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Tablet Kunyah Ekstrak Daun Jambu Biji (*Psidium Guajava* L.) Dengan Amilum Sukun Sebagai Pengikat

(The Chewable Tablet of Guava Leaves Extract (Psidium guajava L.) with Breadfruit Starch as Binder)

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ABSTRAK

Amilum sukun dapat digunakan sebagai pengikat pada tablet kunyah karena terdiri dari amilosa dan amilopektin karena dapat meningkatkan daya kohesifitas dan membentuk ikatan yang baik pada serbuk. Ekstrak daun jambu biji (*Psidium guajava* L.) mampu membunuh pertumbuhan bakteri *Streptococcus mutans* sehingga dapat berfungsi untuk mencegah karies gigi. Penelitian ini bertujuan untuk melihat pengaruh peningkatan amilum sukun terhadap karakteristik fisik tablet kunyah ekstrak daun jambu biji. Tablet kunyah ini dibuat dalam 4 formula yang masing – masing formula terdiri dari mucilago amilum sukun 10 %, 13%, 16% dan 19%. Amilum sukun sebagai pengikat didapat dari buah sukun yang hampir matang dan dihancurkan lalu direndam hingga terjadi pemisahan antara air rendaman dan amilum, selanjutnya amilum dikeringkan dan dibuat mucilago untuk ditambahkan ke dalam formula. Hasil karakteristik amilum, serbuk yang didapat benar adalah amilum sukun. Granul yang dihasilkan dievaluasi kemampuan mengalir dan distribusi ukuran partikel. Selanjutnya, granul dibuat menjadi tablet kunyah. Hasil evaluasi tablet kunyah menunjukkan bahwa peningkatan konsentrasi mucilago amilum sukun mampu meningkatkan kekerasan dan menurunkan keregasan dari tablet kunyah.

ABSTRACT

Breadfruit starch can be used as a binder on the chewable tablet because it consists of amylose and amylopectin which can increase the cohesiveness and make a good bond with the powder. Guava leaves extract can kill the bacterial growth of Streptococcus mutans so it can be served to prevent dental caries. This research aimed to know whether increased concentrations of breadfruit starch can affect the physical characteristics of the chewable tablet of guava leaves extract. The chewable tablets were formulated into 4 formulas with different concentration of mucilago breadfruit starch, such as 10%, 13%, 16% and 19%. Breadfruit starch as a binder obtained from an almost ripe the breadfruit and then was crushed and soaked to occur separation between water immersion and amylum, and then amylum was dried and made as mucilago and the mucilago was added into the formula. The result of the characteristic of starch, the powder was true breadfruit starch. The flowability and particle size distribution of granule was evaluated. Then, the granule was made into the chewable tablet. The research result showed that the increase of mucilago breadfruit starch concentration increased the hardness and decreased friability of chewable tablet.

INTRODUCTION

Caries is a dental and oral health problem that still faced by our country. Based on Household Health Survey 2004, the prevalence reached 90.05%. One of the bacteria that play a role in the pathogenesis of caries is *S. mutans*. Inside dental plaque, this bacteria will ferment sucrose to acid. The resulting acid causes the process of dissolution and demineralization of the tooth so that there was caries.

An alternative material that can be used to prevent dental caries is guava leaves extract (*P. guajava* L.). This plant can be used as a mouthwash for a toothache and as an astringent. From the results of previous research had been proved that guava leaves extract (*P. guajava* L.) be able to kill the growth of *S. mutans* so it can prevent dental caries (Tampedje et al. 2016). In previous research guava leaves extract has been used as anti-dental caries against *S. mutans* in the form of toothpaste with a concentration of 2% (Nursal et al. 2014). Preparations in the form of toothpaste allow for non-uniform doses and impractical usage so that chewable tablets developed.

Chewable tablets are generally chewed in the mouth prior to swallowing and are not expected to swallow intact. Main purpose of chewable tablet is to provide proper unit dosage form of medication which can easily be administered to children or to the elderly who have difficulty in swallowing a tablet intact. Chewable tablet have some specific advantages as Improved patient acceptance, Patient convenience; need no water for swallowing, Possible to use as a substitute for liquid dosage forms where rapid onset of action is needed, Absorption of drug is faster, Product distinctiveness through marketing prospective, Effectiveness of therapeutic agent is improved by the reduction in size that occurs during mastication of tablet before swallowing, Better bioavailability through by passing disintegration (that increase dissolution) (Renu 2015). Characteristics of the chewable tablet have a smooth shape, has a delicious taste and does not leave a bitter and unpleasant taste.

