THESIS UNNECESSARY

CHEWABLE TABLET FORMULATIONS SEED EXTRACT of AVOCADO (*Persea americana* Mill.) WITH THE VARIATION of MANNITOL FILLERS USING WET GRANULATION METHOD

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FORMULASI SEDIAAN TABLET KUNYAH EKSTRAK BIJI ALPUKAT (*Persea americana* Mill.) DENGAN VARIASI BAHAN PENGISI MANITOL MENGGUNAKAN METODE GRANULASI BASAH

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ABSTRAK

Biji buah alpukat (*Persea americana* Mill.) merupakan salah satu bagian dari tumbuhaan yang mempunyai manfaat sebagai pengobatan. Bijinya yang dianggap masyarakat sebagai limbah faktanya, dalam biji tersebut mempunyai senyawa metabolit sekunder yang termasuk dalam kelas alkaloid triterpenoid, tanin, flavonoid, dan saponin yang memiliki efek farmakologis (Marlinda *et al.,* 2012. Pengembangan zat aktif yang mengandung *zat bitter*, sehingga menutupi rasa pahit tersebut dan agar lebih tahan lama maka dibuat dalam bentuk sediaan formulasi tablet kunyah, sehingga dapat dikonsumsi dalam semua kalangan dan mempermudah sebagian orang yang sulit untuk menelan obat, tanpa harus membutuhkan air untuk menelannya. Tujuan dari penelitian ini untuk mengetahui pengaruh penggunaan manitol sebagai bahan pengisi terhadap karakteristik fisik tablet kunyah, serta mengetahui konsentrasi manitol yang baik untuk formulasi tablet kunyah ekstrak biji alpukat (*Persea americana* Mill.). penelitian ini merupakan penelitian eksperimental dengan menggunakan analisa data parametrik *oneway ANOVA*. Tablet kunyah yang diformulasikan sebagai berikut: ekstrak biji alpukat (15,6%), Aerosil (1%), Mucilago amilum 10% (8%), amilum (3%), Mg. Stearat (1%), Talk (8%), Asam sitrat (1%), dalam 3 variasi formula yaitu, F1 (Manitol 40%), F2 (Manitol 50%), dan F3 (Manitol 60%), dan laktosa sebagai *add* 100%. Pada formulasi ini dilakukan dengan metode granulasi basah. Hasil data evaluasi tablet telah menunjukan bahwasannya semua formula secara umum menghasilkan seluruh formula yang memenuhi persyaratan tablet yang baik. Pengaruh penggunaan manitol yang telah dianalisis statistik dalam formulasi tablet berpengaruh pada peningkatan kerapuhan dan keseragaman bobot tablet, serta cita rasa yang dihasilkan. Tetapi tidak berpengaruh terhadap keseragaman ukuran, kekerasan. Sedangkan formulasi tablet kunyah ekstrak biji alpukat yang mengandung konsentrasi manitol pada formula 1 sebesar 40 % merupakan formulasi yang paling baik dari hasil uji karakteristik fisik tablet. Sedangkan pada formulasi 3 dengan konsentrasi manitol 60% mendapatkan rasa yang paling disukai oleh responden. Konsentrasi variasi manitol yang digunakan belum dapat menghasilkan rasa tablet yang manis sesuai dengan ciri khas tablet kunyah pada umumnya yaitu, mempunyai rasa khas yang manis ketika dikunyah dan nyaman dikonsumsi sehingga tidak meninggalkan rasa pahit

Kata kunci: *Biji alpukat (Persea americana Mill.), Bahan pengisi Manitol, , Tablet kunyah.*

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ABSTRACT

Avocado seeds (*Persea americana* Mill.) Is one part of the plant that has benefits as a treatment. The seeds are considered by the community as a waste of fact, in these seeds have secondary metabolites which are included in the class of triterpenoidal alkaloids, tannins, flavonoids, and saponins as pharmacological effects (Marlinda et al., 2012). Development of active substances containing bitter substances, covering the bitter taste and to be more durable it is made in the form of chewable tablet formulations, it can be consumed in all circles and make it easier for some people who are difficult to swallow the drug. Filling material on the physical characteristics of chewable tablets as well knowing the good concentration of mannitol for the formulation of avocado seed extract chewable tablets (*Persea americana* Mill.).This study was an experimental study using parametric data analysis oneway ANOVA. Chewable tablets were formulated as avocado seed extract (15.6%), Aerosil (1%), Mucilago starch 10% (8%), starch (3%), Mg. Stearic (1%), Talk (8%), Citric acid (1%), in 3 variations of formula, F1 (Mannitol 40%), F2 (Mannitol 50%), and F3 (Mannitol 60%), and lactose as add 100%. In this formulation carried out by a wet granulation method. The results of tablet evaluation data have shown that all formulas generally produce all formulas that meet good tablet requirements. The effect of the use of mannitol which has been analyzed statistically in tablet formulations affects increasing the fragility and uniformity of tablet weight, as well as the waste produced. But it does not affect the uniformity of size, and violence. While the formulation of avocado seed extract chewable tablets containing 40% concentration of mannitol in the 1st formula was the best formulation from the test results of the physical characteristics of tablets. Where in 3rd formulation with a concentration of 60% mannitol gets the most preferred taste by respondents. The concentration of mannitol variation that has been used has not been able to produce a sweet taste of tablets by the characteristics of chewable tablets in general, which has a distinctive sweet taste when chewed and is comfortably consumed so as not to leave a bitter taste.

Keywords: *Avocado seeds (Persea americana Mill.), Chewable tablets, Mannitol fillers,*

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FOR UNDERGRADUATE THESIS EXAMINATION

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ORIGINAL STATEMENT SHEET

With this,

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CHAPTER I

PRELIMINARY

1.1. Background of Research

One of the names of plants that was widely spread in Indonesia is avocado, avocado plants that have great potential in the treatment because it has efficacy as a medicine. The plant is commonly utilized in traditional medicine communities. In this section of the plant is an exciting part is the seeds that are considered by the community as waste; it can treat the diseases. Allah SWT created the entire world has its own benefits, one of which is a plants which are a source of natural materials that can produce chemical components in it and according to 92% consumer survey of state that natural ingredients can be trusted as safe drugs and do not cause plant side effects which function as a treatment can also be called herbal medicine (Dubick, 1986).

The existence of plants is a blessing and favor of Allah SWT given to all of its creatures. As Allah SWT said:

فَأَنْۢبَتْنَا فِيْهَا حَبًّا ٧٢ وَعِنَبًا وَقَضْبًا ٨٢ وَزَيْتُوْنًا وَنَخْلً ٩٢ وَحَدَآئِقَ غُلْبًا ٠٣ وَفٰكِهَةً وَّاَبًّا ١٣ مَّتٰعًا لَّكُمْ وَلِاَنْعٰمِكُمْ ٢٣ (سورة عبس: ٧٢-٢٣)

Artinya: "And caused to grow within its grain. Vines, fresh vegetation, Olive trees, palm trees, and gardens of dense orchards, Fruits and fodder, as for you and your grazing livestock "(QS. 'Abasa (80): (27-32).

The verses of the Qur'an in Sura ' Abasa: (27-32) has been explained about the power of the Almighty Allah SWT created whole grains, vegetables, fruits, and grasses can become food for humans and livestock. Food items have unique benefits to the human body that can be researched in life (Imani, 2005).

Plants in the preparations of the drug that is generally in the form of extracts from natural materials, in general, have a low solubility in fat, then the necessary development to improving biovaibilitas is better than extract preparations ingredients worlds (Rajiv, 2013). Some events of studies showing that avocado seeds contain compounds are secondary metabolites that are included in a class of alkaloids, tannins, flavonoids, triterpenoid, saponins (Marlinda et al., 2012), which has the effect of pharmacological.

According to research Suhendra et al., (2016) seed extract of avocado (Persea americana Mill.) can lower total cholesterol levels in wistar rats which have induced propylthiouracil with a dose of 125 mg/kg BW and 250 mg/kg BW amounting to 18.1% and 31.2%, due to the presence of flavonoids content. Flavonoids prevent adhesions lipoprotein polyethylene.

Flavonoids have actions to reduce cholesterol levels in the body by inhibiting activity of the enzyme HMG-Co-A reductase as cholesterol biosynthesis (Sekhon et al., 2012), according to Elekofehinti et al., (2013) saponins have action by inhibiting fat peroxidation and increasing the concentration of antioxidant enzymes, while tannins are able to reduce the accumulation of cholesterol in the blood by accelerating the removal of cholesterol through feces (Rahayu, 2005).

Judging from previous studies that avocado seeds have significant benefits, the development of these active substances requires dosage forms are durable, easy to consume, and easy to store. Some of the development of avocado seed extract has been made in other dosage forms as in the research of Hidayah (2018) avocado of seed extract has been made in conventional tablet dosage forms with the effect of Na-CMC binder concentration and 1500 Starch Crushing material with Factorial Design method, besides Microgranul Mucoadhesive Avocado Seed Extract with Differences in Carbopol Concentration (Aditya, 2016), and effervescent granules a combination of avocado seed extract and rosella flower petals (Mas'adah, 2015).

So for the development of avocado seed extract innovations in this study chewable tablet dosage forms were shown to cover the bitter taste caused by avocado seed content on (Zuhrotun, 2007). Because the purpose of chewing tablets is to provide residues with good taste in the oral cavity so that they are easily swallowed and do not leave a bitter or unpleasant taste (Agoes, 2008), in addition, the dosage form of chewable tablets is very appropriate to be used to make it easier for children or parents who are difficult to swallow whole drugs. Extracts formulated into chewable tablets are more easily released as active ingredients in body tissues and absorbed by the body.

The advantage of chewing tablets when compared with other oral substantial dosages is it can improve patient comfort by eliminating the need for drinking water to swallow drugs, besides that it can be used as a substitute for liquid dosage forms if fast drug work (onset) is needed, increasing patient acceptance due to taste which is fun and has a unique product from a marketing standpoint (Siregar, 2010).

In this formulation, it is varying the filler to get the concentration of the material which can cover the bitter taste of the active substance. The cartridges used are mannitol, mannitol is a substance that is not hygroscopic and can be combined with active ingredients that are sensitive to moisture, the concentration used ranges from 10% -90% (Rowe, 2006).

The mannitol taste is about 70% of the sugar with a cooling taste in the mouth, has sufficient solubility in water and is usually used as a filler in chewable tablets so that the manufacture of mannitol granulation has the advantage that granules will dry more quickly. Because chewable tablets have a distinctive taste that makes them comfortable for consumption, thus producing a feeling that consumers like (Ansel, 1989).

The use of wet granulation method in this formulation is one method that can be used to make chewable tablets, and with this method can increase compressibility, obtain better flow, and can increase the uniform distribution of the womb. The purpose of this formulation study was to determine the

effect of the physical properties of avocado seed extract (*Persea americana* Mill.) by varying the concentration of mannitol fillers, to obtain the physical properties of standard.

1.2. Problem Formulation

The problems in this research are:

1. Are avocado seed extracts (*Persea americana* Mill.) With variations in the concentration of mannitol, fillers can be formulated into chewable tablet preparations?
2. How does the comparison of variations in mannitol filler material on the physical properties of avocado seed extract chewable tablets (*Persea americana* Mill.)?

1.3. Research Objectives

The purpose of this research is:

1. Making avocado seed extract (*Persea americana* Mill) chewable tablet formulations with variations concentration of mannitol fillers material.
2. Find out the influence of mannitol fillers to the physical properties of avocado seed extract tablets (*Persea americana* Mill.)

1.4. Benefits of Research

1.4.1. Theoretical Benefits

Add to the treasure of knowledge about natural herbal medicine, and avocado seeds are one of Allah SWT creation that should be examined because it has the benefits of secondary metabolites contained in the content of avocado seeds. The avocado seed extract (*Persea americana* Mill) chewable dosage form is made, which produces the best physical properties that can make it easier for sufferers who have difficulty swallowing tablets.

1.4.2. The Practical Benefits

Practically, the results of this research are expected to be input to research further in researching avocado seeds (*Persea americana* Mill.), So they can produce various avocado seed products.

CHAPTER II

LITERATURE REVIEW

2.1. Previous Research

On the research of Zuhrotun (2007) with the title "The Activity of Ethanol Extract of Avocado Fruit Seeds (*Persea americana* Mill.) The Shape of The Round" antidiabetic testing ethanol extract of avocado seeds (*Persea americana* Mill) round shape with each dose used was 0.245 g / kg BW: 0.0490 g/kg BW and 0.980 g / kg BW administered orally to white male rats using the glucose tolerance test method. On giving the variation in this dose on the ethanol extract of rounded avocado seeds showed that at a dose of 0.980 g / kg BW the most substantial decrease in blood glucose levels (40.00%), followed by a dose of 0.490 g / kg BW (26.82%) and 0.245 g / kg BW (22.82%) at the 0.05 level. The results of this study showed that an increased dose with ethanol extract of avocado seeds could increase antidiabetic activity.

In research conducted by (Aprilya et al., 2011) on "The Effect of Mannitol as a Filler Divested on Physical Properties of Antacid Tablets" this research aimed to determine how the effect of mannitol as a filler on the physical properties of antacid tablets was made using wet granulation method. Tablets were made with three formula of mannitol concentration such us, Formula I (11.70%), F II (8.12%), and F III (4.23%). The Data was analyzed by one-way ANOVA statistical method. The results indicate it shows that the greater mannitol, the longer flow of granule, the tablet gets louder, the tablet's disintegration time is longer, the friability becomes smaller, the uniformity of tablet weight meets the requirements according to Pharmacopoeia Indonesian Edition V.

Research conducted by (Widyanari, 2017) on "Chewable Tablet Formulation of Red Dragon Fruit Meat Powder (*Hylocereuspolyrhizus*) with Mannitol Fillers Concentration Variations" This research aimed to

determine the effect of using mannitol as a filler on physical quality and flavor chewable tablets in response. And the best results from the test of physical properties and taste response to the variation of mannitol to 3 formulations were the formulations using the largest mannitol at (F3: 50%)

On the research that has been researched by (Jannah *et al*., 2017) on "Effects of Avocado Seed Extract (*Persea americana* Mill) as Blood Antihiperkolesterol in Mice (*Mus musculus*)," this research aims to identify the content of avocado seeds as antihypercholesterol in the blood of mice. Phytochemical substances found in avocado seed extract (*Persea americana* Mill) which can reduce the blood hypercholesterolemia of mice (Mus musculus) optimally is 10%.

On the research of Sunusmo (2018) on "Anticholesterol Effectiveness Test of Avocado Seed Extract in Wistar Male Rats In Vivo and Phytochemical Screening" this study used 12 Wistar strain male rats which were divided into 3 different doses to measure the decrease in cholesterol and triglyceride levels with avocado seed extract for 14 days so that the most effective treatment obtained was 250 mg / kgBW can reduce cholesterol levels as much as 88.2 mg / dL.

