THE INFLUENCE OF PRE-TREATMENT AND CO-TREATMENT OF AMBON BANANA FRUIT JUICE TO FUROSEMIDE BIOAVAILABILITY

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Abstract

Introduction. *Some patients used banana to administered tablet or pill . It is possible that there will be pharmaceutical interaction between the drug and banana. This study was aimed to know the influence of pre-treatment and co-treatment of ambon banana fruit juice (Musa paradisiaca L.) on the furosemide bioavailability..*

Method. *This study was carried out using cross over design.. The subjects used in this study were five local male rabbit with same in body weight and divided into 4 treatments. The A group was treated by furosemide 80 mg (control), The B group was treated by ambon banana fruit juice 100% (5 ml) 2 hours before furosemide administration. The C and D groups were treated by ambon banana fruit juice 100% and 50% (5 ml) in the same time with furosemide administration. The blood was taken through marginalis vein of ears at the time 0,5; 0,75; 1; 1,5; 2; 3; 3,5; 4; 8; and 24 hours after furosemide administration. Furosemide in the blood was determined using Kelly's method modified by Hakim. Then, the bioavailability parameters were measured from pharmacokinethics profiles . Furthermore, t max and Cp max were analized using one-way Anova while AUC0-8 was analized using Kruskal-wallis.*

Result. *The average of furosemide bioavailability in male rabbit are Cpmax ; 15,21.10-2 (ìg/ml), 13,97.10-2 (ìg/ml), 11,08.10-2 (ìg/ml), 12,10.10-2 (ìg/ml), tmax; 2,30 hours, 3,50 hours, 3,35 hours , 5,30 hours, and AUC0-8 ; 10,53 ìg.ml-1 hour, 4,00 ìg.ml-1 hour, 4,95 ìg.ml-1 hour, 3,37 ìg.ml-1 hour respectively for treatment A,B,C, and D. There were no significant differences of tmax and Cpmax and AUC0-8 among groups (p value> 0.05).*

Conclusion. *There were no influence of pre-tretment and co-treatment of ambon banana fruit juice (Musa paradisiaca L.) on the furosemide bioavailability.*

Key word : *Furosemide, Ambon Banana fruit Juice (Musa paradisiaca L.), Bioavailability*

INTRODUCTION

Peroral administration is the most natural administration of the medicines. Most of the peroral dosage forms such as tablets, capsules, pills, should be swallowed with water. However, some patients can not take their per oral medication without bananas. This could becaused by the physical properties of the banana fruit is soft and pliant so that it can help patients in swallowing the medicine. The use of bananas along with the drug is not only found in homes, but also at the hospital. Patients who need banana to take the medicines generally those who are elderly, children and patients who have difficulty swallowing medication with water.
The habit of medicine administration along with banana could be a problem, because the presence of food-drug interactions. We could not understand the abnormalities or changes of our body, because of the the light effects of drug-food interaction. However, people consider banana in this issue because it was easy to obtain, the price is also accessible by the whole society (Handayani,2009).

The prevalence of hypertension in Indonesia reached 31.7% of the population at the age of 18 years and over 60% of them were ended in stroke. While the rest were ended by heart, kidney failure and blindness.
According to Joint National Committee (JNC) 7, the first line therapy for hypertension is a diuretic, one furosemida. The Biopharmaceutics Drug Classification System (BCS) categorizes furosemida as class II, due to low solubility, furthermore furosemida also has a 95% protein binding (McEvoy, 2002), thus furosemide is potential for interacting with other agents.

According to the premise that people often take the medicine with a green banana, including furosemide allows the interaction between them. Theoretically, consumption of bananas along with the favorable interaction furosemide is because bananas contain lots of potassium (Anonymous, 2002), whereas a loop diuretic is likely causes hypokalemia. The co-administration with banana juice could be expected to affect the bioavailability of the furosemide tablet. The aim of this study was to evaluate the effect of pre-treatment and co-treatment of ambon banana fruit juice (*Musa paradisiaca* L.) on the furosemide bioavailability.

MATERIALS AND METHODS

MATERIALS

The instruments used in this study were: glass tools, scapel, micro pipettes, syringes, vortex (Thermolyne 37 600), centrifuge equipment (centrifuges) Mettler Toledo AG 285, spectrofluorometer (Hitachi F 2500) and analytical balance (CEN Phoenix 91 501).

