A REVIEW ON FORMULATION AND EVALUATION OF SPIRULINA PLATENSIS CHEWABLE TABLET

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ABSTRACT

Among various natural food sources, spirulina contains β-carotene which is higher than other sources that is used to overcome malnutrition. However, spirulina was widely marketed in the conventional form such as capsules and tablets which are less favorable for consumption. In order to increase its acceptability, it is formulated in the chewable tablet using direct press method that meets requirements and is acceptable to the community. This study aims to determine the valid of optimal formula for spirulina chewable tablets through the development of formulas on aerosil 200 (lubricant), and PEG 6000 (glidant). This was an experimental research which was carried out by optimizing the dry extract formula of *Spirulina platensis* using the Simplex Lattice Design (SLD) method with Aerosil 200 as a lubricant and PEG 6000 as a glidant. The tablet's physical properties observed were organoleptic, weight uniformity, tensile strength, friability, disintegration time. The result of physical properties test were analysed using one sample t-test with a 95% confidence level. Then, the optimum formula was conduct to hedonic test. The result of the spirulina chewable tablets optimum formula was consist of 25 mg aerosil 200 (lubricant) and 5 mg PEG 6000 (glidant) with 0.58% weight uniformity deviation, 4.52 kgf/cm^2 tensile strength, 0.74% friability and all the tablets meets specification for disintegration time. The validation results showed that there were no significant differences in the physical properties of the SLD prediction results with the actual results. The hedonic test showed that optimum formula still need to add mask odour to minimize the characteristic aroma and the coating material to beautify physical appearance of spirulina the chewable tablet. The optimal formula for spirulina chewable tablets and fulfilling the quality requirements of traditional medicines is using 25 mg aerosil 200 (lubricant) and 5 mg PEG 6000 (glidant).

Keywords: *Spirulina, chewable tablet, aerosil 200, PEG 6000, simplex lattice design*

INTRODUCTION

Many countries have used Spirulina to overcome malnutrition, especially in children. In Kongo, 10% of children who consumed spirulina have been saved from malnutrition. Spirulina contains high amount of βcarotene which can provide weight gain and increase hemoglobine level. According to Lorenz the food Drug Association (FDA), 3 grams of spirulina powder contains 10 mg β-carotene, which is higher than other sources. In addition, Spirulina is proven to be a safe food for direct consumption that contains essential amino acids; rare essential lipids such as gamma linolenic acid; mineral salts such as calcium, phosphorus, magnesium, zinc, copper, iron, chromium, manganese, sodium, potassium, and selenium; and vitamins such as beta carotene, vitamin A precursors, vitamins B1, B2, B6, B12, C, and E and enzymes. Another fact, spirulina can provide weight gain and improve body function fat-free mass, increase hemoglobin levels and reduce anemia in HIV-infected or immune deficient adult patients within 12 weeks.

is widely marketed in the form of conventional capsules and tablets which are less favorable for consumption. In order to increase spirulina's acceptability, it is necessary to make another dosage form that is chewable tablets. The direct compressing method is the best method to make the tablets and to decrease β-carotene oxidation and not stable to heat. The direct compressing method has shorter process stages than granulation, therefore it is expected that it can maintain its stability. However, the use of direct compressing method requires the formula of intermediate product flowability properties meet the quality target, therefore the weight uniformity and the tablet's dosage can be guaranteed.

This study used Aerosil 200 and PEG 6000 as a combination of lubricant ingredients. Aerosil 200 are able to increase the tablets friability. Aerosil 200 was chosen as a lubricant because it has a free-flowing, anticaking and anti-clogging properties. Aerosil 200 concentration as a lubricant (glidan) is 0.1 - 1.0%. Meanwhile, polyethylene glycol (PEG) is an addition polymer of ethylene oxide and water. PEG 6000 as a lubricant helps to improve the flowability properties and the texture of the tablet's surface at 3% concentration. The combination of the two lubricants is expected to maintain the flowability properties of the products to produce chewable tablet.

In the end, the spirulina chewable tablet must meet requirements and be acceptable to the community. The quality requirements of traditional medicine have several physical properties requirements of tablets that must be fulfilled, including organoleptic test parameters, weight similarities and disintegration time. On the other hand, the physical characteristics parameter of chewable tablets according to the FDA are organoleptic, weight similarities, hardness, fragility and disintegration time of the tablets. Based on these requirements, the formula can be developed based on the tablet's physical

characteristics which consist of organoleptic tests, weight similarities, hardness and disintegration time of the tablet. According to tablet's physical characteristics data, the best formula was obtained by the Simplex Lattice Design (SLD) method and conducted to hedonic test to ensure the chewable tablet dosage form are well received by the community.