On the research of Hidayah (2018) on "The Effect of Na-CMC and Starch Crusher 1500 Concentration Concentration on Tablets of Avocado Seed Extract (Persea americana Mill.) With Factorial Design". In tablet formulas which were optimized with the factorial design method using the Design Expert 11 program (trial). The optimum formula will be analyzed using SPSS one simple & test with a confidence level of 95%. And the results of this research show that the combination of Na-CMC and Starch 1500 can increase flow speed and reduce stationary angles, tapping, CV weight uniformity, hardness and disintegration time. 17.5 mg of Na-CMC and 37.5 mg of Starch 1500 produced the optimum formula.

2.2. Theoretical Basis

2.2.1. Avocado Plant

Avocados (*Persea americana* Mill.) is originated from Central America. This plant entered Indonesia around the 18th century. An avocado grows wild in the forests and is planted in gardens and yards where the soil is loose and fertile nothing waterlogging. This plant can grow in the tropics and subtropics with rainfall between 1,800 mm to 4,500 mm each year. In general, this plant is suitable for a cold and wet climate. This plant is not resistant to low or high temperatures. In Indonesia, these plants will grow at an altitude between 1 m to 1000 m above sea level (Nurrasid, 1998).

Avocado trees are 3 m to 10 m high, have rooted roots, woody stems, round, brown in color, and have many branches. The single leaf which is located crammed at the end of the branch, its shape is elongated, the tip and base are pointed. Flat edges sometimes roll up. Fruit flesh if it's soft, it's green and yellowish (Monica, 2006).

Avocado flowers are located near the tip of branches, the flowers 1-1.5 cm in diameter, yellowish, downy and stamens in 4 pieces, fruit of the avocado-shaped bulb to ovoid, yellowish green with purple spots, double / smooth, and fragrant, spherical seeds and only one seed in 1 piece (Materia Medika Indonesia, 1989; Hika Citra, 2009). Images of avocados can be seen in figure 2.

Figure 2.1. The seed of avocado *(Persea americana* **Mill.)**

There is *Scientific Classification* of plant avocado *(Persea americana* Mill*.):*

Kingdom	: Plantae (Plants)
Subkingdom	: Tracheobionta (Vascular plants)
Superdivision	: Spermatophyta (Produce seeds)
Division	: Magnoliophyta (Flowering plants)
Class	: Magnoliopsida (Blown two)
Subclass	: Magnoliidae
Ordo	: Laurales
Family	: Lauraceae
Genus	: Persea
Species	: *Persea americana* Mill
Sinonim	: *P.gratissima* Gaertn

Avocados have two pieces of seeds, and they are included in the Dicotyledoneae class. Avocado seeds are round or oval, while seed pieces of white beans. The substrate is easily seen when the seed skin is removed or skinned. When the fruit is young, the seed coat sticks to the fruit. When the fruit is old, the seeds will release themselves. Generally, this trait is used as a sign of fruit maturity. Long-shaped fruit has longer seeds than the seeds contained in round fruit. All avocado seeds have similarities; the lower part is rather flat and then rounded or soaring (Indriani & Suminarsih, 1997).

Phytochemical screening of avocado seed extract shows that avocado seeds contain polyphenols, flavonoids, triterpenoids, quinones, saponins, tannins and monoterpenoids and sesquiterpenoids which can inhibit bacterial growth so avocado seed extract (Persea americana Mill.) Is indicated to have antibacterial power. Avocado seeds have bitter alkaloids, so they taste very bitter (Zuhrotun, 2007). Avocado seeds also contain such as 59.87% starch, 12.67% ash and 0.54% minerals and contain a mixture of polyphenolic components such as catechins and epilation (Atsuhendra, 2007).

The most widely utilized part of the avocado plant is the fruit as fresh fruit. In the world of medicine, avocados have been widely used as a traditional medicine to treat a variety of diseases. Fruit flesh can reduce pain and treat cancer sores, while the leaves of avocados can be used to treat nerve pain, gastric pain, reduce high blood pressure and treat kidney stones, besides fruit and leaves, avocado seeds also have properties that can be used to reduce sugar levels in the blood (Nurrasid, 1998).

In the research conducted by (Anggraeni, 2006) avocado seeds contained 13.6% tannins, 13.25% starch. Tanin is called by collagen, which can precipitate or multiply the mucous membrane protein on the surface of the small intestine and form a layer that protects the pipe, thus inhibiting glucose absorption and the rate of increase in glucose and the rate of growth in blood glucose is not high while phytochemical screening of simplicia and ethanol extract of round shape avocado seeds contain polyphenol compounds, namely, flavonoids, tannins, alkaloids whereas saponin compounds are only detected in extracts (Zuhrotun, 2007).

1. Flavonoid

   According to Marais et al., (2006), the flavonoid is used to describe the products produced by plants which are included in compounds with the chemical formula C6-C3-C6. Flavonoid compounds have glycoside bonds that can be integrated by enzyme activity obtained from plant material in both fresh and dry forms. Flavonoid extraction requires solvents that are by their polarity. Some flavonoids are less polar such as isoflavones, flavanones, methylated flavones, and flavonols which can be extracted with chloroform, dichloromethane, diethyl ether, or ethyl acetate solvents, but more polar flavonoids and aglycones can be obtained using alcohol solvents of alcohol or alcohol-water mixture (Marston and Hostettmann, 2006).

   Flavonoids are phenolic compounds that can change when essential compounds or ammonia are added. Flavonoids are compounds that are soluble in water and can be extracted using 70% ethanol

(Harbone, 1987). According to Sabir (2005), flavonoids can cause damage to bacterial cell wall permeability.

2. Tanin

Tanin is a complex of many compounds found in plants, a mixture of polyphenols which is difficult to separate because it is not in the form of crystals. Tanin is separated from proteins and cytoplasmic enzymes, but if plant tissue is damaged, then tanning reactions can occur. This reaction causes the protein to be difficult to achieve by the digestive juices of plant-eating animals. One of the main functions of tannins is as a repellent of plant-eating animals because it feels osphronemids (Harborne, 1987). The content of tannins in avocado seeds varies depending on the type. Total tannin for dried avocado seeds, dry butter avocado seeds, fresh avocado seeds and avocado seeds for sweet butter respectively 117 mg/kg, 112 mg/kg, 41.335 mg /kg, and 41 mg/kg (Malangngi et al ., 2012). mg/kg (Malangngi *et al*., 2012).

3. Alkaloid

The alkaloid is a secondary metabolite that is spread on plants. Alkaloids function as addition compounds to herbivores or predators. Some of the alkaloids can be antibacterial, antifungal, and antiviral, which can be toxic to animals. The largest group of alkaloids are secondary metabolites containing nitrogen (Wink, 2008). Alkaloids are a group of secondary substances or the largest secondary metabolites of plants. In general, alkaloid is a chemical compound, with an alkaloid structure containing one or more nitrogen atoms, which are usually combined as part of a cyclic system. Alkaloid usually has no color, often is optically active, most crystals are formed, and only a small amount of liquid is a sample of nicotine at room temperature Harborne (1987).

Alkaloids are toxic to humans, but alkaloid compounds can be used widely in the field of medicine. Some studies use alkaloid isolated

from plants as medicine. Alkaloids have effects in the health sector in triggering the central nervous system, increasing blood pressure, reducing pain, antimicrobials, sedatives, and heart disease drugs (Simbala, 2009).

4. Saponin

Saponins are sterol glycosidestriterpene and have been detected in more than 90 genera in plants. Glycosides are a complex between production sugar (glycone) and instead of sugar (aglycone). Many saponins have a unit of sugar up to 5, and a common component is a glucuronic acid. Saponins are indicated by foam formation when extracting plants or concentrating extracts (Harborne, 1987). Some saponins work as antibacterials and used as raw materials for the synthesis of steroid hormones used in the health field (Robinson, 1995).

2.2.2. Extract

The extract is thick preparations obtained by extracting the active compound from animal vegetable simplicia using the appropriate solvents, almost all of the solvents are evaporated, and the remaining mass or powder is treated in such a way as to meet the prescribed standards (Depkes RI, 1995). Extracts are grouped according to their properties, such as:

a. Dilute extract is a preparation that has a concentration of honey and can be poured.
b. The concentrated extract is a preparation that is cold and cannot be poured. The water content is up to 30%
c. Dry extract is a preparation that has a dry concentration and is easy to pour, preferably having a moisture content of no more than 5%
d. Liquid extract, extract made in such a way that 1 part of simplicia is equivalent to 2 parts liquid extract (Voight, 1995).

Extraction methods are chosen based on several factors such as the nature of the raw material of the drug and the power to adjust each

type of extraction method and interest in obtaining the perfect extract from the drug (Ansel, 1989). The extraction methods commonly used include maceration, percolation, and soxlhetation:

1. Maceration

The maceration has come from the Latin macerare means soaking, which is the most appropriate process where the refined medicine allows it to be soaked with solvents until it seeps in and softens the cell arrangement, substance which are soluble will dissolves. Double maceration is carried out by the simplicity twice macerated with the same solvent, meaning first with half the part, then with the remainder. The simplicia material is extracted with a small amount of solution (20%) and finally with the entire amount of the rest (Voigt, 1984).

2. Percolation

Percolation is the process of a drug that has been finely extracted in a suitable solvent by slowly passing through the medicine in a column. Medications used in individual extraction devices are called percolators. In the process of percolation, the flow of mainstream through the general column of medicine from top to bottom towards for exit is drawn by the gravity as heavy and the liquid in the column (Ansel, 1989). Before filling the percolator, the advance powder is moistened with mainstream and allowed to expand, to facilitate the entry of extraction material into the cell collection during percolation (Voight, 1994).

3. Soxhletation

Soxhletation is carried out by entering the material to be extracted into an extraction bag (paper board) in an extraction device from a glass is between a distilled flask or a water cooler and connected via a pipette. The pumpkin contains volatile solvent, and when it is heated it evaporates to reach the coolant through the pipette, this solvent condenses in it and drips into the powder being screened. The solution

is gathered in a glass container, and after reaching the maximum height, it is automatically pulled in the pumpkin so that the substance is buried in the pumpkin (Voight, 1994).

2.2.3. Chewable Tablet

Chewable tablets are special tablets that are chewed to pieces and swallowed. These preparations have a pleasant aromatic flavor, do not contain crushers and are preferred by patients who have difficulty swallowing drugs (Voight, 1984). Chewable tablets are designed with lower hardness than conventional tablets to ensure ease in chewing tablets (Agoes, 2008).

The purpose of the chewable tablets is to provide a form of treatment that can be easily given to children or parents who may find it difficult to swallow medicine (Banker & Anderson, 1986). Characteristics of chewable tablets, when chewed, will form a smooth mass, have a good taste and do not leave a bitter or unpleasant taste. Chewable tablets are made by pressing, generally using mannitol, sorbitol or sucrose as binders and fillers, containing coloring agents and scented ingredients to improve appearance and taste (Ansel et al., 1995).

According to Agoes (2008) excipients commonly used for tablet, formulations are also used for chewable tablets because they can produce the chewable tablet properties needed in terms of sweetness and chewability. Additional ingredients used in making chewable tablets include:

1. Filler Material (diluent)

Fillers (diluents) is required if the drug dosage is not enough to build bulk and to improve the cohesion power that can be pressed directly or to trigger flow. Also, fillers were added to the formulation to form the desired size of the tablet (Ansel et al., 1995).

According to Banker and Anderson (1986) filler material must meet the requirements, namely: not toxic, available in sufficient quantities, the price is quite cheap, not contraindicated with other components, must be physiologically inert, stable in physical and chemical, both in combination with color, may not interfere with the bioavailability of the drug. The fillers commonly used include sucrose, lactose, calcium carbonate, dextrose, mannitol sorbitol and other suitable ingredients (Banker and Anderson, 1986).

2. Binder

Materials Binder is required in the manufacture of tablets with the intent to improve the kohesifitas between the particles of the powder thus providing compactness and durability of tablets (Voight, 1984). Use of excessive binding will make too wet granule mass and granule too hard, but if too little will make the masses too wet granule and granule too hard but if too little will make the adhesive strength of the weak, so the granule becomes soggy, and tablets become brittle (Aulton, 2003). Commonly used Binder materials is mucilage amyli 5 – 10% gelatin solution, 2-10%, 5-20%, pyrrolidone polyvinyl metal cellulose (solution) 2 – 10%, ethyl cellulose (solution) 5 – 105, poliakrilamid 2 – 8% (Sheth et al., 1980).cellulose (solution) 5 – 105, poliakrilamid 2 – 8% (Sheth *et al*, 1980).

3. Lubricant

Lubricant functions as a flow regulator, and the separator of the printed material. Some lubricants are hydrophobic, so they tend to reduce the speed of disintegration and dissolution of tablets. Therefore excessive levels of lubricants should be avoided. Ring materials commonly used include talc, magnesium stearate, aluminum stearic, stearic acid, palmitic acid, and starch (Voight, 1994).

2.2.4. The Method of Manufacture of Tablets

In the manufacture of tablets, there are three methods, the method of wet granulation, dry granulation method and continuous

direct on:

1. Wet granulation method

Wet granulation or powder agglomeration is carried out by stirring/agitating the powder or mixture powder in the presence of a liquid which is usually in the form of a binding solution that has been mixed with dry powder. The formation of granules takes place because of the effect of the bonding of liquid-cars that are formed between primary particles. The process includes the following stages: a) Deagglomeration of the starting material by grinding or sifting, b) Mixing dry starting material, c) Addition of liquid and formation of wet/moist periods, d) Sieving wet period to remove large chunks, e) Drying f) Dry granulation/sieving to achieve the appropriate granule size (Agoes, 2008).

2. Dray granulation method

On dry granulation method, it is formed by moisture or the addition of a binder to the medicinal powder mixture but by compressing a large amount of mass from the powder mixture and then breaking it down and making fragments into smaller granules. This method is primarily for materials that cannot be treated with wet granulation methods because their sensitivity to water vapor or due to drying requires a significant temperature (Ansel, 1989).

3. Press directly

This method is used for materials that have available flowing properties as well as cohesive properties that allow it to be directly compressed in tablets without the need for wet or dry granulation (Ansel, 2005). The advantage of this method is that medicinal materials that are sensitive to moisture and heat, whose stability is disrupted due to granule operations can be made into tablets. But with the increasing demand for tablet quality, this method is not preferred (Voight, 1994).

2.2.5. Problem With Tablet Printing (Aulton, 2008)

In the tablet printing process several problems are often found, namely:

a. Capping, which is the separation of part or all of the tablet's upper or lower surface.
b. Laminating, separating the tablet into two or more layers
c. Picking or sticking, namely the mass of the printed tablet attached to the stamp or punch so that the resulting tablet exfoliates the surface
d. The binding that is the mass of the tablet imprinted attached to the matrix wall (die) is marked by a parallel stroke on the side of the tablet.
e. Mottling, which occurs uneven color spots on the surface of the tablet.
f. Whiskering, which is a thin mustache on the top and bottom of the tablet produced.