The materials used were obtained from the ambon banana one supermarket in the city of Yogyakarta. The chemicals used were of pharmaceutical furosemide degrees (Indofarma), ethyl acetate pa (E Merck), HCl pa (E Merck), phosphate buffer pH 8, NaOH pa, heparin, distilled water (Lab Asia) and the local strain male rabbits aged 3 months with the same weight.

Identification and Preparation of Ambon Banana Fruit Juice

Identification of plant was performed at the Laboratory of Biology, University Ahmad Dahlan. Identification was done in an organoleptic, based on physical characteristics, odor, color and distinctive flavor of banana fruit. Banana juice was made by weighing 50 g of bananas and water to 50 ml. The concentration of 50% w / v was obtained by the dilution of 100% w / v.

Bioavailability Furosemida Parameter Determination in Blood

The five same weight of local strain male rabbits were examined using Cross Over design with 4 treatments (Table I).

Table I. Cross over the design and treatment with banana juice on the bioavailability of the furosemide tablet

Rabits	Week			
	I	II	III	IV
1	A	B	C	D
2	B	C	D	C
3	C	D	A	B
4	D	A	B	A
5	A	B	C	D

A = 80 mg tablet furosemide (control), B = Pretreatment of 100% w / v banana juice 2 h before the furosemida tablet, C = Co-treatment of 100% w / v banana juice with a furosemida tablet, D = Co-treatment of 50% w / v banana juice with a furosemide tablet, The total volume of solution was 5 ml

Before the treatment, the rabbits were fasted for one day. We consider 7 days for washing out in each treatment. After the drug administration, the blood was taken at hours 0.5, 0.75, 1, 1.5, 2; 2.5; 3; 4; 8 and 24, through the vena marginalis rabbit ears. The blood as collected in tubes with heparin ependrof.

Determination of the furosemida bioavailability

The bioavailability parameters included in this study were Cp max, t max and AUC 0-8 which were obtained directly from the relationship curve between drug concentration and time, and AUC 0-8 was obtained by the trapezoidal method.

DATA ANALYSIS

Data were analyzed statistically with tests of homogeneity of variance and data normality. After considering the homogeneity of variance and data normality the differences between the treatments were analyzed using or Kruskal Wallis test.

RESULTS AND DISCUSSION

This study showed that there were no influence of pre-treatment and co-treatment of ambon banana fruit juice (*Musa paradisiaca* L.) on the furosemide bioavailability.

PLANT IDENTIFICATION

Figure 1. Ambon banana fruit

The ambon banana used in this study was white when ripe yellow discharge. Its skin was smooth and would change the color into yellow when ripe at room temperature. Taste slightly sour was sweet and strong odor. These bananas have an average length of 15-20 cm and a diameter of 3.5 to 4 cm (Anonymous, 2010). The banana is creamy colored, fragrant and sweet (Anonymous, 2011).

From the determination of the excitation and emission wavelengths in the blood plasma, furosemide was consecuted at 272 nm and 404 nm, whereas the linear regression equation for the standard curve was: $Y = 0.247 + 4.767\ x$; $r = 0.996$.

Recovery requirements analysis method that is between 80-120% of the levels was listed

in the table (FDA requirements) (Pusporini, 2006). The recovery ranges from 89.96 to 107.28% indicated that the method chosen has accurate range of % recovery (% recovery.

Table II and Figure 3 are presented the furosemide concentration in blood plasma. Next, the bioavailability of furosemide tablet on male rabbits are shown in Table III.

Table II. Furosemide levels in blood plasma vs time (mean ± SE) on treatment with banana juice