BENEFITS OF SPIRULINA TABLET

Rich in many nutrients : Spirulina is packed with nutrients. A single tablespoon (tbsp), or 7 grams (g), of dried spirulina powder, contains:Trusted Source

- **Protein:** 4 g
- **Thiamin:** 14% of the Daily Value (DV)
- **Riboflavin:** 20% of the DV
- **Niacin:** 6% of the DV
- **Copper:** 47% of the DV
- **Iron:** 11% of the DV

It also contains small amounts of magnesium, potassium, and manganese.In addition, the same amount contains only 20 calories and less than 2 g of carbohydrates.Spirulina also provides a small amount of fat — around 1 g per tbsp (7 g) — including both omega-6 and omega-3 fatty acids in an approximately 1.5 to 1 ratio.Plus, the quality of the protein in spirulina is considered excellent and providesTrusted Source all of the essential amino acids that your body needs.Note that it is oftenclaimed that spirulina contains vitamin B12, but this is false. It has pseudovitamin B12, which has notbeen shown to be effective in human.

Bost powerful antioxidant and anti-inflammatory properties : The main component of spirulina is called phycocyanin, which is an antioxidant that also gives it its unique blue color.Phycocyanin can help fight oxidative stress by blockingTrusted Source the production of molecules that promote inflammation and providingTrusted Source impressive antioxidant and anti-inflammatory effects.

Lowers cholesterol and triglyceride level : Spirulina can help lowerTrusted Source total cholesterol, low-density lipoprotein (LDL) or bad cholesterol, and triglycerides, while also increasing high-density lipoprotein (HDL) or good cholesterol, which are all risk factors for heart disease.According to one reviewTrusted Source, spirulina was able to significantly improve these markers in people with metabolic syndrome and related disorders.

Protects LDL cholesterol from oxidation : Fatty structures in your body are susceptible to oxidative damage. This is known as lipid peroxidationTrusted Source, a key driver of many serious

diseases.ResearchTrusted Source found that the antioxidants in spirulina may be particularly effective at reducing lipid peroxidation.In fact, one small studyTrusted Source showed that spirulina supplementation was able to reduce exercise-induced lipid peroxidation, inflammation, and muscle damage in 17 rugby players.

Anti-cancer properties : While more studies are needed, some evidence suggests that spirulina has anti-cancer properties.Research in animals indicatesTrusted Source that it may help reduce cancer occurrence and tumor size in various cancers.

Reduce blood pressure : One review of five studiesTrusted Source found that taking 1-8 g of spirulina per day could significantly reduce both systolic and diastolic blood pressure, especially for people with high blood pressure levels.This reduction is thought to be driven byTrusted Source an increased production of nitric oxide, a signaling molecule that helps your blood vessels relax and dilate.

Effective against anemia : Anemia is fairly commonTrusted Source in older adults, leading to prolonged feelings of weakness and fatigue.A 2020 study found that taking spirulina may improve anemia in pregnant people during the second trimester. In 2021, researchersTrusted Source also found it may also improve iron deficiency in young children.However, more high-quality, recent studies are still needed

Improve muscle strength and endurance Exercise-induced oxidative damage is a major contributorTrusted Source to muscle fatigue.Spirulina may help reduce this, as researchTrusted Source points to improved muscle strength and endurance.In another studyTrusted Source, spirulina supplementation was able to improve oxygen uptake during an arm cycling exercise, with researchers noting that it could act as an ergogenic aid to enhance athletic performance.

Helps in controlling blood sugar level : Animal researchTrusted Source suggests that spirulina could help lower blood sugar levels.However, according to one review of eight studiesTrusted Source on humans, spirulina supplementation in doses ranging from 0.8-8 g daily could significantly reduce fasting blood sugar levels in people with type 2 diabetes.However, there was no significant effect on blood sugar levels after eating or levels of hemoglobin A1c, which is usedTrusted Source tomeasure long-term blood sugar control.

NUTRITIONAL VALUE

PROTEIN :

Spirulina contains up to 70% of highly assimilable proteins (94% of the absorption coefficient). This easy digestibility is particularly important for people who suffer from intestinal malabsorption.The protein content is 2.5 times higher than that of lean meat. It contains all the essential amino acids **or those that** our body needs to take it from. Taken within a strict vegetarian diet, it provides lysine and methionine.

To assess the potential we report the protein content of various foods:

– Eggs 13.3%

– Soybean 43.2%

– Grain 29.2%

– Peanuts 25.3%

– Spirulina 65%

The comparison is clear that the Spirulina constitutes the highest and most powerful source of digestible protein.