2.2.6. Evaluation of Granul Properties

1. Flow time

Flow time is the time needed for powder or granule to flow through the funnel. Flow properties are influenced by particle shape and particle size through lubricating agents which reduce friction (Banker and Anderson, 1986). A reasonable granule flow rate is not less than ten each second for 100 grams of granules (Depkes RI, 2014).

2. Quiet Corner

Determination of the stationary corner is the maximum quiet corner found on the surface of the assault and horizontal plane, which indicates the friction force between the particles of powder. If the powder flows freely from a cone-shaped funnel. Measurement of the stationary Quiet corner by measuring the height and diameter of the cone produced. The smaller the quiet corner, the better the flow properties of the powder and vice versa. The stationary edge is influenced by the

shape and size of the particles, and the cohesiveness of the dust, where the higher the cohesiveness the particles become more easily attached (Aulton, 1988).

Table 2.1. Requirements for Inter-Corner Quiet

Relationships	Quiet Corner (o)
Special	25 -30
Good	31 – 35
Good Enough	36 – 40
Rather Good	41 – 45
Bad	46 – 55
Very Bad	56 – 65
Very-very Bad	>66

(United States Pharmacopoeia:32th, 2009)

3. Tapping

Tapping shows a decrease in the volume of several granules or powders due to tapped and vibrating. The smaller the index of determination, lowers the flow characteristics. Granules with a tapping index of less than 20% showed excellent flow properties (Depkes RI, 1995).

4. Moisture Content Test

Evaluate the water content used to prevent moisture from powders can accelerate microbial and fungal growth. Water content is measured using a tool called by moisture balance. With the condition are standard water content in dry granules is <3% (Depkes RI, 1995).

2.2.7. Evaluation Physical of Tablets

1. Uniformity of Weight

Uniformity of weight has been determined by weighing 20 tablets and calculated the average weight. The considered is calculated one by one, no more than two tablets may deviate from the average

weight, and more than the price set in column A and there must not be a single tablet whose pressure varies from the average weight set from columns A and B. Repeated with 10 tablets and no one should have the average weight set in columns A and B (Depkes RI, 2014).

2. Uniformity of Size

Uniformity of tablet size aims to determine the uniformity of both the diameter and thickness of the tablet that is not uniform, it will affect the number of doses active substances on tablets, and it's a volume that is inconsistent, making it difficult in the packaging process. Good requirements for uniformity are tablet diameter not more than three times and not less than $1^{1/3}$ times the thickness of tablets (Depkes RI, 2014)

3. Violence

Hardness is a limitation used to describe the resilience of tablets to resist mechanical stresses such as shocks, erosion, and tablet cracks during the packaging, transporting and distribution to consumers. Generally, the strength scale of tablets ranges from 4-8 kg (Depkes RI, 2014).

4. Fragility

Fragility is the mass of all particles released from the tablet (Voigt, 1994). This test is carried out to determine the fragility of tablets because tablets that are fragile and damaged contain substances with reduced efficacy which affect the therapeutic effect. This test uses a device called a rotating friabilator tester, and the tablet rolls down. Screening is done 100 times with the requirements of tablets that cannot lose more than 1% (United State Pharmacopeia 30^{th}, 2007)

5. Favorite Analysis Test

The preference analysis test was carried out by accidental sampling technique, with a heterogeneous population of 20 respondents. Each respondent had the same opportunity to experience samples from several chewable tablet formulations (Nugroho, 1995).

2.2.8. Material Description

1. Mannitol

Mannitol contains no less than 96.0% and no more than 101.5% C6H14O6 is calculated against the dried substance. Description of crystal powder or free-flowing granule, white, odorless, sweet taste. Mannitol sweetness is about 70% of the generosity of sugar with cold taste in the mouth, has sufficient solubility in water, dissolves in alkaline solution, dissolves in pyridine, is very difficult to dissolve in ethanol. Practically insoluble in ether, storage containers in well-closed containers (Depkes RI, 2014).

2. Magnesium stearate

Magnesium stearate is a mixture of magnesium with solid organic acids containing magnesium stearate and magnesium palmitate (C32H6Mgo4). Magnesium stearate is used as a lubricant in capsules and tablets with a concentration of 0.25-5.0% w / w. Description: fine powder, slippery, white, and easily attached to the skin, a distinctive weak odor. Solid solubility is insoluble in water, ethanol (95%) and in ether difficult to dissolve in benzene and ethanol (95%) (Allen & Luner, 2006).

3. Talcum

Talc is natural hydrate magnesium silicate, in the form of excellent crystal powder, white or gray-white, shiny, easily attached to the skin and free from granules. Not soluble in almost all solvents. Talk has three advantages including being able to function as a flow regulating materials, lubricating materials and mold separators (Voight, 1984). Talc is used as glidant and lubricant at concentrations of 1.0-10% (Kibbe, 2006).

4. Aerosil

High dispersed silicium dioxide (Aerosil) has an upper specific surface and has proven its advantages as a flow regulator. Aerosil reduces the stickiness of the particles with each other, and less friction

between particles. Aerosil binds moist through silanol groups (can draw water 40% of its time) although as powder still maintains its flowing power (Voight, 1994).

5. Amylum Manihot

Manhinot starch (cassava starch) is the starch found in the root tuber manhinot utilizes Pohl which is in the form of fine powder and white, containing amylose and amylopectin which is very efficient as a helper for tablet preparations. Amylum as a suitable binder and glidan is used at concentrations of 2-5% (Sheth et al., 1980).

6. Citric Acid

Citric acid has a form such as anhydrous or monohydrate in the form of clear crystal, colorless, white, odorless, highly acidic, very soluble in water, easily soluble in ethanol, rather difficult to dissolve in ether and hygroscopic. Citric acid has monohydrate crystals which will be lost when heated at a temperature of 40-500^{o}C (Depkes RI, 1995).

7. Lactose

Lactose is a sugar obtained from milk. Has a crystal mass, hard, creamy white, does not smell and tastes a little sweet. Stable in the water, but easily absorbs. Smooth (and slow) dissolves in water and is easier to dissolve in boiling water, very difficult to dissolve in ethanol and insoluble in chloroform and ether (Depkes RI, 1995).

In the wet granulation process, the lactose used is lactose hydrate because anhydrous lactose can absorb moist so that it increases the moisture. Formulas that use lactose excipients can show the rate of release of active substances, the granules dry quickly and are not sensitive to variations in temperature changes that will affect tablet hardness. Lactose is used as a filler (Banker and Anderson, 1986).

2.2.9. Halal Product Analysis

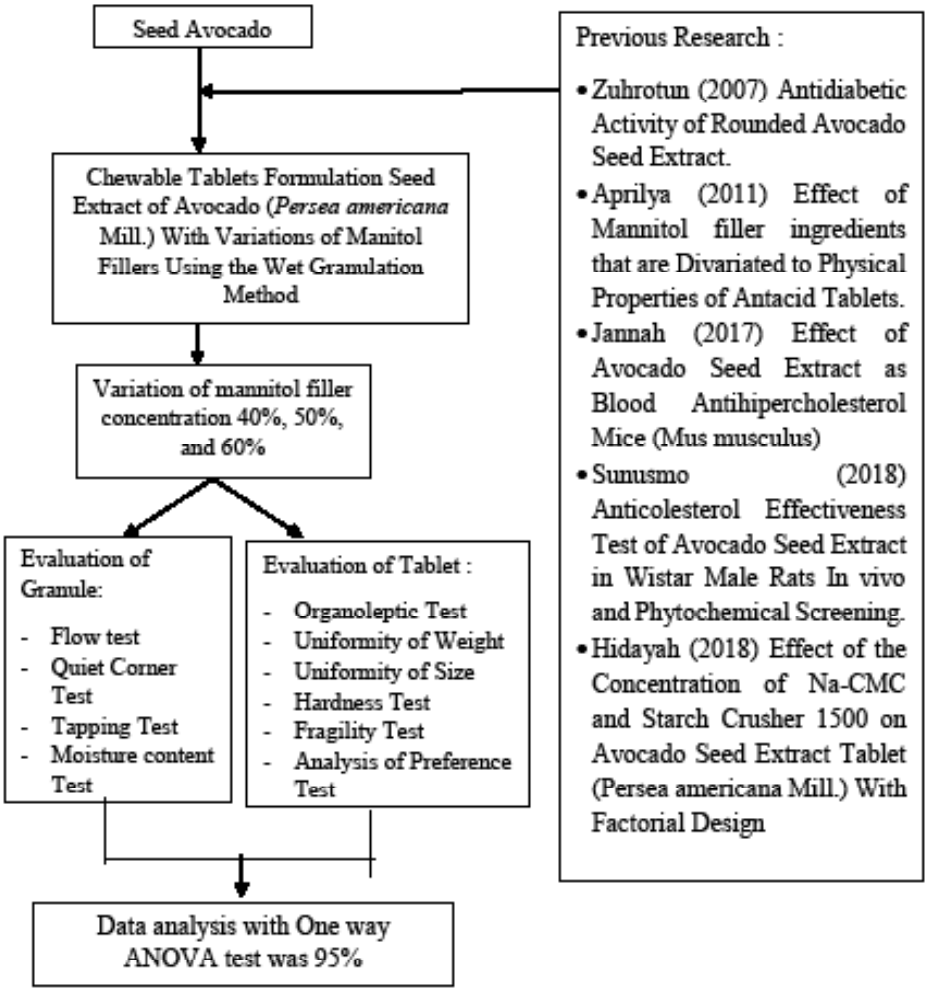
According to LPPOM MUI (2002), halal products are products that meet halal requirements, in terms of production (slaughter,

transportation, storage, processing, and presentation) and materials used (raw materials and additional materials). Based on the Qur'an and Sunnah guidelines, it is easy to determine the halal nature of a drug. Medicines must at least choose three related aspects, such as:

1. Not made from unclean ingredients (for internal medicine)
2. Not made of contaminated parts (medicine and deep)
3. Not contaminated by contaminated materials (in the process of production, storage, and distribution).

All legal halal plants for consumption, except plants that have adverse side effects, such as poison. Herbal medicines including extracts, essential oils, infusions, or plant solutions can be said to be halal (Taylor, 2001). Extraction using solvents, that is, alcohol as one of the ingredients that cause the *khamar* to have a specific determination in its use. The Indonesian Ulema Council allows the use of ethanol as a solvent if the final product is not contained in alcoholic residues. Alcohol used cannot be a product of the liquor industry (AIFDC ICU 2008; AIFDC ICU 2009).

2.3. Conceptual Framework



CHAPTER III

RESEARCH METHODS

3.1. Time and Places of Research

Manufacture of avocado seeds extracts and granulations was carried out in the Chemical Laboratory the Faculty of Pharmacy FIK University of Darussalam Gontor and the manufacture of tablets along with the evaluation of avocado seed extract chewable tablets was conducted at the Pharmacy Laboratory of University Muhammadiyah Surakarta. The study was conducted from September to March 2018.

3.2. Instruments and Material

The Instruments used include: analytic balance, oven, 30 mesh sieve, 16 mesh sieve, 14 mesh sieve, grinder, and other glass tools, single punch tablet machines, granule testing using funnel bunchers, digital analytic balance, term analog thrust, digital hardness tester, friability tester, volumenometer, rotary evaporator, water bath, moisture analyze.

The ingredients used were avocado seeds obtained from UPT Materia Medica Batu, mannitol, lactose, aerosol, 10% amyl mucilago, starch, magnesium stearate, talcum, citric acid, aquadest, ethanol 96%.

3.3. Research Design

The research belongs to the category of experimental research. The design of avocado seed extract chewable formulations was taken from Widyanari (2017) study which will be made with 3 variations of mannitol concentration as fillers using a concentration ratio in F1 (40%), F2 (50%), F3 (60%).

The independent variables used were variations in the concentration of mannitol, and the dependent variable was to determine the effect on the physical properties of granules which included organoleptic test, flow time test, tapping test, stationary angle, and water content test. As well as the

physical properties of tablets which included uniformity of weight, tablet hardness, tablet fragility, and preferred analysis test. The formula used is as follows (Widyanari, 2017):

Table 3.1. Formulation of Chewable Tablets of Avocado (*Persea americana* Mill.)

Ingredients	Type	Content of Tablet (%)		
		FI	**F II**	**F III**
Active substance	Extract seed of Avocado	15,6	15,6	15,6
Adsorbent	Aerosil	1	1	1
Binder	Mucilago amili 10%	8	8	8
	Starch	3	3	3
Lubricant	Mg Stearate	1	1	1
	Talcum	8	8	8
flavor	Citric Acid	1	1	1
Fillers	Mannitol	40	50	60
Fillers	Lactose	Add 100%	Add 100%	Add 100%

Description: F1: Concentration of filler mannitol = 40%, F2: Concentration of filler material mannitol = 50%, F3: Concentration of filler material mannitol = 60%.

3.4. Research Procedure

3.4.1. Determination of Plant

Determination of avocado seeds (*Persea americana* Mill) is carried out at the Materia Medika Batu Malang. The determination was carried out to determine the truth of characteristics in avocado seeds (*Persea americana* Mill).

3.4.2. Manufacture Extract of Avocado Seed

Avocado seeds were macerated with 96% ethanol by participating (1: 7.5)L in a 5-day maceration with frequent stirring (Depkes RI, 1979).

Maserates formed are filtered with a buncher funnel and evaporated with vacuum rotary evaporator. Then the liquid extract is placed on the water bath at 60^{o}C to be evaporated to concentrated extract is formed.

3.4.3. Manufacture of Dry Avocado Seed Extract

The first step is to make mucilago amyli, by adding 10 grams of cassava starch to 10 ml water, stirring to it forms a translucent gel and then boiling water to 100 ml, then cooling. Furthermore, weighing amyli mucilago as used in the formula. The active substance is added with aerosil which functions as an adsorbent which can reduce the stickiness of the particles with each other and attract moisture up to 40% of its mass. If the lubricant material is not used in the manufacture of granules, the possibility of the granule will not flow freely and the stationary Quiet corner formed will be higher than 30^{o} which will produce a granule that will be difficult to flow (Depkes RI, 1979).

After obtaining the dry extract, mixed with fillers, a mixture of flavoring and coloring ingredients, and dry binder, added little by little amyl mucilago as a binder to form a mass that can be fisted. The sieve mass was sieved no.14 to form a wet granule, and weighed. Then dried in a drying oven for one day at ± 60^{o}C and granules dry out. Dry granules sieved with no. 16 (Widyanari, 2017).

3.4.4. Halal Analysis of Materials in Chewable Tablet Formulations

Analysis of ingredients in avocado seed extract chewable formulation by analyzing the original of a material used and looking at the 3 aspects of halal medicine, such us: Not made from unclean ingredients (for internal medicine), not made from contaminated parts (inside and outside drugs) , not contaminated by unclean materials (in the process of production, storage and distribution) (AIFDC ICU 2008; AIFDC ICU 2009). One of the legal bases required by the use of halal drugs is the hadith of the Prophet Muhammad; he said: "Indeed Allah

SWT does not make diseases unless there is a cure, Allah SWT creates medicine for every disease. Therefore, you should seek treatment and do not seek treatment with the unclean (History of Abu Ad Darda). In the drug formulation, the most important virtue is the guarantee of the halal ingredients used.