The binder is one of the essential additives in the manufacture of tablets. Binders are added to the tablet formulation to impart plasticity as well as increases interparticulate bonding strength in the 20 tablet (Enauyatifard et al. 2012). The binder is added in the tablet formula to add cohesiveness of the powder thus providing an important bond for forming granules under forging to form a cohesive or compact period, commonly binders that used are starch, PVP, gelatin, Na. CMC and tragacanth (Siregar 2010).

The binder used in this study is breadfruit starch. The breadfruit starch is the starch that obtained from breadfruit, is a natural material that is widely available at a relatively cheap price. In the form of fine powder, easy to stick, white, odorless and tasteless, dissolves in hot water, insoluble in cold water and alcohol, positive against iodine reaction. The breadfruit starch can be used as a binder because it contains amylose and amylopectin so that can increase cohesiveness and form a good bond with the powder (Siregar 2010).

Breadfruit plants have several scientific names commonly used, namely *Artocarpus communis* Forst, *A. incise* Linn, and *A. altilis* (Pitojo 1992). Breadfruit (*A. altilis* (Park.) Fosberg.) is an alternative source of carbohydrates besides rice, sago, cassava, and corn. The comparison of amylose and amylopectin in breadfruit is 27,7% amylose and 72,3% amylopectin (Guntara 2012). The smaller of amylose content or the higher of amylopectin make the higher of adhesion (Winarno 2004).

The concentration of mucilago amylum that used as the binder is 5 - 10% (Siregar 2010). Mucilago starch can be used as a maximum binder at a concentration of 10%. Based on the background above, research on a variation of breadfruit starch concentration as a binder on chewable tablets of guava leave extract (*P. guajava* L.) was conducted.

METHOD

Tools

Analytical scales (OHAUS), glassware, rotary tablet press (Rimek mini press-II), oven (Memmert), sieves shaker, blenders (Miyako), sieve no 12 and 16, millimeter blocks paper, vernier caliper (tricle brand), desiccator, hardness tester (YD-2 Tablet Hardness tester), friability tester (CS-2 Friability tester), tapped density tester, granule flow tester, crussible.

Materials

Guava leaves extract (*P. guajava* L.) was obtained from Indonesian Spice and Medicinal Crops Research Institute (ISMCRI). The plant determination was done at the Indonesian Institute of Science (LIPI) and no.adm: 54/T/LAB/III/2017. Breadfruit obtained from market in Cakung Jakarta Timur. Mannitol, lactose, aerosil, magnesium stearate, iodine reactant and talcum obtained from Brataco.

Procedure

Isolation of breadfruit starch

Bread starch was made from an almost ripe breadfruit and green (Ifmaily. 2018). To dissolve the flour and separate it from the dregs, water added to the result of the grater breadfruit. Next, the starch was precipitated for 24 hours with attention to the water layer at the top.The clearer of the water means the better precipitation. The stand was inserted in the oven for 24 hours at 60°C. Starch obtained in the form of lumps, then it was mashed and sieved with number 60 so that the powder that obtained was amylum.

Identification of breadfruit starch

Identification of breadfruit starch was qualitative analysis, lost on drying test and ash content test. A total of ± 1.0 g of starch was dispersed into 50 ml of water, heated to a clear gel, then cooled. 0.05 ml of a 0,005 M Iodine solution was added and will produce a blue color (Depkes RI 2014). Then, ash content test was done by weighing the crus that has been inserted in the oven for 30 minutes at 105°C with three times treatment until the weight is fixed. A ± 1.0 g sample is inserted into the crus, then leveled. Then it is heated until the substance of fabric is perfect. Then it is inserted in blast furnace until found ash. The filling process was carried out at a temperature of 800°C for 30 minutes then cooled in a desiccator and weighed. The treatment is repeated until the weights are fixed (Depkes RI 2014).

Design of the formula

The chewable tablet formula was made into 4 formulas of formula I, II, III, IV with the weight of each tablet is 700 mg. All formula can be seen in **Table 1.**

Procedure for making chewable tablets

Procedure for making chewable tablets was done by wet granulation method, that was by making 10% of mucilago amylum. The guava leaves extract (*P. guajava* L.) and aerosol were inserted into the mortar and mixed to homogeneous, and then mannitol and lactose are inserted and mixed to homogeneous, add a binder (mucilago) to a compact mass that can be clenched. The homogeneous period was sieved with a sieved number 12 then dried in an oven at 50°C for 18 hours. The obtained dried granules were then sieved with sieve number 16. Magnesium stearate and talc were added to dry granules and then mixed until homogeneous, then granular evaluation was performed. The granules were molded into tablets weighing 700 mg and evaluated.