CARBOHYDRATES :

Spirulina contains from 10 to 15% of carbohydrates in the form of polysaccharides. The main function of carbohydrates is to provide energy to the body. They provide about 50-70% of the total energy required by the body (1 g of carbohydrate provides 4 kcal of energy). In addition to providing ready fuel, carbohydrates play a vital role in maintaining the proper functioning of the liver, central nervous system, heart and muscle contraction.Due to its composition Spirulina is a great source of quick energy for our body.

LIPID :

The lipids are soluble organic substances in solvents such as alcohol, ether and chloroform, but insoluble in water. Humans are biological membranes of all cells, they are accumulated in the storage tissue as an energy reserve and are found in the blood stream into complex structures known as plasma lipoproteins.The most common sources of lipids are: milk, cheese, olive oil, walnuts, canola, soybean, flaxseed, salmon and mackerel.Lipids are the richest source of energy and humans it is immagazinata as a deposit in order to provide power if you can not get from carbohydrates (1 g of fat provides 9 kcal of energy). A drastic reduction of the consumption of fats leads to weight loss and weakness.

Fat is necessary because:

– Serve as vehicles for the absorption of vitamins as A, D, E and K;

– Help the proper development in the growth;

– Help in the formation of all cell membranes.

Spirulina contains about 7% of lipids of which numerous essential fatty acids. Among these the most significant are the linoleic acid and gamma-linolenic acids which give the Spirulina the caratteristicha to normalize the cholesterol content in the blood.

PIGMENTS :

Spirulina also contains some important natural pigments: chlorophyll, carotenoids and phycocyanin. This mixture of pigments provides an important antioxidant activity, increases the natural defenses, stimulates the formation of red blood cells and promotes muscle activity possessing beta-carotene fifteen times more than carrots.

Chlorophyll : It has an important role in the maintenance hemoglobin in the body. For this reason the Spirulina can be useful in certain anemias (e.g. low concentrations of hemoglobin in the blood).It has beneficial effects on the digestive system. It normalizes the secretion of acid in the stomach by stimulating the bowel peristaltic movements that facilitate the passage of stool.It helps the regeneration of damaged cells.It can increase the efficiency of the heart's pumping function

Phycocyanin : The phycocyanin is the most important pigment in Spirulina and is well contained 14% of its whole weight.This pigment is involved in various functions of the body such as digestion of amino acids, stimulation of the defense system and the construction of the blood cells.

Carotenoids : Spirulina has a high content of natural carotenoids, precursors and the producers of vitamin A,The advantage of carotenoids lies in the fact that are convertible into vitamin A only when the body needs it. In this way it is reduced to a minimum the possibility of an overdose of vitamin A, and then the side effects resulting from it.In addition, carotenoids have a high antioxidant that fights free radicals responsible for cell aging. They contribute to the prevention of cardiovascular disease by inhibiting the damage caused by cholesterol on artery walls. They stimulate the immune system and induce a ‘protective action of the eyes.

VITAMINS :

Vitamins are organic compounds that our body requires in relatively small quantities. Vitamins are used for a proper functioning of the metabolism and the maintenance of general health.Spirulina contains many essential vitamins and among these is vitamin A, vitamin D, vitamin E, vitamin K, biotin, thiamin B1, riboflavin B2, B3 niacin, B5 pantothenic acid, pyridoxine B6, B9 and B12, folic acid, cobalamin .Its exceptionally rich in vitamin B12 is a good ally for vegetarians.B1 and B2 vitamins are anti-stress vitamins.Vitamin B9 plays an essential role in the production of genetic material and in cell growth.Vitamin E acts as an anti-aging.Spirulina contains all these vitamins, healthy keeps the human body and also helps to prevent disturbances arising from their deficiency.

MINERALS :

Minerals are essential elements for life and human health. Spirulina contains a large number and its intake can help in the prevention of various disorders arising from their deficiency.The man needs many minerals essential for proper functioning of all the enzymatic systems and many other physiological functions. Spirulina contains numerous minerals such as, calcium, magnesium, manganese, zinc, and traces of many other minerals.Among the most important are the calcium, content in spirulina well 2 times more than milk.Magnesium promotes the absorption of calcium and helps regulate blood pressure. Iodine and sodium are contained at low levels and therefore is not a problem for those who place a low-salt diet.

SIDE EFFECTS, PRECAUTIONS AND DOSE

SIDE EFFECTS :

An allergic reaction may be possible in those allergic to spirulina.[1] Allergic reactions would include rash or swelling. If you experience side effects, stop using spirulina, and contact your healthcare provider immediately.