3.4.5. Evaluation The Physical Properties of Granules

Test of granule physical properties include :

1. The Flow Time Test

The flow time test aims to find out which powder is used to have a good flow time. A good flow time will result in tablets that have filled the weight uniformity requirements. Granules can be said to qualify if the flow time is more than 10 seconds. The 100 g granule is put into a measuring device until the corner is full and flattened, then the lid is opened, and the granule is allowed to flow until it runs out and is calculated when the flow uses a stopwatch. (Depkes RI, 2014).

2. Quiet corner Test

100 g granule is put into a Quiet measuring device to full and flattened, the lid is opened, and the granule is allowed to flow until it runs out. The height of the formed diameter is measured, and the stationary corner is calculated by the calculation formula as follows:

$$\text{Tan } \alpha = \frac{h}{r}$$

information :

h = Cone hight (cm)

r = Cone radius (cm)

α = Quiet corner (^{0}) (Pinate et al., 2012).

3. Tapping Test

The granule is inserted into a 100 ml measuring cup and is considered as V^o. Measuring cups are installed on the volumenometer and are drawn ten times, 500 times and 1250 times to see the strength

and stability of the granule. There is a difference between V^{500} and V^{1250} less than 2 mL then V^{1250} is the volume after tapping (Vf), and if more than 2 ml is repeated, an increase such as tapping 1250 is repeated until the difference between measurements is repeated less than 2 mL. The final determination results are considered V^t. Tap values are calculated using equations.

The formula calculates the value of the index:

$$T\ \% = \frac{Vo - Vt}{Vo} \times 100\%$$

(Depkes, 2014)

4. Moisture Content Test

One gram of granule is inserted into the moisture analyze tool and then leveled and measured by the water content by pressing the start button; it will get percent moisture content (Depkes RI, 1995).

3.4.6. Manufacture of Chewable Tablet of Avocado Seed Extract

Granules that have been tested for their physical properties added Talk and magnesium Stearate as a lubricant and mixed until homogeneous, then tested for their physical properties. The granule was then printed with a single punch tablet printing machine with a weight of ± 500 mg.*single punch*.

3.4.7. Evaluation of Physical Properties of Tablets

Test the physical of chewable tablets include :

1. Organoleptic Observation Test

Organoleptic observation is visually by observing the taste, shape, and color. As well as the physical appearance of tablets include the absence of capping, cracking, picking and another characteristic as indicating damage to the tablet (Siregar, 2010)

2. Uniformity of Weight Test

Weighing 20 tablets is calculated by the average weight of tablets, tablets meet the requirements for uniformity of weight, if there

are no more than two tablets, each of which weights deviates from the average weight greater than the price specified in column A, and none the weight deviates from the average weight of more than the price set in column B. Even if 10 tablets are used, not one tablet whose weight deviates is greater than the average weight set in column A and column B (Depkes RI, 2014)

$$CV = \frac{SD}{X}$$

Information :

CV = Coefficient of variation

SD = Standards Deviation

X = Average weight of tablets

3. Uniformity of Size Test

Twenty tablets were selected from each formula, then the thickness and diameter of each tablet were measured using a measuring instrument, a micrometer screw. According to Indonesian Pharmacopoeia V, the conditions set out in terms of uniformity of size unless stated. Otherwise, the diameter of the tablet must not be less than $1^{1/3}$ the thickness of the tablet and should not be more than three times the thickness of the tablet (MOH, 2014)

4. Hardness Test

Evaluation of the hardness of the tablet using a digital hardness tester. A tablet is placed on a device with a horizontal position; the tool is calibrated to the position of 0.00. The tool is rotated until the tablet is broken. Read the values listed on the monitor tool (Depkes RI, 2014).

5. Fragility Test

Twenty tablets were removed from the sticky particles, then weighed. The tablet is inserted into the tester friability; the device is rotated for 4 minutes or 100 times the rotation (25 rpm), the tablet is removed from the tool, cleaned and reconsidered (Ministry of Health, 2014). The formula calculates fragility:

$$\text{Fragility} = \frac{(M1 - M2)}{M1} \times 100\%$$

Information :

M1 = Weight before testing

M2 = Weight of the tablet after the test

6. Favorite Analysis Test

In the preferred analysis test carried out by giving chewable tablet preparations for each formula to be tested by the panelist and provided drinking water to rinse and clean the remaining chewable tablets in the mouth, then wait ± 5 minutes for checking the following formula. The purpose of this test is to find out which recipe is the most preferred, then the analysis of preference is done by distributing questionnaires to 20 panelists conducted randomly (Purba et al., 2014). The results of the indications carried out are the average values obtained from the multiplication of the frequency (number) of respondents with the amount of the hedonic test scale divided by the total number of respondents.

3.5. Analysis of Data

Data obtained from research results on avocado seed extract granules and chewable tablets will be compared with the requirements contained in Indonesian Pharmacopoeia and other supporting libraries. And the analysis will be done statistically using the One Way ANOVA test with a confidence level of 95%.

CHAPTER IV

RESULTS AND DISCUSSION

4.1. Results of the Characteristic Evaluation of Avocado Seed Extract

The results of the determination that has been made at UPT Materia Medika Batu that the simplicia studied are avocados with the Latin name *Persea americana* Mill. The simplicia used is avocado seeds taken from fresh fruit, with the Latin names *Persea cement* so the key determinations obtained from these plants are as follows: 2a-27a-28b-29b-30b-31a84b-88b-89b-91a-109b-119b -120b-128b-129a-135b-136b-139b-140b-142a-143a-146-154b-155b-156b-162b-163a-164b-165a-2a-2.

Explanation of the key to the determination of avocado plants is Habitus: Tree. ±10 m high. Stem: Woody, round, branched, dirty brown. Leaves: Single, ovoid, stemmed, scattered location, pointed tip and base, hairy, 10-20cm long, 3-10 cm wide, green. Flowers: Compound, panicle shape, twins, growth of twigs, twelve stamens, four anthers, dirty white, hair crowns, 1-1.5 cm diameter, yellowish white. Fruit: Bunny, ovoid, 5-20 cm long, speckled or bald, fruit flesh if red soft, green or purplish yellow. Seeds: Round, 2.5-5 cm in diameter, reddish-white seed pieces. Root: Rumped, round and brown. Determination of plants is shown in Appendix 21.

The avocado seed extract is made by macerating for seven days with five days using the first 20% of some solvents, and two days for the rest of the solution while stirring occasionally. The comparison used is (1: 7.5) L using ethanol 96% as a solvent, the reason for using ethanol 96% solvent is that compounds such as catechins and fitosterol will be better observed in polar solvents (Hussain and Mohamad, 2015).

The moderate obtained is then evaporated so that the concentrated extract is obtained. The evaporation process is carried out using a rotary evaporator. The principle of using this tool is to regulate the temperature of

the rotary evaporator water bath at a temperature of 50°C, not to exceed the optimum temperature of the active substance. The working principle of this evaporator is by adding heat or heat to concentrate a solution consisting of a high boiling solute and a lower solvent which results in a more concentrated solution and high concentration.

The concentration of the solution is based on the huge difference in boiling points between the substances. The boiling point of a pure liquid is affected by pressure. The tool is run for a particular time until the results are in the form of a concentrated extract, in this study used a water bath which is set at the optimal temperature and rotation speed, which is 50oC with a rotation speed of 50 rpm (Lisa, 2006) — making 1000 grams of a thick extract of avocado seeds obtained 78 grams of concentrated extract.

Thus obtained a yield of 7.8%. Evaluation of avocado seed extract was conducted to determine the quality of the extract purchased so that it can meet the variety of concentrated extract. Phytochemical screening conducted by Sunusmo (2018) that avocado seed extract contains tannins, flavonoids, and saponins. The concentrated extract of avocado seeds contains flavonoids with the truck test producing yellow colored fluorescence (Hidayah, 2018).

According to Sekhon et al. (2012) research, flavonoids have actions to reduce cholesterol levels in the body by inhibiting the activity of the enzyme HMG-Co-A reductase as cholesterol biosynthesis, saponins according to elekofehinti et al., (2013) have action by inhibiting fat peroxidation and increase the concentration of antioxidant enzymes, while tannins are able to reduce the accumulation of cholesterol in the blood by accelerating the removal of cholesterol through feces (Rahayu, 2005).

The full extract examination is carried out through organoleptic characteristics (shape, smell, color, and taste). The results of an organoleptic analysis of a thick extract of avocado seeds are shown in table 4.1

Table 4.1 Result of Organoleptic Evaluation of Thick Avocado Seed Extract

Parameter test	Result
Form	Thick
Smell	Typical of Avocado seed extract
Color	Blackish Brown
Flavor	Bitter

The characteristics of the concentrated extract of avocado seeds in table 4.1 are dense, blackish brown with a distinctive aroma of avocado seeds and bitter taste. The emergence of a sour taste because saponins that have a bitter taste and tannin have a flavor that is as tight as avocado seeds (Zuhrotun, 2007).

4.2. Manufacture Methode of Chewable Tablet of Avocado Seed Extract

The method of making chewable tablets, avocado seed extract is made using wet granulation of this method, aiming to improve the flow properties, prevent the tablet from sticking to the mold, and reduce the air space so that the tablet is not quickly broken. The selection of the granules was made using a wet granulation method to produce an excellent and stable tablet.

The chewable tablet formulation used was extracted from avocado seeds according to Suhendra et. al., (2016) by effective doses of lowering cholesterol levels for mice at a dose of 125 mg/kg bw each day, has been converted to human treatments shown in Appendix 1 to cover the bitter taste of the active substance then using fillers as well as sweeteners is mannitol and lactose (Siregar, 2010).

Mannitol used in this formulation was varied into three concentrations, such us, 40%, 50%, 60% to determine the amount of concentration that can mask the bitter taste of avocado seeds (*Persea americana* Mill.). Mannitol

is inert, can be used as a chewing tablet as it gives a good taste, is mild and cold sweet, soft and melts in the mouth, and the sweetness level of mannitol is the same as glucose and half of the sweetness of sucrose (Armstrong, 2009).

Manufacture of granules begins by drying the active substance (concentrated extract of avocado seeds) using aerosol as an adsorbent with a ratio of 1: 1. The water content of dried avocado seed extract obtained is 3.62%; this is consistent with Voight's (1994) research, the water content got according to the dry extract water content of 5%. The principle of wet granulation is to mix active substances and other additives to be homogeneous and moistened with a binding solution, then sifted to obtain granules with uniform shapes and sizes, and the drying process is carried out. Drying with a temperature of 50^{o} - 60^{o} C aims to reduce the water content contained in the granule. The dried granules are then sieved with a smaller sieve size so that the granules are obtained with excellent flow properties.

The chewable tablet form avocado seed of extract, mannitol and lactose function as fillers, citric acid as a flavoring, and amyl mucilago as a binder. Amyli mucilago with a concentration of 5% - 10% is a suitable binder, neutral and nonreactive so that it can be used with most active substances (Sheth et al., 1980). Magnesium stearate is added as a lubricant to prevent the mass of the tablet from sticking to the mold and the use of talc as glidan to increase the ability to flow in the granule.

4.3. Result of Halal Analysis of Ingredients Chewable Tablet Formulation

Halal is the concept of the principle rules have a been established on the religion of Islam, which is used to declare that something is permitted or prohibited to be consumed by Muslims based on the Qur'an, hadith or ijtihad (ulama agreement) (Salehudin, 2010). According to the dictionary, al al-Munjid fi al-Lughah ’halal is the opposite of haram.

In unlawful cases, it has been explained in the Qur'an and al-Sunnah

and the results of the ijtihad of the scholars based on their understanding. The whole nature and elements of forbidden thing and evil. So clearly Allah SWT forbids him, "And he justifies for them all good things, and forbids the mall bad things (al 'Raf: 157). Then it is obligatory for Muslims to consume drugs or use halal cosmetics.

One of the legal bases required by the use of halal drugs is the hadith of the Prophet Muhammad, and he said: "Indeed Allah SWT does not make diseases unless there is a cure, Allah SWT creates medicine for every disease. Therefore, you should seek treatment and do not seek treatment with unclean (History of Abu Ad Darda). The drug formulation the most important virtue is the guarantee of the halal ingredients used.

According to Ranasasmita (2014) there are at least 3 critical points that determine halalness of the drug, is the processes and materials of insulation through extraction, process and supporting fermentation materials (excipients), so that more definite information is needed on the manufacturing process, and additional sources of equipment, because of this can raise doubts about the halalness of products in avocado seed extract chewable tablet formulations. The results of the analysis of chewable tablet formulation materials are shown in table 4.2.

Table 4.2. Halal Analysis of Chewable Tablet Formulation

Criteria	Original of Description	Parameter			Information
		A	B	C	
Ingredients					
The extracted seed of Avocado	Avocado seed powder extracted with solvent ethanol 96%				Cannot be analyzed

Criteria	Original of Description	Parameter			Information
		A	B	C	
Aerosil	Crystalline powder, has a high specific surface, and binds moistly via groupilanol, and is obtained from the UMS laboratory because the pure compound is used.	√	√	√	Halal
Mannitol	Types of sugar alcohol found in fruits (Department of Religion, 2003).	√	√	√	Halal
Lactose	Sugar from milk, which used is pure compound obtained from the UMS laboratory (LPPOM MUI, 2015).	√	√	√	Halal
Starch Manihot	The product comes from vegetable ingredients through a physical process without adding elements or by adding additives which are generally chemicals. Physical process in the form of destruction, cutting, filtering, deposition, drying, etc. (LPPOM MUI, 2013)	√	√	√	Halal

Criteria	Original of Description	Parameter			Information
		A	B	C	
Citric Acid	Depending on the halal media used in the manufacture of citric acid by fermentation (LPPOM MUI, 2003) obtained from the UMS laboratory				Cannot be analyzed
Magnesium Stearate	Derived from mining/ quarrying materials, depending on the halal of stearic acid used in its manufacture (LPPOM MUI, 2013), which was obtained from the UMS laboratory				Cannot be analyzed
Talcum	Excellent crystal powder, easily attached to the skin and free from granules, which are used are pure compounds obtained from PT. Brataco which has been certified Halal	√	√	√	Halal

Criteria	Original of Description	Parameter			Information
		A	B	C	
Instrument					
Analytical scales		√	√	√	Halal
Stirring rod		√	√	√	
Mortar and Pestle		√	√	√	
Porcelain		√	√	√	
Measuring cup		√	√	√	
Beaker glass		√	√	√	
Erlenmeyer		√	√	√	
Tablet single punch		√	√	√	
Friability tester		√	√	√	
Volunometer		√	√	√	
Rotary evaporator		√	√	√	
Calipers		√	√	√	
Digital hardness tester		√	√	√	
moisture analyze		√	√	√	
Water bath		√	√	√	
Mesh no 14 & 16		√	√	√	
Process					
Extract of avocado Seed		√	√	√	Halal

Description: A = Not made from unclean ingredients, B = Not made of contaminated ingredients, C = Not contaminated with impure and unclean ingredients

When viewed from the stages of making avocado seed extract, what needs to be criticized is the maceration process using 96% ethanol, which is evaporated by using a rotary evaporator and concentrating the extract using a water bath, and the avocado seed concentrated extracts in the final product do not contain ethanol. Requirements from the Indonesian Ulema Council allow the use of ethanol as a solvent if the final product is not included in alcohol. The original of the alcohol used should not be the product of the liquor industry (*Khamar*) (AIFDC ICU 2008; AIFDC ICU 2009).