Evaluation of granule

Flow properties were done by inserted 100.0 grams granule into the funnel. Granule was allowed to flow freely from the funnel, the granule allowed to fall onto the millimeter block paper. Then a stable cone will be formed and formed an angle of repose, then calculated the rest angle and the flow time (Siregar 2010). Then, the compressibility of granule was done by putting the granule into a 100 ml measuring cup, measured up to 100 ml. Then granule was tapped with tapped density tester as much as 500 times beats as much as 3 times treatment. Then recorded the volume and the weight of granules after it was tapped (Siregar 2010).

Next evaluation was a distribution of granule. This evaluation was done by 100.0 grams of granule were weighed, then inserted into a multi-mesh screen with mesh sieves no 18, 20, 24, 30, 40. Then switched on 30 Hz for 25 minutes. Then weigh the granules left on each Sieve. And the last was lost on drying test. This evaluation was done by drawn glassed weighing bottle that has been cleaned and dried in an oven at 105°C for 30 minutes. The treatment is conducted three times until the weight is fixed. Next, 2.0 grams of granules are

Table 1. Formula of Chewable Tablet Guava Leaves Extract (*Psidium guajava* L.)

Material	FI (%)	F2 (%)	F3 (%)	F4 (%)	Function
Guajava leaves extract (*Psidium guajava* L.)	2	2	2	2	Active Pharmaceutical Ingredients
Mucilago of breadfruit starch	10	13	16	19	Binder
Aspartame	0.5	0.5	0.5	0.5	Sweetener
Aerosil	0.1	0.1	0.1	0.1	Absorber
Talk	2	2	2	2	Lubricant
Mg Stearate	2	2	2	2	Glidan
Mannitol ad	100	100	100	100	Filler

taken and weighed thoroughly and put into a weighing bottle, then flattened. Then put in the oven, open the stopper and let the plug in the oven. Then the drying was carried out at 105°C for 2 hours. After that, the weighing bottle was cooled in a desiccator and weighed three times treatment until the constant weight (Depkes RI 2014).

Evaluation of tablet

The physical appearance of observing color, shape, and taste of tablet. Then, size tablet uniformity was performed by taking 10 tablets from each formula, then measured a vernier caliper and micrometer scrub (Depkes RI 1979). And the next evaluation was weight uniformity. This evaluation was done by weighed 20 tablets one by one. Calculated the average weight of the weight, the weight of each tablet compared with the average weight (Depkes RI 1979).

The next evaluation was the hardness of tablet test. This evaluation was done by placing a tablet in an upright position on the hardness tester tool. Readable tool scale that shows tablet hardness in kilograms (Siregar 2010). And the last is friability of tablet test. This evaluation was done by weighing 20 tablets that have been free from dust then put into the tool friability tester. The device is set at 25 rpm for 4 minutes or 100 revolutions, then it is free from dust, then weighed. Then calculate the percentage of weight loss (Siregar 2010).

Data Analysis

The results of evaluation of hardness and friability data of chewable tablets of guava leaves extract (*P. guajava* L.) with a binder from breadfruit starch were analyzed using one way ANOVA which then continued with Tukey test with 95% (α = 0,05) to know the significant difference between formulas.

RESULT AND DISCUSSION

Characteristic of Guava Leaves Extract

The results of the organoleptic test can be seen in **Table 2**. Guava leaves contain Guaijaverin which is the flavonoid compounds have bacteriostatic activity flavonoid as anti-dental caries (Prabu et al. 2006), this test is done to identify the flavonoid compound that contained in guava leaves extract. The result of identification of guava leaves extract is positive containing flavonoid and tannin compound. Test of the ash content is done to know the impurities in the extracted material. The ash content data shows the

Table 2. Evaluation result of Guava Leaves Ekstract (*Psidium guajava* L.)