Common side effects :

Spirulina is generally safe, but some people have reported the following with its use:

- Allergy
- Headache
- Muscle pain
- Sweating
- Trouble sleeping

Sever side effects :

While severe side effects from spirulina are rare, be aware that the following have occurred:

Anaphylaxis (severe allergic reaction)

- Throat swelling

Immediately stop using spirulina if you experience severe side effects, and call your healthcare provider.

PRECAUTIONS :

People with phenylketonuria (inability to process the amino acid phenylalanine) and individuals with other amino acid disorders (ex., classical homocystinuria (HCU), maple syrup urine disease (MSUD)) may need to avoid spirulina due to its high protein—and thus amino acid—content.

The safety of spirulina in pregnant or nursing people has not been established. Speak with your healthcare provider before using spirulina if you're pregnant, plan to get pregnant, or are breastfeeding.

Please don't give children supplements–including spirulina–without discussing this with their pediatrician first.

Spirulina can sometimes be contaminated with things like lead or other heavy metals (it grows in lakes, after all) or toxins.

DOSAGE :

Always speak with a healthcare provider before taking a supplement to ensure that the supplement and dosage are appropriate for your individual needs.

As a general guideline, don't use more than what's listed on your product's label. Manufacturer recommendations might vary. And there's no recommended "effective" dosage of spirulina. Avoid spirulina if you're allergic or sensitive to it or any of its ingredients.

Studies have used from one to 10 grams a day for up to six months to 19 grams of spirulina a day for up two months, with a relatively good safety profile in people with different conditions.

Again, please do not give supplements to children without first discussing this with their pediatrician.

What happens if I exceed the dosage limit of spirulina

An upper limit or recommended intake is lacking for spirulina. Taking around 40 grams per day for an unknown period has been noted.[1] Contact your healthcare provider for information if you believe you've taken too much spirulina.

FORMULATION AND EVALUATION

Intruments and materials : The instrument used in this study were digital scales (Ohause), a set of extraction tools, evaporators (Heidolph), Buchner orifice, vacuum, mixing machines (Erweka AR 401), and tablet compressing machines (DELTA type VFD007S21A), hardness tester (PUSFIT), friability tester (CS-2), and disintegration tester (BJ-3). The materials used in this study were Spirulina platensis from Musthofa Herbal Klaten, ethanol 96% (Chemic Laboratories), ludipress, aerosil 200, PEG 6000, and saccharine.

Simplicia Identification: Simplicia identification was carried out at the Biology Laboratory, FMIPA, Universitas Ahmad Dahlan.

Spirulina Extraction: The extraction method used the maceration method. The simplicia was taken as much as 1,405 kg, then immersed in 5 L of 96% ethanol. It should be stirred approximately 2 hours then was soaked for 24 hours. The filtrate was filtered using Whattman filter paper with Buchner and vacuum funnel assistance. Filtrate remaceration of the first maceration with 96% ethanol (in the same ratio) 2x. The maserat mixture 1, 2 and 3 was evaporated and then the thick spirulina extract was pulverized by adding aerosil 200 gradualy until it becomes a dry extract.

Chewable tablet formulation: The orientation of lubricants with the lowest and highest concentrations of Aerosil 200 and PEG 6000 was done by inputting data on Design Expert 7.1.5. The result of 8 formulas of spirulina chewable tablet as predicted by SLD can be seen in table 1. All ingredients were mixed using a cube mixer at 50 rpm speed. The tablets were printed indoors with 25 ^{0}C ± 2 ^{0}C temperature and 75% RH ± 5% RH humidity.

and keep them to make the tools not move. The angle of repose is calculated by means.

Table I. Formula of spirulina chewable tablet

COMONENTS		QUANTITY						
		F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**
Spirulina dry extract (mg)	250	250	250	250	250	250	250	250
Ludipress (mg)	245	245	245	245	245	245	245	245
PEG 6000 (mg)	20	25	5	15	25	5	10	15
Aerosil 200 (mg)	10	5	25	15	5	25	20	15
Saccharin (mg)	1	1	1	1	1	1	1	1
Total (mg)	526	526	526	526	526	526	526	526

$$\tan(\propto) = \frac{2h}{d}$$

Note: h = height of the granule formed, d = base's diameter of the granule formed.

The test of material's flowability properties: Flow through an orifice done by one hundred grams of powder was put in the orifice.The flow through an orifice is qualified if it passes through the funnel in less than 10 sec. Angle of repose done by the granules were put into the orifice until it was full or as per the marker. Remove the granule holder in orifice.