The avocado seed extract is used as an active ingredient in tablet dosage formulations. All halal plants for consumption, except having a toxic effect. According to Taylor (2001), galenic preparations (extracts, essential oils, infusions or plant solutions, etc.) can be said to be halal. The products of the avocado seed extract tablets that were criticized were the manufacturing processes related to the addition of excipients which were mixed until homogeneous to form a product judging from the results of the analysis of the materials shown in table 4.2, the chemicals obtained from PT. Brataco and University of Mauhamadiyah Surakarta laboratories that do not contain ingredients from pig derivatives, and do not carry other components are forbidden or include unclean things such as carcasses, blood, components from human organs, dirt and so on. In the process of making chewable tablet preparations used are instrument found in the laboratory, which has never been used for materials containing pig derivatives.

4.4. Evaluation Results of Chewable Tablet of Avocado

Manufacture of avocado seed extracts chewable tablet granules, whose physical characteristics have been evaluated, data obtained that meet the requirements include flow time test, stationary Quiet corner test, tapping test, and moisture content test. The evaluation results are shown in (table 4.3).

Table 4.3 Evaluation Result of Granules a Chewable Tablets of Avocado Seed Extract

Formulation	Flow Time (second)	Quiet Corner (^{0})	Tapping (%)	Moisture Content (%)
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
F1	5,67 ± 0,39	32 ± 2,00	8,67 ± 0,57	1,97 ± 0,09
F2	5,12 ± 0,49	29 ± 2,89	8,50 ± 1,32	2,34 ± 0,01
F3	4,90 ± 0,17	29 ± 2,52	8,33 ± 0,57	2,44 ± 0,17
Sign	0,10	0,24	0,89	0,00
Terms	<10 second/ 100gram (Depkes RI, 2014)	<45° United States Pharmacopoeia : 32th, 2009)	< 20% (Depkes RI, 1995)	<3% (Depkes RI, 1995).

Information : F1 = Formulation 1st with mannitol filler material 40%, F2 = Formulation 2nd with filler mannitol 50%, F3 = Formulation 3rd with mannitol filler material 60% Mean = Average value, SD = Standard Deviation, Test statistical analysis Oneway ANOVA homogeneity (p <0.05) followed by the Post-Hoc Test Games-Howell, Oneway ANOVA homogeneity test (p> 0.05) followed by the Bonferroni Post Hoc Test.

1. Flow Time Test

Based on the results obtained from the evaluation of the granule flow time found in table 4.3, the results of the granule flow time test are shown in Figure 4.1 as follows:

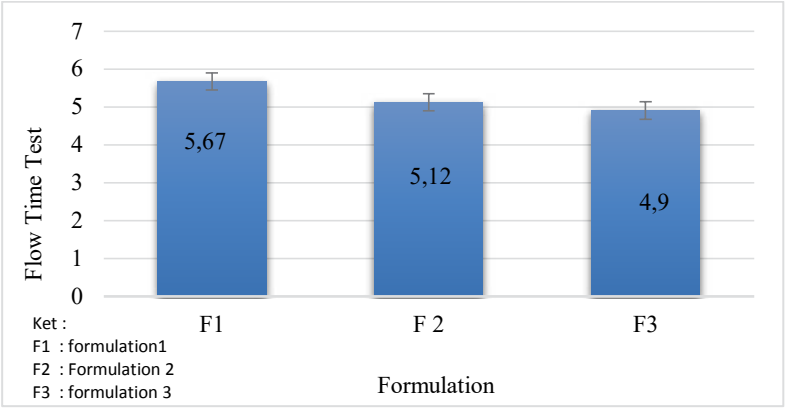


Figure 4.1. Graphic result of Flow Time Test

The flow time check aims to find out which powder is used to have a good flow time. A good flow time will result in tablets that have fulfilled the weight uniformity requirements. Based on the results obtained, the granules on the three formulas gave the flow time of formula 1 (5.67 seconds), formula 2 (5.12 seconds), formula 3 (4.9 seconds), so that the granules in the formulation met the flow time requirements which is under 10 seconds / 100 grams (Ministry of Health, 2014).

In formulation 3 has the best flow properties compared to formulation 2 and formulation 1. Because at the flow time of fewer than 10 seconds / 100 grams granules can easily flow, and in the tablet printing process it is more comfortable. According to Nokhodchi (2005), the presence of moisture adsorbed by the drug will affect the flow properties, compressibility, and granule hardness on the tablet. Granules which have the most concentration of mannitol are more comfortable to flow while granules that have a mass of mannitol at least the flow time is the least. Formula 3, which contains the highest levels of mannitol, makes granules dry more efficiently, and has homogeneous particles, so the flow properties are faster.

The nature of granule flow is influenced by the shape and size of particles and the friction that occurs between granules. Flow properties in granules have essential characteristics as a control in the process of filling granules into the mold and produce uniformity of weight and will not experience damage to the tablet when printing tablets.

From the results of statistical analysis using the one way ANOVA test contained in the attachment, that the results of the statistical analysis of the flow time test produce data that is typically distributed and homogeneous. So that the significant value obtained $p = 0.107$ or $p > 0.05$, it can be concluded that the formulations 1, 2, and three that have been compared are not significant, which means there is no difference in the flow time of granules between formulas.

The results of this study that regardless of the variation in mannitol given will not affect the time of flow of granules, because the mannitol properties are nonhygroscopic so that it can be used using dry granulation methods or direct presses. The wet granulation method used in this study cannot influence the granular flow properties.

2. Quiet Corner Test

In addition to the flow rate, the flow properties determined by the stationary corner, the smaller the quiet corner formed by particles, the better granular features and the easier it flows so that it simplifies the tableting process, so the resulting tablets can meet the requirements. Data obtained from all formulas meet the requirements, which are less than 45^{o} (USP, 2009). The results obtained are shown in graphical form in Figure 4.2.

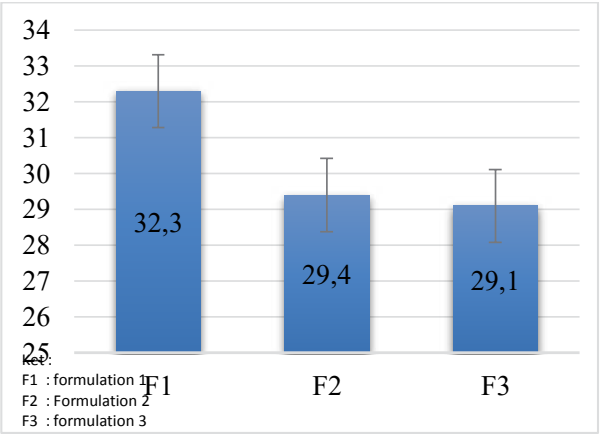


Figure 4.2. Quiet Corner Test result Graph

Based on the results obtained in the calculation of three formulas having an F1 quiet corner of 32^{o}, F2 of 29^{o}, and F3 of 29^{o}. From the results, it is found that the method which has the smallest edge of silence is F3 and the formula that has the most considerable stationary advantage is F1. The results of the stable corner obtained in each of these formulas meet the requirements of flow properties, where granules have excellent flow properties in the range of 25-30^{o}, except

for formula 1 with a stationary angle of 32^{o} which has excellent flow properties in the range 31- 35^{o}.

The results of the stationary corner are affected because the characteristics of mannitol are non-hygroscopic, where for F1 using mannitol filler material is 40%, F2 50%, and F3 60%, so F3 produces a smaller angle of silence compared to other formulas. Because mannitol is used more, the granules produced are drier compared to different recipes.

The results of statistical analysis of granule stationary corner using the Oneway ANOVA test resulted in significant values obtained at p = 0.276 or (P> 0.05) which showed that there were no significant differences between the three formulas. The variation of mannitol filler concentration has less effect on the silence corner of the granule, so that no matter how much the frequency of mannitol given will not affect the silence corner of the granule. The wet granulation method used in this study also did not change the silence angle of the granule. The stationary edge on the granule is related to the flow time of the granule; if the flow time of the granule is good, then the resulting fixed corner will also be useful.

3. Tapping Granule Test

The results of the granule tapping test obtained from the three formulas fulfilled the requirements, is with a tapping index where less than 20% can produce excellent flow properties (Depkes RI, 1995). The test results of tapping index can be seen in graph Figure 4.3.

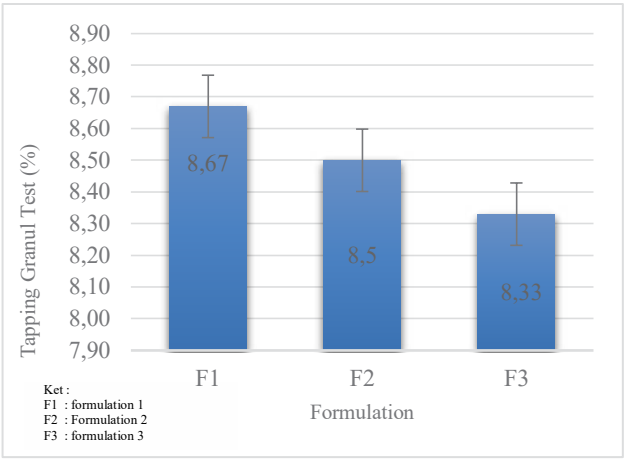


Figure 4.3. Graph of Granule Tapping Test Result

Based on the results obtained from the three formulations, the F1 index was 8.67%, F2 was 8.50%, and F3 was 8.33%. Of the three formulations, the smallest percentage of index tap was F3 with a concentration of mannitol filling material of 60% and the formula that had the most extensive tap index was F1 with variations in mannitol concentration of 40%. In the granule tapping test, a decrease in granule volume showed that between the granule particles there were still air cavities which could cause the granule to become compressed, allowing the granule to clog the hopper hole.

The data shows that F3 (60% mannitol) with the highest concentration of mannitol has the best flow properties because the smaller value of the index will have a faster flow and more comfortable to press. Because the flood of mannitol which is not hygroscopic causes the lowest index value the granule will easily flow (Rowe et al., 2006).

The results of statistical analysis using the Oneway ANOVA test resulted in significant values obtained at p = 0.903 or (P> 0.05). The interpretation of the data shows that there is no significant difference between the formulas. The variations in the concentration of mannitol have less effect on the granule t ap index, so that regardless of the frequency of mannitol given it will not affect the silence corner of the

granule. The wet granulation method used in this study also cannot modify the granular index tap value.

4. The Moisture Content of Granules Test

The results of water content test on the three formula data filled the requirements, is with a percentage of <3% (Depkes RI, 1995). The moisture content test results are shown in graphical form in Figure 4.4.

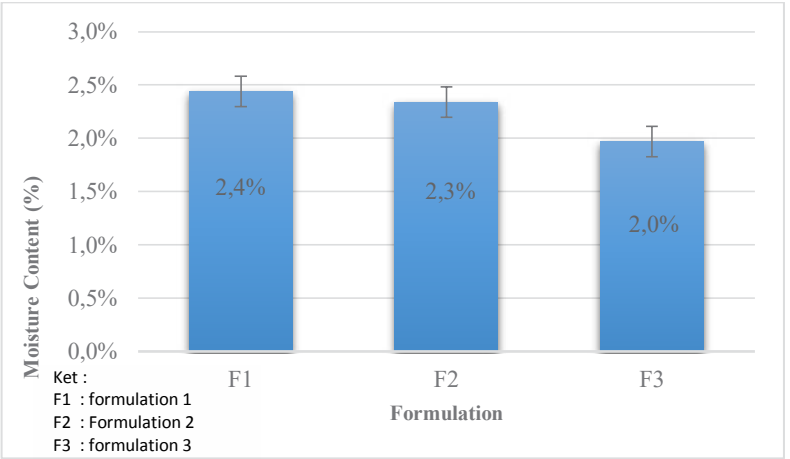


Figure 4.4. Graph of Moisture Content Test Result

Based on the results obtained from the three formulations, the water content in F1 was 2.4%, F2 was 2.3%, and F3 was 2.0%. From the effects of the third data formulation that the highest water content is found in F1 at 2.4% and the smallest at F3 at 2.0%. Because by mannitol fillers which make the granules very easy to dry by their non-hygroscopic nature, making the granules drier and containing lower moisture, the higher the concentration of mannitol used will be the lower the water content obtained. The water content in the granule is high so that the flow speed will be longer. Because a large amount of water content will prolong the granule flowing from the funnel to the tablet device.

The results of the statistical analysis used the Oneway ANOVA test by producing significant values obtained at p = 0.00 or (P <0.05). Interpretation of the data shows that there are substantial differences

between formulas. Significant differences in the formula were continued with the Bonferroni post hoc test shown in Appendix 9, that there were significant mean differences from the effect of mannitol variation on formulation 3 and formulation 1. The changes in mannitol filler ingredients affect the granule moisture content.

4.5. Evaluation Result of Chewable Tablet of Avocado Seed Extract

Avocado seed extract chewable tablets were evaluated by measuring tablet hardness test, tablet fragility test, tablet weight uniformity test, tablet size uniformity test and observing the physical appearance of avocado seed extract chewable tablets shown in table 4.4.

Table 4.4. Evaluation Result of Avocado Seed Extract Tablets

Formulation	Uniformity of Weight (mg)	Uniformity of Size (mm)		Hardness (Kg)	Fragility (%)
	Mean ± SD	Tebal	Diameter	Mean ± SD	Mean ± SD
F1	503± 4,84	1,2	4,3	5,04 ± 0,18	1,18 ± 0,07
F2	499± 9,50	1,2	4,3	4,20 ± 0,70	2,40 ± 0,02
F3	496± 3,82	1,2	4,3	4,07 ± 0,10	2, 62 ± 0,07
Sign	0,00			0,05	0,000
Term	Tablet deviation requirements deviation of 5% and 10% (Depkes RI, 2014)	Diameter <3 times, >1 $\frac{1}{3}$ thick (Depkes, RI 2014).		4-8 Kg (Depkes RI, 2014).	<1% (USP 30th, 2007).

Description: F1 = Formulation 1 with mannitol filler material 40%, F2 = Formulation 2 with mannitol filler material 50%, F3 = Formulation 3 with mannitol filler material 60%, Mean = Average value, SD = Deviation Standard, Statistical analysis test Oneway ANOVA homogeneity ($p < 0.05$) followed by Post Hoc Test Games-Howell if the data is not homogeneous (heterogeneous). Test on Oneway ANOVA statistical analysis if the resulting value is significant ($p < 0.05$) followed by Bonferroni's Post Hoc Test.