No	Parameter	Result	Picture
1	Organoleptic	Colour: Dark brown Odor: The typical smell of guava leaf Taste: Bitter Shape: Gore extract	
2	Water content	15.19 %	
3	Ash Content	0.59 %	
4	Loss On Drying	2.49%	
5	Flavonoid Test	+	
6	Tanin Test	+	

Information :
+ (positive): Contains a class of compounds

internal and external mineral/organic content from the initial process until the formation of the extract (Depkes RI 2008). The results of the ash content test of 0.59% guava leaves extract stated that the mineral/organic element content in the extract was small, the requirement of the provision of the ash content of guava leaves was not less than 9.0% (Depkes RI 2008). The result of lost on drying of guava leaves extract was 2.49%, the requirement of lost on drying value on guava leaves was not less than 10% (Depkes RI 2008). The purpose of this drying rate is to provide the maximum (range) limit of the amount of the lost compound in the drying process.

Characteristics of Breadfruit Starch

Characteristics based on organoleptic performed include microscopic test, a test of odor and observation of color of breadfruit starch. In general, microscopic test aimed to look the typical anatomy of each plant that useful for the identification process. The results of the organoleptic test can be seen in **Table 3.**

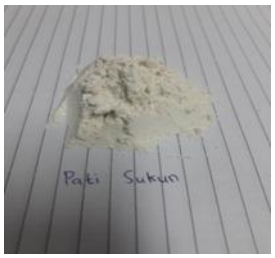
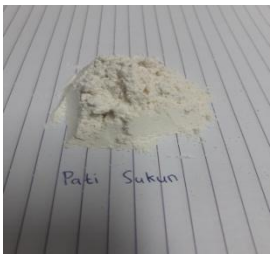
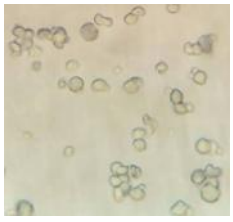
In the qualitative test of the identification of starch, the dispersed powder in water provides a purple color when it was dropped by the iodine reagent, indicating that the resulting powder positively contains starch. The result of an organoleptic test, it was found that breadfruit starch was odorless and white color and texture of breadfruit starch in the form of a fine powder which was rather rough when touched by hand.

Microscopic test on breadfruit starch was aimed to determine the shape of starch microscopically. If seen by using a microscope, the shape of breadfruit starch was round and irregular in a single circumstance or compound.

Formula Orientation Results

In this research chewable tablet from guava leaves extract was prepared using breadfruit starch as binder. Breadfruit starch predicted to provide higer durability to the tablet. In the manufacture of chewable tablets was increased at 10% mucilago breadfruit starch to get good physical properties of chewable tablets (Siregar, 2010). Based on the results of the orientation using the breadfruit starch mucilago 10% with concentrations of 2.5%, 5%, 7.5% and 10%. Only formula with 10% concentration that produces a hard tablet while other concentrations produce tablet that is fragile and easily

Table 3. Evaluation result of breadfruit starch

Evaluation	Result	Picture
Organoleptic		
Odor	Odorless	 
Taste	No taste	
Color	White	
Texture	Rude	
Content of water	0.91(%)	
Micsorcopic	Round and irregular in single or multiple circumstances	
Yield	12.966% b/b	
Iodine reaction	Purple color	

destroyed. So the results of the orientation of the used concentration of 10%, 13%, 16% and 19%, of which each formula was made as much as 700 g.The results of orientation can be seen in **Table 4.**

Result of Evaluation

Evaluation of chewable tablets was done to determine the physical properties of chewable tablets. Evaluation of chewable tablets performed was the granule evaluation of tablets and the evaluation of chewable tablets. Granule evaluation includes flow time test, the angle of repose test, compressibility test and particle size distribution. Evaluation of chewable tablets included organoleptic test, weight uniformity test, size uniformity test, friability test, and hardness test.

Granule evaluation

Granule evaluation was performed to determine the quality of tablet mass in each formula. Evaluation performed on granule include, flow time, the angle of repose and compressibility can be seen in **Table 5**.

The flow time test is one of the evaluations that performed on the granule of tablets. The flow time test is required to find out some length of granule can pass through the funnel granule flow tester. A granule is said to have a good flow time if it has a powder flow rate of ≤ 10 g / sec (Siregar 2010). The flow time test was performed with 100 gram of granule, so all the formulas met the requirements of a good flow time.