Time (hours)	C(μg/ml)			
	A mean±SE (10_{-2})	B mean±SE (10_{-2})	C mean±SE (10_{-2})	D mean±SE (10_{-2})
0	0	0	0	0
0,5	4,70 ± 0,88	4,01 ± 0,48	5,53 ± 0,66	6,44 ± 2,13
0,75	5,06 ± 0,83	4,39 ± 1,23	5,49 ± 1,68	5,18 ± 1,25
1	8,03 ± 2,41	4,18 ± 1,04	4,11 ± 0,71	6,81 ± 2,15
1,5	10,14 ± 5,52	7,35 ± 2,33	4,73 ± 1,20	9,34 ± 2,01
2	**12,69 ± 5,04**	**10,78 ± 3,43**	5,79 ± 1,48	6,07 ± 1,08
2,5	9,57 ± 2,09	6,23 ± 2,17	6,72 ± 1,95	8,07 ± 1,81
3	8,27 ± 1,32	9,88 ± 1,46	7,27 ± 2,37	**11,12 ± 2,43**
4	8,14 ± 1,46	8,14 ± 2,00	**10,61 ± 2,51**	8,94 ± 2,08
8	6,31 ± 1,34	7,83 ± 2,35	8,61 ± 2,68	9,06 ± 2,30
24	5,69 ± 0,93	5,15 ± 1,36	6,19 ± 1,44	4,31 ± 1,49

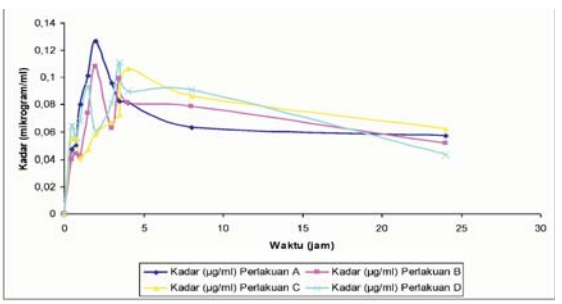

Figure 2. Curve levels furosemide (mean ± SE) in plasma vs time. The 80 mg of furosemide tablet was given orally

The smallest percent degradation of furosemide was found when it was stored at -20 ° (freezer), thus, the sample should be directly extracted the plasma stored in the freezer.

After the calculation, the obtained parameters such as bioavailability of the furosemide tablet are presented in table III

There were no significant differences in bioavailability parameters among 4 treatments.

The results showed that the bioavailability parameter in each treatment produced no significant differences ($p > 0.05$) both at AUC, t max and Cp max. This means that treatment the banana juice did not influence furosemide bioavailability significantly. There was also no significant differences of furosemide bioavailability in the co-treatment of 5 ml banana juice at a concentration of 50% w / v to 100% w / v with furosemide tablet. There were no significant differences of tmax and Cpmax and AUC0-8 among groups (p value> 0.05).

The results are consistent with the study performed by Kelly et al (1974) and

Table III. The mean parameter furosemide tablet bioavailability in banana juice treatment

Parameters	Treatment			
	A	B	C	D
	Mean ± SE	Mean ± SE	Mean ± SE	Mean ± SE
Cp_{max} (µg/ml)	15,21 ± 4,67	13,97 ± 2,62	11,08 ± 2,51	12,10 ± 2,24
t_{max} (Jam)	2,30 ± 0,62	3,50 ± 1,16	3,35 ± 0,65	5,30 ± 1,10
$AUC^{0-\infty}$ (µg/ml. hours)	10,53 ± 5,67	4,00 ± 1,15	4,95 ± 1,08	3,37 ± 1,29

Hammurland et al (1982) which stated that furosemide provided with food did not affect the bioavailability of the drug, although Hammurland et al found that the peak levels decreased and the study of food provided is not mentioned specifically. These results were in contrast to the results obtained by Beermann (1986) which stated that food may decrease the bioavailability of furosemide about 30%, but the decreased bioavailability due to the diuretic effect furosemide not because of the interaction with food intake. The research was conducted on healthy humans with food such as milk, cheese, egg, avocado and fish juice. According McCrandle, et al (1996) furosemida 40 mg supplied with food (orange juice, eggs, milk and butter) were also significantly reduce the bioavailability of 30% but decreased bioavailability of the mechanism is not described further. This study has limitations in the sensitivities analysis methods are used, so for further research are expected to use more sensitive analytical methods, eg HPLC.

CONCLUSION

1. Pre-tretment of banana juice did not affect the bioavailability of the tablet furosemide parameters (p>0.05).
2. There weres no significant difference of furosemide bioavailability in the effect of 5 ml banana juice co treatment at a concentration of 50% w / v to 100% w / v.
3. There was no significant difference in the effect of giving 5 ml banana juice 100% w / v simultaneously or two hours prior to the furosemide bioavailability

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