The results of the evaluation of chewable tablets are as follows:

1. Organoleptic Observation Test

The results of organoleptic observations are shown in Table

4.5. Avocado seed extract chewable tablets in formula 1, and formula two did not cause any damage to the tablet, while in formula three there was caping, that is, partially or entirely separated from the upper or lower surface of the tablet and Laminating, separating the tablet into two or more layers. Because formula 3 has the highest degree of fragility, causing damage to the tablet during the tableting process.

Table 4.5. Observation of Organoleptic Chewable Tablets Avocado Seed Extract

Consideration of Organoleptic	Formulation		
	F1	F2	F3
Shape	Rounded Round	Rounded Round	Rounded Round
	No damage to the tablet	No damage to the tablet	Did not occur damage to the tablet capping and cracking
Color	Whitish Brown	Whitish Brown	Whitish Brown
Flavor	Bitter	Less bitter taste	Leaving bitter taste a little sweet
Typical aroma	Standard extract	Standard extract	Standard extract

Information: F1 = Formula1 (mannitol 40%), F2 = Formula 2 (mannitol 50%), F3 = Formula 3 (mannitol 60%).

The color produced from the chewable tablet provides whitish-brown color because the concentrated extract of the active substance is blackish brown so that the active substance and excipients are white and mixed at homogeneously as shown in the appendix. While the taste produced in formula 3 has a slightly sweet taste which still leaves a bitter taste because the highest concentration of mannitol is 60%.

The concentration of mannitol has not been able to give a sweet taste it does not cover the bitter taste of the active substance. Judging from the observations of the results of organoleptic tablets, the higher the concentration of mannitol fillers, the more sweetness obtained, and

the aroma of chewable tablets has a distinctive smell from avocado seed extract.

2. Uniformity of Weight Test

Based on the results of the weight uniformity test shown in Appendix 6, tablets are said to have average weight when the Relative Standard Standards (SBR) are by Indonesian Pharmacopoeia Edition V requirements. It is known that the weight uniformity of avocado seed extract chewable tablets (*Persea americana* Mill.) pharmacopeia requirements, in each formula no one tablet deviated more than the average weight in each formula (Depkes RI, 2014).

In F1 there were no deviant tablets with a deviation of 5% between 477-528 mg while the deviation of 10% between 474-523, for F2 there was no weight of the tablet deviating with a deviation of 5% between 474-523 mg while the deviation of 10% between 499-548 mg, and F3 with a deviation of 5% between 472-521 while a deviation of 10% between 447-546 mg. It is stated that the avocado seed extract chewable tablets have excellent weight uniformity and meet the requirements specified in the Indonesian pharmacopeia.

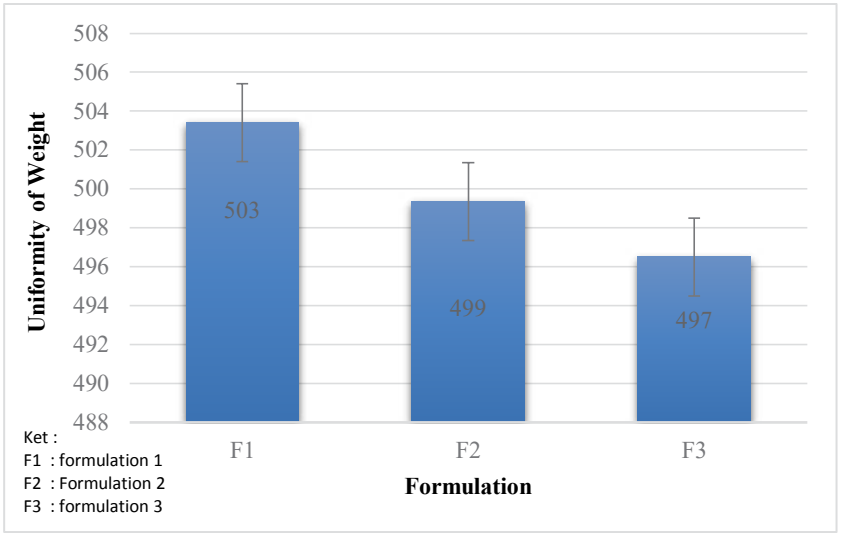


Figure 4.5. Graphic Result of Tablet Weight Uniformity Test

The results of statistical analysis of tablet size uniformity Figure 4.5 produce data that is usually distributed and homogeneous. Oneway ANOVA test results with p = 0.006 or (P <0.05), the interpretation of the data shows there are significant differences between formulas. To find out between the three different formulas is continue the Games Howell post hoc analysis, based on the results obtained from the effect of variations in mannitol fillers there are differences in formula 1 and formula 3. Shows the variations in mannitol filler ingredients affect of uniformity tablet weights.

3. Uniformity of Size Test

The requirements for uniformity of tablet size according to Indonesian Pharmacopoeia Edition V is the tablet diameter should not be less than $1^{1/3}$ thick tablets and should not be more than three times the thickness of the tablet. The results of the research are shown in the graph in Figure 4.6.

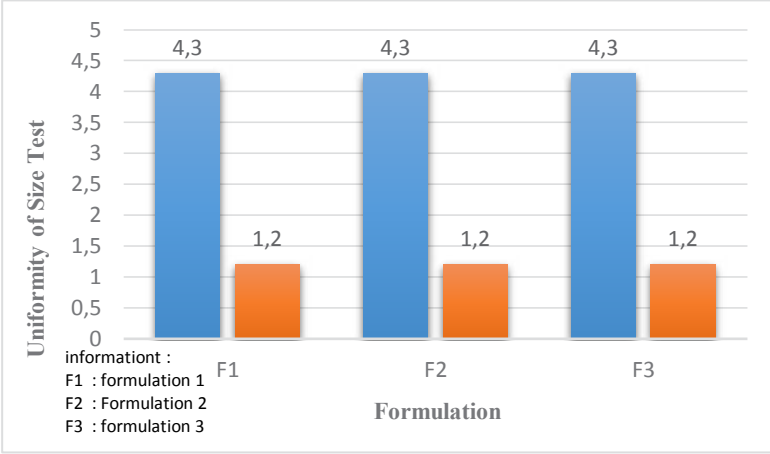


Figure 4.6. Tablet Size Uniformity test Result Graph

Comparison of uniformity size (diameter-thickness) of each formula is F1 for (4.3 - 1.2) mm, F2 for (4.3 - 1.2) mm, and F3 for (4.3 - 1.2)) mm. On the three formulas, the results obtained from the data have the same diameter and thickness, and the three formulas meet the requirements of the tablet size uniformity standard.

4. Hardness Test

The tablet hardness test results in all three formulations have met the requirements, is the percentage between 4-8 kg (Depkes RI, 2014). The graph results obtained from the three formulations are shown in graph 4.7.

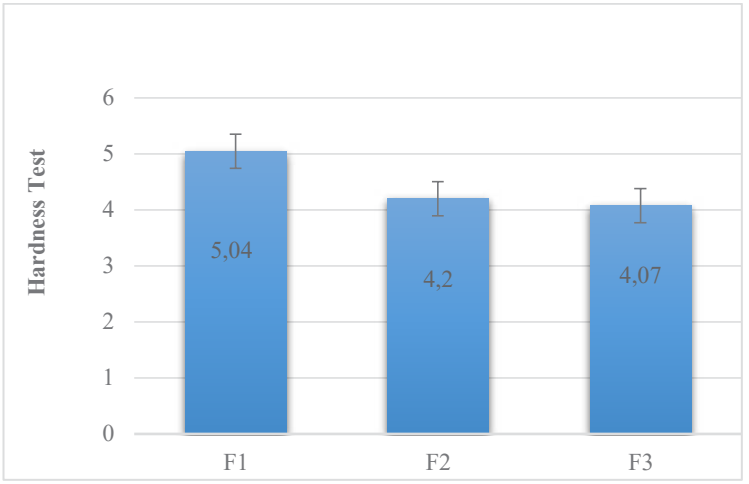


Figure 4.7. Result of Tablet Hardness Test Graph

Based on the results of three formulations, the resistance scale of the tablet was obtained by using a hardness tester. The hardness of F1 tablets was obtained (5.04 Kg), F2 (4.2 Kg), and F3 (4.07 Kg). From the third result, the highest level of hardness formulation was found in F1 at 5.04 Kg, and the lowest level of violence seen in F3 was 4.07 Kg. Mannitol content of the value hardness is getting smaller.

Because there is an interaction between mannitol and lactose which can increase tablet hardness, F1 has the least amount of mannitol which is 40% and more lactose which is equal to 22.4% compared to F2 (7.6%) and F3 (2.4%) where the interaction between mannitol and lactose as fillers as well binding agents which can produce hard granules. Then F1 chewable tablets have a higher level of hardness compared to formulas 2 and 3. Good tablet hardness is caused by uniform granule size and shape with wet granulation method.

The results of the statistical analysis of the test on the way of violent ANOVA on tablets showed a value of p = 0.064 (P> 0.05). The interpretation of these data indicates that there is no significant difference between avocado seed extract chewable tablet formulas. The shows that the variation of mannitol filler material has less effect on the tablet hardness of the formula, so that regardless of the concentration of mannitol given it will not affect the silence corner of the granule.

5. Fragility Test

The tablet fragility test results in the three avocado seed extract chew formulations shown in the graph Figure 4.8 did not meet the requirements, and it's the fragility rate obtained more than 1% (USP 30th, 2007), chewable tablets had a low hardness and often produced tablets with a high degree of fragility.

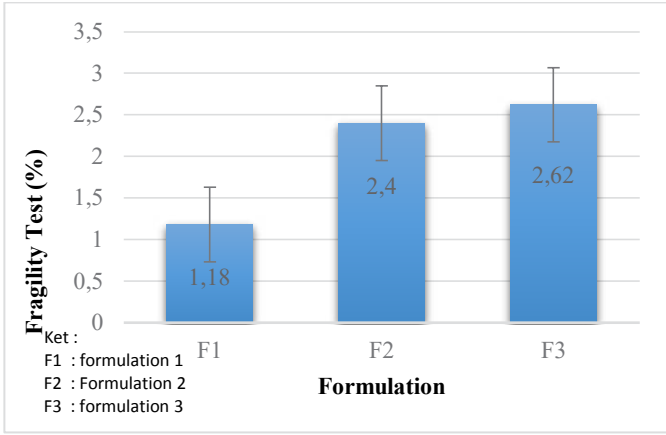


Figure 4.8. Result of Tablet Fragility Test Graph

Based on the results of the three formulas, the fragility level obtained in F1 tablets is (1.18%), F2 (2.4%), F3 (2.62%). The recipe which has a high fragility level is found in the filler, it's F3 of 2.62%, and F1 owns the lowest formula at 1.18%. Because F3 has the highest interaction between mannitol with as many as 60% and the lowest lactose as much as 2.4% as filler. The ratio between mannitol, lactose and starch can reduce the fragility of tablets so that the percentage of

starch that interacts with mannitol and lactose is more significant then the fragility of tablets will be smaller (Gohel, 2005).

The increasing percentage of tablet fragility, then the tablet will be more fragile. The factor that affects the vulnerability of tablets is the moisture content of a tablet. Tablets that have dehydrated granules will cause tablets to be more delicate compared to tablets with higher moisture content. The hardness test is positively correlated with tablet fragility test, the lower the hardness value, the higher the fragility value.

The results of the statistical analysis of the test oneway ANOVA fragility on tablets showed a value of p = 0,000 (P <0.05). The interpretation of the data shows that there is a significant difference in the fragility of tablets between formulas, followed by the Bonferroni post hoct test with differences in the three formulas. Shows that variations in mannitol affect the fragility characteristics of tablets.

6. Favorite Analysis Test

The preferred analysis of the test results shown in Table 4.9 has been done by 20 respondents who were randomly selected to fill in the ideal analysis questionnaire. Questionnaires were taken from similar studies on responsiveness (Widyanari, 2017). The Favorite Analysis Test consists of four parameters, namely; color, aroma, taste, and texture.

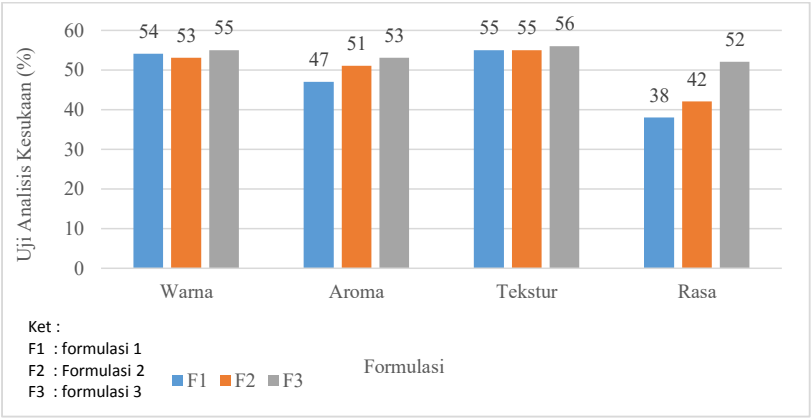


Figure 4.9. Result of Respondents Analysis

Based on the results obtained on the tablet color 65% of respondents liked F3 due to the lighter shade of the other formulas because the concentration of mannitol was higher which was as much as 60%. The majority of excipients used were white that the color covered the color of extracted chocolate; the results obtained from the chewable tablets of avocado seed extract were whitish brown.

The analysis results of the aroma preference of the three formulas have the same aroma, but the smell that responded likes is F3 with a percentage of 60% of respondents because the concentration of mannitol is higher so it can mask the distinctive smell of avocado seed extract.

The texture (hardness) of the tablets on the three formulas is the same, but the preferred formulation is F3 with a percentage of 60% of respondents, because it has the lowest level of violence and the highest fragility, making it comfortable when consuming it.

The analysis of preference for taste parameters was 65% of respondents liked the taste of F3 chewable tablets because the concentration of mannitol 60% caused sweetness compared to other formulas. The concentration used as a filler for avocado seed extract chewable tablets has not been able to cover the bitter taste of the active substance.

CHAPTER V

CLOSING

5.1. Conclusions

1. Based on the results of the avocado seed extract chew formulation in this study that can meet the standard requirements for the physical properties of tablets which include, uniformity of weight, uniformity of size, and tablet hardness except for tablet fragility tests that do not meet the standard requirements. The concentration used has not been able to produce a sweet taste of tablets by the characteristics of chewable tablets in general, which has a distinctive sweet taste when chewed and comfortably consumed so as not to leave a bitter taste.
2. The concentration of fillers varied by F1 (40%), F2 (50%), and F3 (60%), affecting the water content of the granules, friability, and uniformity of weight on the chewable tablets. The best results of the physical evaluation of the formulation of avocado seed extract chewable tablets were F1 with variations in the concentration of mannitol by 40%, and the analysis of the preference of tablets which respondents liked was F3 with a concentration of mannitol (60%). In addition to the physical properties of hardness on tablets, and for the physical properties of granules in the flow time test, tapping, and stationary corner, mannitol has less effect on these material properties.

