidant in blood, decreasing total blood cholesterol, safe for liver in rabbits with high feed cholesterol. Another research was on the effect of purple yam, that could decrease total cholesterol of wistar rats serum which were given repeated cooking oil insignificantly [7]. Actually from taxonomy, monkey is closer to human, they are in the same group, called primate, however from the similarity of endocrinology, (hormone and metabolism), human is closer to rat or mice.

However, the significant results of anthocyanin effect with paired test was showed on decrease of LDL \((p=0.011)\) and ratio of total cholesterol/HDL \((p=0.037)\); whereas in total cholesterol \((p=0.546)\), HDL \((p=0.197)\) and triglyceride \((p=0.712)\) the change was not significant. This was also supported by [8], the increase of black rice anthocyanin extract gave significant effect to the decrease of triglyceride, LDL levels, LDL/HDL ratio, and cholesterol atherogenic index value. These interventions had positive impacts in the malonaldehyde (MDA) of plasma and antioxidant capacity level. Likewise, Widyasari [9], about effect of steeping dry petals, purple rosella flowers contain anthocyanins against total cholesterol levels of hypercholesterolemic rats. There were no differences in total cholesterol after treatment with rosella at various dosages:1340 mg/kg body weight/ day, 2700 mg/kg body weight/ day, and 4020 mg/kg body weight/ day in hypercholesterolemic mice. Also, the effect of rosella petal infusion insignificantly reduces total cholesterol at dosages of 125 mg/kg body weight (12.99%), 250 mg/kg body weight (23.54%) and 500 mg/kg body weight (30.82%) [10].

Anthocyanin is one of the important pigment that has been studied widely, have some beneficial effects on mammals' cells such as antioxidant activity, antimutagenic, hepatoprotective and antihypertensive, and antidiabetic effects [11]. Anthocyanin is abundant in several fruits and vegetables, nuts, grains, and tubers. Anthocyanin is a group of flavonoids that dissolve in water, which play a role in forming red to blue in plants, flowers, seeds, fruits and vegetables, has ability to improve endothelial blood function [12], reduce LDL sensitivity to free radicals and can have hypolipidemic activity, anti-inflammatory, endothelial dysfunction and NO production as well as good antioxidants [13].
The anthocyanin pharmacological mechanism is related to its constituent chemical structure (Fig. 6), this mechanism of action is based on its antioxidant potential, depend on the number and position of hydroxyl group (-OH), the conjugation group, the level of glycosylation and the presence of donor electrons in the ring structure, because of the ability of the aromatic group to maintain loss of electrons. The number of -OH groups at positions C3 and C4 in rings B and C3 in C ring of the flavonoid nucleus appears to be the major structure required for anthocyanin, inhibition of endothelial cell oxidative damage, and free radical intracellular activity. The mechanism of this antioxidant specifically includes suppression of the formation of reactive species, through enzyme inhibition or sequestration of elements involved in the production of free radicals. Anthocyanins also have antiperoxidative activity, capture free radicals and ions, inhibit XO, chelating metal ions, with the target of arachidonic acid and molecular adhesion, directly dispose of the active species of oxygen including hydrogen peroxide, oxygen singlets, superoxide, -OH and peroxyl radical. The next, anthocyanin inhibits NF-κB signal and NF-κB dependent mediator activated by tumour necrosis factor (TNF) -α plays a role in pathogenic atherosclerosis. This process is carried out by malvidin-3-glucoside which suppresses pro-inflammatory mediators, inhibits and blocks NF-KB. Anthocyanins inhibit vasodilator action by preventing damage to ONOO- in endothelial cells through interference with mitochondrial apoptotic pathway, preventing endothelial cell apoptosis and Baxnucler translocation inhibition [15]

4. Conclusion
From the research it could be concluded that the highest content of anthocyanin and antioxidant activity in tropical purple fruit were java plum followed by tomi-tomi, purple sweet potato, and Bali grape, and anthocyanin consumption for 3 weeks (strawberry fruit) gave good effect to lipid profile of elderly human without side effect, it could reduce total cholesterol, LDL, and triglyceride level, but did not have effect on HDL level and ratio of cholesterol total to HDL.
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