Granules exhibit good flow properties if it has an angle of repose value between 25^0 to 40^0 with some type of flow include an angle of repose < 25^0 type of flow was excellent, 25^0 - 30^0 good flow type, 30^0 - 40^0 flow type was good enough, and > 40^0 types of bad flow. The angle of repose is the free surface angle of the powder pile with the horizontal plane (Siregar 2010). The angle of repose was obtained from the measurement of the granules cone at the time of the test. From the table can be seen that the angle of repose of the formula 1 to 3 ranged from 25^0 - 30^0, it can be said that the granule has a good flow type, while the formula 4 has a good flow type.

Compressibility tests were used to predict powder flow characteristics by looking at the compressibility index results. Compressibility tests were performed to determine the ability of granule to fill the space between particles and under the most compressible conditions, without any particle shape change. The result of compressibility test shows the compressibility value of the formula 1 to 4 ranged between 4% - 8%. Compressibility index category of the five formulas that is good, because it is in the range 11-15% (Agoes 2012). The water content in granule in this research is relatively small that was less than 2.5% if granule a moisture content above 2,5% then it is feared there will be peeled at printing process. The test water content test aimed to determine the water content in granules, it was useful for the printing process because the moist granules caused part of the tablet glutine at the punch, resulting in a tablet with a not good physical shape.

The granule size distribution test aimed to determine the granule size distribution, the importance of this evaluation is due to variations in the small granule to large granule ratio, as well as the magnitude of granule size differences affecting how the space between particles is filled, the difference in the proportion of large and small particles can affect the weight of the

Table 4. Formula Orientation Result

No	Concentration of mucilage breadfruit starch	Result (kg/cm^2)	Conclusion
1	2.5 %	0.45	Tablets are very fragile and very easy to destroy
2	5 %	1.19	Tablets are fragile and very easy to break
3	7.5 %	3.23	Tablets are fragile and very easy to break
4	10 %	4.39	Tablets are relatively strong and not easy to broken

Table 5. Result of granule evaluation

Evaluasi	F1	F2	F3	F4	Standard
Flow rate (second)	5.6 ± 0.43	5.9 ± 0.26	7.45 ± 0.12	6.36 ± 0.15	10 second (Siregar 2010)
Angle of repose (0)	28.30 ± 0.65	29.96 ± 0.98	29.92 ± 1.23	34.34 ± 0.97	25-400 (Wells 1987)
Compresibility (%)	4.99 ± 0.02	8.00 ± 0.01	4.34 ± 0.58	4.33 ± 0.57	11-15% good (Agoes 2012)
Water content (%)	0.38 ± 0.031	0.07 ± 0.021	0.41 ± 0.184	1.70 ± 0.045	< 2.5% (Siregar 2010)

contents the die (Lachman *et al.* 1994). This may result in variation in weight, in this study the granule spread more widely in the sieve number 18, this was because the last sieve that used in the process of making the granule was the number 16 sieve, so in the sieve number 16 most of the granules can be passed and accumulated on the next sieve number 18. The result of the particle size distribution can be seen in **Figure 1**.

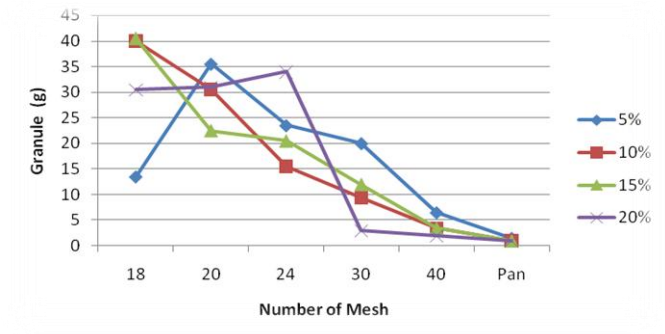


Figure 1. Granule Size Distribution

Tablet evaluation

Evaluation of tablets performed on chewable tablets of guava leaves extract that had been made include color, shape, taste, uniformity of size, weight uniformity, hardness and firmness of tablets, can be seen in **Table 6**.

The chewable tablet that resulted had a brownish white color, round shape and has a sweet taste. The tablet weight uniformity test was performed by testing the weights of 20 tablets. The result of tablet weight uniformity test from formula 1 to formula 4 showed that all tablets were qualify based on the requirement of weight uniformity because there were no 2 tablets that have a weight deviation above 5% from the weight of the average tablet and no one tablet had a deviation weight above 10 % Of the weight of the average (Depkes RI 1979).