5.2. Suggestion

1. Further research is needed by using other fillers and other tablet making methods to get a standard formulation and better
2. New research needs to be done with a variety of other additives to cover the bitter taste of the active substance
3. Required testing of levels on tablets to determine the levels in the tablet so that it matches the original standards.

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APPENDICES

Appendix 1. Calculation of Dosage and Chewable Tablet Formulation

1. Calculation of doses of avocado seed extract each chewable tablet

The calculation of avocado seed extract is effective for mice at a dose of 125 mg/kg bw each day (Suhendra et. Al., 2016). The dose of avocado seed extract in mice with an average weight of 200 g by calculation:

$$\frac{200\ g}{1000\ g} x\ 125 = 25\ mg\ each\ day$$

Konversi from mouse to human : 25 mg x 56,0 = 1400 mg = 1,4 g

So the dose of avocado seed extract for humans is 1400 mg each day. One day took three times with one administration of 466.67 mg. 3 x 2 tablet daily, then one tablet contains avocado seed extract as much as 78 mg.

2. Calculation of supplemental formulations of avocado seed extract chewable tablets (*Persea americana* Mill.)

1. Extract of Seed Avocado (Active Substance) $= \frac{15,6}{100}\ x\ 500 = 78\ mg$
2. Aerosil (Adsorben) $= \frac{1}{100}\ x\ 500 = 5\ mg$
3. Mucilago amyl 10% (Binder) $= \frac{8}{100}\ x\ 500 = 40\ mg$
4. Amylum (Dray Binder) $= \frac{3}{100}\ x\ 500 = 15\ mg$
5. Mg stearat (Lubricant) $= \frac{1}{100}\ x\ 500 = 5\ mg$
6. Talcum (Glidan) $= \frac{8}{100}\ x\ 500 = 40\ mg$
7. Citric Acid (Flavor) $= \frac{1}{100}\ x\ 500 = 5\ mg$
8. Mannitol (Fillers)
   - Formula I $= \frac{40}{100}\ x\ 500 = 200\ mg$

- Formula 2 $= \frac{50}{100} x\ 500 = 250\ mg$
- Formula 3 $= \frac{60}{100} x\ 500 = 300\ mg$

9. Lactose (Fillers)
   - Formula 1 $= \frac{22,4}{100} x\ 500 = 112\ mg$
   - Formula 2 $= \frac{7,6}{100} x\ 500 = 62\ mg$
   - Formula 3 $= \frac{2,4}{100} x\ 500 = 12\ mg$

The total weight each tablet is a follows:

- Formula I = 500 mg
- Formula 2 = 500 mg
- Formula 3 = 500 mg

Appendix 2. Table of Flow Time Evaluation Test Result

Formulation	Trial			Mean ± SD
	1	2	3	
Formula 1	5,28	5,66	6,06	5,67 ± 0,39
Formula 2	4,69	5,66	5,00	5,12 ± 0,495
Formula 3	4,72	5,06	4,91	4,90 ± 0,17

Appendix 3. Table of Quiet Corner Evaluation Test Result

Formulation	Trial			Mean ± SD
	1	2	3	
Formula 1	32,2	34,3	30,3	32 ± 1,90
Formula 2	27,8	28	32,4	29 ± 2,60
Formula 3	31,8	26,4	29,2	29 ± 2,70

Appendix 4. Table of Tapping Evaluation Result

Formulation	Trial (%)			Mean ± SD
	1	2	3	
Formulasi 1	9	8	9	8,67 ± 0,577
Formulasi 2	7,5	10	8	8,50 ± 1,323
Formulasi 3	8	8	9	8,33 ± 0,577

Appendix 5. Table of Moisture Content Evaluation Result

Formulation	Trial			Mean ± SD
	1	2	3	
Formula 1	2,6	2,4	2,1	2,4 ± 0,179
Formula 2	2,3	2,3	2	2,2 ± 0,015
Formula 3	2,1	2	1,9	2,0 ± 0,095

Appendix 6. Table The Uniformity of Weight Evaluation Result

No.	Formula 1	Formula 2	Formula 3
	Weight (mg)	Weight (mg)	Weight (mg)
1	502	494	498
2	506	507	490
3	506	498	503
4	505	487	494
5	505	483	500
6	506	486	492
7	504	507	499
8	502	504	496
9	504	513	494
10	501	495	500
11	503	519	496
12	492	493	495
13	503	503	501
14	504	509	503
15	505	506	492
16	490	498	498
17	506	493	494
18	511	490	494
19	504	497	499
20	509	505	492
Mean	**503,4**	**499,4**	**496,5**
SD	**4,84**	**9,50**	**3,82**
CV	**1%**	**2%**	**1%**

Calculation the uniformity of Weight :

1. Deviation of weight $= \frac{5}{100} x\ 500 = 25\ mg$

   (+) 500 mg - 25 mg = 475 mg

   (-) 500 mg + 25 mg = 525 mg

2. F1 average tablet weight is 503,4

   Deviation 5% = $\frac{5}{100} x\ 503 = 25{,}15$

   (-) 503 mg – 25,15 = 477,85

   (+) 503 mg + 25,15 = 528,15

   The average weight of tablets is 5% deviation

   between 477,85 – 528,15

   Deviation uniformity of weight 10% = $\frac{10}{100} x\ 503 = 50{,}3$

   (-) 503 mg – 50,3 = 452,7mg

   (+) 503 mg + 50,3 = 553,3 mg

   Weight the tablet with a 10% deviation between 425,7 – 553,3

3. F2 average weight of 20 tablet = 499 mg

   Deviation 5% = $\frac{5}{100} x\ 499 = 24{,}95\ mg$

   (-) 499 mg – 24,95 = 474,05 mg

   (+) 499 mg – 24,95 = 523, 95 mg

   The weight of the tablet is 5% deviation between 474.05 - 523.95 mg

   Deviation 10% = $\frac{10}{100} x\ 499 = 49{,}9\ mg$

   (-) 499 mg – 49,9 = 449,1 mg

   (+) 499 mg – 49,9 = 548,9 mg

   The weight of the tablet with a 10% deviation

   between 499,1 - 548,9 mg

4. F3 rata-rata bobot tablet adalah 497 mg

   Deviation 5% = $\frac{5}{100} x\ 497 = 24{,}85$

   (-) 497 mg – 24,85 = 472,15 mg

   (+) 497 mg – 24.85 = 521,85 mg

   The weight of the tablet with a 5% deviation between 472.2 -521.8

   Deviasi 10% = $\frac{10}{100} x\ 497 = 49{,}7$

   (-) 497 mg – 49,7 = 447.3 mg

   (+) 497 mg + 49,7 = 546,7 mg

   The weight of the tablet with a 10% deviation between 447.3 - 546.7

Appendix 7. Table of Hardness Test Evaluation Result Tablet

Formulation	Trial			Mean ± SD
	1	2	3	
Formula 1	5,73	4,34	5,04	5,04 ± 0,70
Formula 2	4,28	4,09	4,23	4,20 ± 0,10
Formula 3	4,1	3,88	4,24	4,07 ± 0,18

Appendix 8. Table of Fragility Test Evaluation Result Tablet

Formulation	Trial			Mean ± SD
	1	2	3	
Formula 1	1,19	1,15	1,18	1,17 ± 0,076
Formula 2	2,4	2,45	2,3	2,38 ± 0,020
Formula 3	2,62	2,5	2,63	2,58 ± 0,072

Appendix 9. Oneway ANOVA Test Results for Statistical Analysis of Granule Tablet Tests

1. Flow Time Test

Tests of Normality

	Formulation	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Flow_time	Formula 1	.177	3	.	1.000	3	.972
	Formula 2	.260	3	.	.958	3	.608
	Formula 3	.198	3	.	.995	3	.870

a. Lilliefors Significance Correction

Oneway

Test of Homogeneity of Variances

Flow_time

Levene Statistic	df1	df2	Sig.
1.284	2	6	.343

ANOVA

Flow_time

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.944	2	.472	3.319	.107
Within Groups	.853	6	.142		
Total	1.797	8			

2. Tapping Test

One-Sample Kolmogorov-Smirnov Test

			Tapping Test	Tapping
N			9	9
Normal Parameters[a,,b]	Mean		2.00	8.500
	Std. Deviation		.866	.7906
Most Extreme Differences	Absolute		.209	.292
	Positive		.209	.292
	Negative		-.209	-.181
Kolmogorov-Smirnov Z			.628	.876
Asymp. Sig. (2-tailed)			.826	.427
Monte Carlo Sig. (2-tailed)	Sig.		.757[c]	.359[c]
	95% Confidence Interval	Lower Bound	.748	.350
		Upper Bound	.765	.369

a. Test distribution is Normal.
b. Calculated from data.
c. Based on 10000 sampled tables with starting seed 2000000.

Oneway

Test of Homogeneity of Variances

Tapping

Levene Statistic	df1	df2	Sig.
2.857	2	6	.134

ANOVA

Tapping

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.167	2	.083	.103	.903
Within Groups	4.833	6	.806		
Total	5.000	8			

3. Quiet Corner Test

Tests of Normality

	Formulation	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Quiet_ corner	Formula 1	.195	3	.	.996	3	.884
	Formula 2	.372	3	.	.783	3	.073
	Formula 3	.178	3	.	1.000	3	.959

a. Lilliefors Significance Correction

Test of Homogeneity of Variances

Quiet_corner

Levene Statistic	df1	df2	Sig.
.280	2	6	.765

ANOVA

Quiet_corner

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	18.916	2	9.458	1.605	.276
Within Groups	35.353	6	5.892		
Total	54.269	8			

Moisture Content

One-Sample Kolmogorov-Smirnov Test

			Formulasi	Kadar_air
N			9	9
Normal Parameters[a,,b]	Mean		2.00	2.256
	Std. Deviation		.866	.2186
Most Extreme Differences	Absolute		.209	.247
	Positive		.209	.143
	Negative		-.209	-.247
Kolmogorov-Smirnov Z			.628	.742
Asymp. Sig. (2-tailed)			.826	.641
Monte Carlo Sig. (2-tailed)	Sig.		.757[c]	.560[c]
	95% Confidence Interval	Lower Bound	.748	.551
		Upper Bound	.765	.570

a. Test distribution is Normal.

b. Calculated from data.

Oneway

Test of Homogeneity of Variances

Moisture_content

Levene Statistic	df1	df2	Sig.
1.217	2	6	.360

ANOVA

Moisture_content

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.309	2	.154	12.636	.007
Within Groups	.073	6	.012		
Total	.382	8			

Post Hoc Tests

Multiple Comparisons

Moisture_content
Bonferroni

(I) Formulation	(J) Formulation	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
1	2	.1000	.0903	.931	-.197	.397
	3	.4333*	.0903	.009	.137	.730
2	1	-.1000	.0903	.931	-.397	.197
	3	.3333*	.0903	.031	.037	.630
3	1	-.4333*	.0903	.009	-.730	-.137
	2	-.3333*	.0903	.031	-.630	-.037

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

Appendix 10. Test Results of Statistical Analysis Oneway ANOVA Test of Physical Properties of Tablets

One-Sample Kolmogorov-Smirnov Test

			Formulasi	Keseragaman_ Bobot
N			60	60
Normal Parameters[a,,b]	Mean		2.00	499.75
	Std. Deviation		.823	7.034
Most Extreme Differences	Absolute		.221	.111
	Positive		.221	.076
	Negative		-.221	-.111
Kolmogorov-Smirnov Z			1.712	.862
Asymp. Sig. (2-tailed)			.006	.447
Monte Carlo Sig. (2-tailed)	Sig.		.005[c]	.418[c]
	95% Confidence Interval	Lower Bound	.004	.408
		Upper Bound	.007	.427

a. Test distribution is Normal.

b. Calculated from data.

c. Based on 10000 sampled tables with starting seed 2000000.

Oneway

Test of Homogeneity of Variances

Uniformity_of_Weight

Levene Statistic	df1	df2	Sig.
10.674	2	57	.000

ANOVA

Uniformity_of_Weight

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	480.900	2	240.450	5.621	.006
Within Groups	2438.350	57	42.778		
Total	2919.250	59			

Post Hoc Tests

Multiple Comparisons

Uniformity_of_Weight
Games-Howell

(I) Formulation	(J) Formulation	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Formulation 1	Formulation 2	4.050	2.385	.223	-1.85	9.95
	Formulation 3	6.900*	1.378	.000	3.53	10.27
Formulation 2	Formulation 1	-4.050	2.385	.223	-9.95	1.85
	Formulation 3	2.850	2.290	.439	-2.86	8.56
Formulation 3	Formulation 1	-6.900*	1.378	.000	-10.27	-3.53
	Formulasi 2	-2.850	2.290	.439	-8.56	2.86

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

1. Uji Kekerasan

Tests of Normality

	Uji Kekerasan	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Kekerasan	Formulasi 1	.175	3	.	1.000	3	.992
	Formulasi 2	.286	3	.	.930	3	.490
	Formulasi 3	.364	3	.	.800	3	.114

a. Lilliefors Significance Correction

Test of Homogeneity of Variances

Hardness

Levene Statistic	df1	df2	Sig.
2.900	2	6	.131

ANOVA

Hardness

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1.501	2	.751	4.506	.064
Within Groups	1.000	6	.167		
Total	2.501	8			

2. Fragility Test

Tests of Normality

	Formulasi	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	Df	Sig.
Fragility	1		3	.	.923	3	.463
	2	.253	3	.	.964	3	.637
	3	.361	3	.	.807	3	.132

a. Lilliefors Significance Correction

Test of Homogeneity of Variances

Fragility

Levene Statistic	df1	df2	Sig.
2.556	2	6	.157

ANOVA

Kerapuhan

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	3.492	2	1.746	455.504	.000
Within Groups	.023	6	.004		
Total	3.515	8			

Post Hoc Tests

Multiple Comparisons

Fragility
Bonferroni

(I) Formulation	(J) Formulation	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Formulation 1	Formulation 2	.20000*	.05055	.022	.0338	.3662
	Formulation 3	1.41000*	.05055	.000	1.2438	1.5762
Formulation 2	Formulation 1	-.20000*	.05055	.022	-.3662	-.0338
	Formulation 3	1.21000*	.05055	.000	1.0438	1.3762
Formulation 3	Formulation 1	-1.41000*	.05055	.000	-1.5762	-1.2438
	Formulation 2	-1.21000*	.05055	.000	-1.3762	-1.0438

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

Appendix 11. Explanation Sheet to Research Subjects

Saya Selvi Sugiyarti, mahasiswa Fakultas Ilmu Kesehatan, Program Studi Farmasi Universitas Darussalam Gontor, akan melakukan penelitian untuk skripsi dengan judul **"Formulasi Sediaan Tablet Kunyah Ekstrak Biji Alpukat (*Persea americana* Mill.) Dengan Variasi Bahan Pengisi Mannitol Menggunakan Metode Granulasi Basah"** yang bertujuan untuk mengetahui pengaruh variasi bahan pengisi mannitol terhadap sifat fisik pada tablet.

Biji alpukat yang biasanya dianggap limbah ternyata mengandung senyawa metabolit sekunder yang dapat menurunkan kadar kolesterol. Tanaman dalam sediaan obat umumnya dalam bentuk ekstrak bahan alam secara umum memiliki kelarutan yang rendah dalam lemak, maka dibuat inovasi baru pengembangan bentuk sediaan farmasi untuk meningkatkan biovaibilitas yang lebih baik dari sediaan ekstrak bahan alam yaitu salah satunya adalah sediaan tablet kunyah yang ditunjukan untuk menutupi rasa pahit yang ditimbulkan pada kandungan biji alpukat.

Adapun penelitian pada salah satu uji yang saya lakukan adalah uji analisis kesukaan dengan mengamati bentuk, aroma, warna , dan rasa dari tablet kunyah untuk melengkapi data penelitian ini. Partisipasi saudari pada penelitian ini sukarela tanpa adanya pemaksaan dengan cara mengisi lembar formulir uji analisis kesukaan. Jawaban saudari akan saya jamin kerahasiaannya dan hanya akan digunkan untuk kepentingan penelitian.

Demikian informasi ini saya sampaikan. Atas bantuan, partisipasi, dan kesediaan waktu saudari sekalian, saya ucapkan terima kasih.

Appendix 12. Respondent Statement Sheet

LEMBAR PERNYATAAN PERSETUJUAN

(*Informed Consent)*

Saya yang bertandatangan dibawah ini

Nama :.....

Umur :.....

Jenis Kelamin :.....

Prodi/Semester :.....

Bersedia untuk dijadikan responden dalam pengambilan data pada penelitian yang berjudul "Formulasi Sediaan Tablet Kunyah ekstrak Biji Alpukat (*Persea americana* Mill.) Dengan Variasi Bahan Pengisi Mannitol Menggunakan Granulasi basah". Pengambilan data tersebut dilakukan untuk melengkapi data skripsi yang mana menjadi salah satu syarat dalam memperoleh gelar sarjana farmasi.

Persetujuan ini saya buat secara sukarela dan tanpa paksaan dari pihak manapun. Saya telah diberikan penjelasan tentang prosedur uji tersebut. Dengan ini saya menyatakan bahwa saya bersedia berpartisipasi dan memberikan jawaban sejujur-jujurnya.

UNIDA, ...

Peneliti Responden

(Selvi Sugiyarti) ( )

Appendix 13. Favorite Analysis Test Questionnaire Sheet

Lembar Kuesioner Uji Analasis Kesukaan Sediaan Tablet Kunyah Ekstrak Biji Alpukat *(Persea Americana Mill)* dengan Variasi Bahan Pengisi Mannitol Menggunakan Metode Granulasi Basah

Nama : ..... Hari/Tanggal : .....
No. Mhs : ..... Tanda tangan : .....

Dihadapan saudara terdapat 3 formulasi pada tablet kunyah ekstrak biji alpukat. Saudara diminta untuk memberikan penilaian terhadap bentuk dan warna dengan cara diamati, aroma dengan cara indra pencium, dan rasa dengan cara mencicipinya.

Table 1. Uji Analsis Kesukaan (Bentuk, warna, aroma, rasa)

Kode	Warna	Aroma	Tekstur	Rasa	
				Manis	Dingin
F 1					
F2					
F3					

Keterangan :

1 = tidak suka/tidak menarik
2 = kurang suka/kurang menarik
3 = suka/menarik
4 = sangat suka/sangat menarik

Komentar :

.....
.....

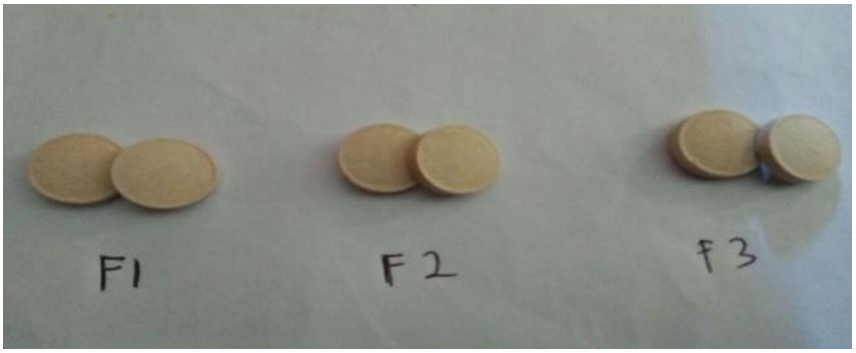
Responden

( )

Appendix 14. Results of Maseration Avocado Seed Extract

Appendix 15. Avocado Seed Thick Extract

Appendix 16. Chewable Tablet of Avocado Seed Extract

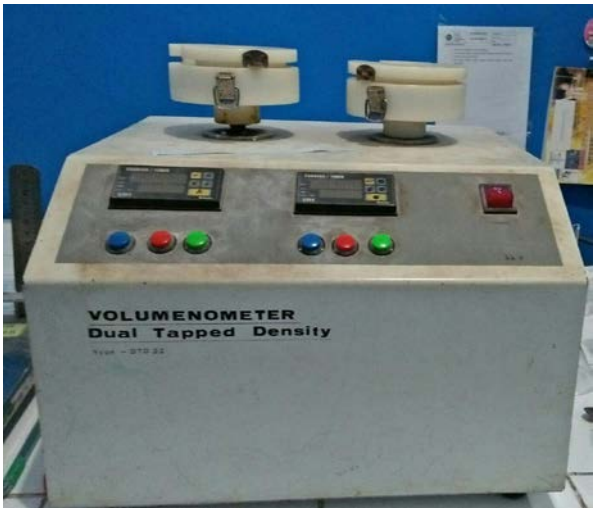


Appendix 17. The instrument of Rotary Evaporator

Appendix 18. The instrument of the Water bath

Appendix 19. The instrument of Flow Time Test

Appendix 20. The Instrument of Tapping Test



Appendix 21. The instrument of Fragility Test

Appendix 22.The instrument of Single Punch Tablet

Appendix 23. Result of Determination Avocado Seeds

PEMERINTAH PROVINSI JAWA TIMUR
DINAS KESEHATAN
UPT MATERIA MEDICA BATU
Jalan Lahor No.87 Telp. (0341) 593396
KOTA BATU 65313

"/18

Nomor : 074/ 346A/ 102.7/ 2018
Sifat : Biasa
Perihal : **Determinasi Tanaman Alpukat**

Memenuhi permohonan saudara :

Nama : SELVI SUGIYARTI
NIM : 362015712265
Fakultas : FAKULTAS ILMU KESEHATAN, PROGRAM STUDI FARMASI
UNIVERSITAS DARUSSALAM GONTOR

1. Perihal determinasi tanaman alpukat

Kingdom	: Plantae (Tumbuhan)
Subkingdom	: Tracheobionta (Tumbuhan berpembuluh)
Super Divisi	: Spermatophyta (Menghasilkan biji)
Divisi	: Magnoliophyta (Tumbuhan berbunga)
Kelas	: Magnoliopsida (berkeping dua / dikotil)
Sub Kelas	: Magnoliidae
Ordo	: Laurales
Famili	: Lauraceae
Genus	: Persea
Species	: *Persea americana* Mill.
Sinonim	: *P. gratissima* Gaertn.
Nama Daerah	: Apuket, alpuket, jambu wolanda (Sunda); apokat, avokat, plokat (Jawa); apokat, alpokat, avokat, advokat (Sumatera).
Kunci determinasi	: 2a-27a-28b-29b-30b-31a84b-88b-89b-91a-109b-119b-120b-128b-129a-135b-136b-139b-140b-142a-143a-146-154b-155b-156b-162b-163a-164b-165a-2a-2.

2. Morfologi : Habitus: Pohon, tinggi ±10 m. Batang: Berkayu, bulat, bercabang, coklat kotor. Daun: Tunggal, bulat telur, bertangkai, letak tersebar, ujung dan pangkal runcing, berbulu, panjang 10-20 cm, lebar 3-10 cm, hijau. Bunga: Majemuk, bentuk malai, berkelamin dua, tumbuh di ujung ranting, benang sari dua belas, ruang kepala sari empat, putih kotor, mahkota berambut, diameter 1-1.5 cm, putih kekuningan. Buah: Buni, bulat telur, panjang 5-20 cm, berbintik-bintik atau gundul, daging buah jika sudah masak lunak, hijau atau kuning keunguan. Biji: Bulat, diameter 2.5-5 cm, keping biji putih kemerahan. Akar: tunggang, bulat, dan berwarna coklat.
3. Nama Simplisia : Perseae Semen / Biji Alpukat.
4. Kandungan : Biji mengandung triterpenoid, flavonoid, tannin, serat, dan pati (amilosa dan amilopektin).
5. Penggunaan : Penelitian.
6. Daftar Pustaka
   - Syamsuhidayat, Sri Sugati dan Hutapea, Johny Ria. 1991. *Inventaris Tanaman Obat Indonesia I.* Departemen Kesehatan Republik Indonesia: Badan Penelitian Dan Pengembangan Kesehatan.
   - Van Steenis, CGGJ. 2008. *FLORA: untuk Sekolah di Indonesia.* Pradnya Paramita, Jakarta.

Demikian surat keterangan determinasi ini kami buat untuk dipergunakan sebagaimana mestinya.

Batu, 05 November 2018
Kepala UPT Materia Medica Batu

Dr. Husin R.M. Drs., Apt., M.Kes.

Appendix 24. Result of Ethical Clearance

KOMISI ETIK PENELITIAN KESEHATAN (KEPK)
Health Research Ethics Committee
FAKULTAS KEDOKTERAN
Universitas Muhammadiyah Surakarta
Faculty of Medicine Universitas Muhammadiyah Surakarta
Komplek kampus 4 UMS Gonilan Kartasura, Telp.(0271)716844, Fax.(0271)724883 Surakarta 57102, email:kepk@ums.ac.id

ETHICAL CLEARANCE LETTER
Surat Kelaiakan Etik
No. 2091/B.1/KEPK-FKUMS/III/2019

Komisi Etik Penelitian Kesehatan (KEPK) FK UMS, setelah menelaah rancangan penelitian yang diusulkan menyatakan bahwa:
Health Research Ethics Committee Faculty of medicine of Universitas Muhammadiyah Surakarta, after reviewing the research design, state that:

Penelitian dengan judul:
The research proposal with topic:

FORMULASI SEDIAAN TABLET KUNYAH EKSTRAK BIJI ALPUKAT *(Persea americana* Mill.) DENGAN VARIASI BAHAN PENGISI MANITOL MENGGUNAKAN METODE GRANULASI BASAH

Peneliti:
The researcher:

Nama/ *Name* : **Selvi Sugiyarti**

Alamat/ *Address* : Universitas Darussalam Gontor

Institusi/ *Institution* : Ilmu kesehatan Universitas Darussalam Gontor

Telah memenuhi deklarasi Helsinki 1975 dan Pedoman nasional etik penelitian kesehatan Departemen Kesehatan RI 2004
Has met the declaration of Helsinki 1975 and national health research ethics Department of Health of the Republic of Indonesia in 2004

dan dinyatakan lolos etik
and ethically approve

Surakarta, 28 Maret 2019
Ketua/*Chairman*,

Prof. Dr. dr. EM. Sutrisna, M,Kes.

Appendix 25. Certificate of Halal Material from LPPOM MUI

مجلس العلماء الإندونيسي
LEMBAGA PENGKAJIAN PANGAN, OBAT-OBATAN DAN KOSMETIKA
MAJELIS ULAMA INDONESIA
Gedung Majelis Ulama Indonesia Jl. Proklamasi No. 51, Lt. III, Menteng, Jakarta Pusat Telp. : 021-3918917, 021-3918890, Fax : 021-3924667
Kampus IPB Baranangsiang Jl. Raya Pajajaran Bogor 16144 Telp. : 0251 - 8358748 (Hunting); Fax. 0251 - 8358747
Website : www.halalmui.org

SURAT KEPUTUSAN

LEMBAGA PENGKAJIAN PANGAN, OBAT-OBATAN DAN KOSMETIKA

MAJELIS ULAMA INDONESIA

Tentang

DAFTAR BAHAN TIDAK KRITIS
(*Halal Positive List of Materials*)

Nomor : SK07/Dir/LPPOM MUI/I/13

Dewan Pelaksana LPPOM MUI, setelah :

MENIMBANG : 1. Bahwa untuk meningkatkan efisiensi dan efektifitas dalam proses pendaftaran Sertifikasi Halal Lembaga Pengkajian Pangan, Obat-obatan dan Kosmetika Majelis Ulama Indonesia (LPPOM MUI) dipandang perlu untuk menetapkan Daftar Bahan Tidak Kritis (*Halal Positive List of Materials*) bagi perusahaan.

2. Bahwa ketentuan yang tersebut di dalam surat keputusan ini dianggap perlu untuk memperlancar kerja dan sistem administrasi yang telah ditetapkan.

MENGINGAT : 1. Surat Keputusan Direktur LPPOM MUI No. SK14/Dir/LPPOM MUI/IV/12 tentang Penetapan Persyaratan Sertfikasi Halal MUI (HAS SERI 23000).

2. Hasil Rapat Pleno Lembaga Pengkajian Pangan, Obat-obatan dan Kosmetika Majelis Ulama Indonesia (LPPOM MUI) tertanggal 8 November 2012.

MEMPERHATIKAN : Program Kerja Lembaga Pengkajian Pangan, Obat-obatan dan Kosmetika Majelis Ulama Indonesia (LP POM MUI) tahun 2013.

مجلس العلماء الإندونيسي
LEMBAGA PENGKAJIAN PANGAN, OBAT-OBATAN DAN KOSMETIKA
MAJELIS ULAMA INDONESIA
Gedung Majelis Ulama Indonesia Jl. Proklamasi No. 51, Lt. III, Menteng, Jakarta Pusat Telp. : 021-3918917, 021-3918890, Fax : 021-3924667
Kampus IPB Baranangsiang Jl. Raya Pajajaran Bogor 16144 Telp. : 0251 - 8358748 (Hunting); Fax. 0251 - 8358747
Website : www.halalmui.org

MEMUTUSKAN

MENETAPKAN : 1. Penetapan pemberlakuan Daftar Bahan Tidak Kritis (*Halal Positive List of Materials*).

2. Surat Keputusan ini berlaku sejak tanggal ditetapkan dan apabila dikemudian hari terdapat kekeliruan akan diadakan perubahan dan perbaikan sebagaimana mestinya.

Ditetapkan : di Jakarta
Tanggal : **30 Januari 2013**

DEWAN PELAKSANA LPPOM MUI
Direktur,

LPPOM

Ir. Lukmanul Hakim, M.Si