The hardness of tablet is one of the parameters for chewable tablets. Tablet hardness test was performed using 20 samples of tablets. Tablet hardness test results can be concluded that only formula 1 that qualify based on the hardness of chewable tablet requirements that is, 4-7 kg (Mendez 1990). Formulas 2, 3 and 4 have the hardness above 8 kg. This showed that the concentration of breadfruit starch that used can affect the granule binding strength so that it can affect the hardness of chewable tablets.

Friability of the tablet is also one of the parameters of chewable tablets. Friability of the tablet was done to determine the ability of the tablet to withstand the effects of mechanical shock during the process of manufacturing, packing and transporting (Siregar 2010). Friability of tablet test was performed using 20 samples of tablets. The result has shown that the friability of tablet from formula 1, 2, 3 and 4 are qualify because the value of test result is below 4% (Mendez 1990). The higher breadfruit starch concentration used, the lower of friability value of chewable tablets. This shows that breadfruit starch affects the friability of chewable tablets.

The tablet size uniformity test is performed by measuring the diameter and thickness of the tablet. The results of the test indicated that all of the formulas were qualify based on tablet size uniformity requirements, 11 / 3x thick tablet ≤ tablet diameter ≤

Table 6. Result of evaluation tablet

Evaluasi	F1	F2	F3	F4	Standard Requirement
Color	Brownish white	Brownish white	Brownish white	Brownish white	-
Shape	Round	Round	Round	Round	-
Taste	Sweet	Sweet	Sweet	Sweet	-
Weight Uniformity (mg)	702.03±3.58	699.05±2.70	697.30±2.52	700.05±3.10	-
Hardness (kg/cm^2)	5.20±0.36	8.16±0.32	11.11±0.40	13.05±0.17	4-8 kg/cm2 (Mendez 1990)
Friability (%)	1.08±0.15	0.79±0.07	0.75±0.03	0.59±0.01	< 4% (Mendez 1990)
Thickness (mm)	4.63±0.02	4.33±0.02	4.53±0.02	4.32±0.04	11 / 3x thick tablet ≤ tablet diameter ≤ 3x thick tablet (Depkes RI 1979)
					-

3x thick tablet (Depkes RI 1979).

Then data analysis was done on the hardness of chewable tablets. The Statistical analysis used in this study were ANOVA and Tukey HSD (Honestly Significant Differences) tests, can be seen in **Table 7**. The result of normality test on hardness indicates significant value was 0.069 higher than 0.05. This indicated that data were distributed normally. Homogeneity test indicated that significant value was 0.061 higher than 0.05, it is shown that H_0 was accepted, and it means that the hardness had the same variant (homogeneous). The result of the variance analysis test of hardness has resulted in a significant value of 0.000 smaller than 0.05, it indicated that H_0 was rejected, meaning there was a significant difference between first up to the fourth formula. Then the Tukey HSD test followed and the results indicated that there were real differences between formula 1, formula 2, formula 3 and formula 4**.**

CONCLUSION

The powder that obtained was a breadfruit starch which can be used as a binder on the chewable tablet granule of guava leaves extract (*P. guajava* L) which met good granule requirements at 10% to 19% amylum concentration. In this study, it can be concluded that increasing the concentration of breadfruit starch to concentration of 19% could increase the hardness and reduce the friability of chewable tablets.

Table 7. ANOVA and Tukey HSD Test

ANOVA

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	709.158	3	236.386	2254.597	.000
Within Groups	7.968	76	.105		
Total	717.126	79			

Multiple Comparisons

Dependent Variable:Nilai

	(I) Kekerasan	(J) Kekerasan	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Tukey HSD	F1	F2	-2.96600*	.10239	.000	-3.2350	-2.6970
		F3	-5.91700*	.10239	.000	-6.1860	-5.6480
		F4	-7.85350*	.10239	.000	-8.1225	-7.5845
	F2	F1	2.96600*	.10239	.000	2.6970	3.2350
		F3	-2.95100*	.10239	.000	-3.2200	-2.6820
		F4	-4.88750*	.10239	.000	-5.1565	-4.6185
	F3	F1	5.91700*	.10239	.000	5.6480	6.1860
		F2	2.95100*	.10239	.000	2.6820	3.2200
		F4	-1.93650*	.10239	.000	-2.2055	-1.6675
	F4	F1	7.85350*	.10239	.000	7.5845	8.1225
		F2	4.88750*	.10239	.000	4.6185	5.1565
		F3	1.93650*	.10239	.000	1.6675	2.2055

*, The mean difference is significant at the 0.05 level,

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