The test of tablet quality parameters: Based on BPOM, the physical properties test on spirulina chewable tablets including organoleptic observation, the uniformity of tablet weights, tablet breaking force and tensile Strength, tablet friability test, tablet disintegration time test**.** Organoleptic observations of tablets were included the shape, color, odor, taste, diameter and thickness of the tablets. Test the uniformity of tablet weights were took 20 chewable tablets of spirulina extract and weighed them one by one randomly. Then, calculate the average weight. If each spirulina chewable tablet is 526 mg, the requirement for weight similarity are not more than 2 tablets which each weight deviates 5% from the average weight and no tablet deviates 10% from the average weight.

(F). Input the data in the Tensile Strength formula $\sigma x = 2F / \pi D$

Note: σx: Tensile Strength, F = breaking force, π 3, 14, D: tablet diameter

Tablet friability test were measured based on USP 38, a tablet that weigh equal to or less than 650 mg, the number of tablets tested is all tablets that weigh close to 6.5 g, therefore the number of tablets tested are suitable with the formula (12 tablets). When the tablet is dust free, it is ready to be scaled (Wo). The tablet test used a friability tester with 25 rpm speed for 4 minutes. Then, freed the tablets from dust and scaled (Wt).The formula to calculate the tablets friability is as follows:

$$\text{Friability} = \frac{(Wo - Wt)}{Wo} \times 100\%$$

Tablet disintegration time test used a disintegration tester by putting 6 tablets into a basket-shaped tube, raising the tubes regularly 29-32 times per minute in a water medium with temperature of 35 ° - 39 ° C. Make sure the tablet is destroyed before 15 minutes.

Optimum Formula Verification: The actual physical properties test results of optimum formula tablets based on Design Expert 7.1.5., were compared with the predicted values obtained from the program using SPSS statistical analysis of one sample t-test at a 95% confidence level.

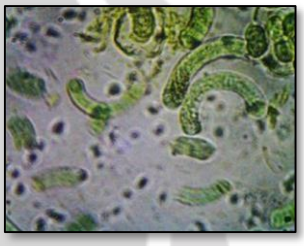
Hedonic Test: The hedonic test was carried out using a random sampling technique with a heterogeneous population of 20 respondents by filling out the questionnaire provided. The inclusion criterion was the condition of the healthy respondent's mouth, while the exclusion criterion was the

condition of the unhealthy respondent's mouth condition, such as stomatitis. Each respondent gets the same opportunity to try the sample. The contents of the questionnaire included age, gender, date of birth, oral condition, appearance, odor, taste responses and suggestions. Appearance, smell and taste responses are grouped from the level of very dislike, dislike, like slightly, like, like very much.

RESULT AND DISCUSSION

Simplicia identification: Simplicia Spirulina platensis was derived from the freshwater cultivation with low minerals content compared to the seawater cultivation, therefore the simplicia does not smell too fishy. The results of macroscopic identification were following the results of parameters in the Certificate of Analysis (COA) Spirulina platensis from Musthofa Herbal Klaten. The microscopic identification of Spirulina platensis can be seen in table II. The results of identification were following refrences which is in filament and helix shape.

Table II. Simplicia macroscopic and microscopic identification of *Spirulina platensis*

Identification		Certification of Analysis	Sample
Microscopic	Odor	odorless	odorless
	Shape		
		filament shape, heli[x10]	filament shape, helix
Macroscopic	Size	99.8% pass mesh 120	Pass 120 mesh
	Color	Dark blue green	Dark blue green
	Taste	Mild, seaweed	Mild, seaweed

Extraction and drying of spirulina simplisia : compound is not stable against heat. 101,19 g obtained The results of maserat were filtered and evaporated to thick extracts were dried and pollinatedwith 94.23 g decrease the ethanol levels. Maserat evaporated in the Aerosil 200. Thus, the yield obtained was 6.707% as water bath at a temperature of 50 ^{0}C since β- carotene seen in table III.

Table III. Rendement of spirulina dry extract powder with aerosil 200 as dryer

Simplisia (gram)	Dry powder (gram)	Rendement (%)
1,405	94.230	6.707

Active material ingredient flowability properties: β- carotene have easily oxidized properties, therefore it should be less exposed to the active materials during the tablets production process. The

direct pressing method was considered as the most efficient method based on production period. Thus, it is necessary to ensure the flowability properties of spirulina dried extract active materials and intermediate product from the mixing results. The powders flowability in tablet compress process will affected to tablet weight and content uniformity of the dosage form.

Test of Powder flow

Flow through an orifice (9.2± 0.36) second

Angle of repose (34.42± 1.98)

Based on table IV, the test result of flow through an orifice on spirulina dried extracts was 9.2 seconds, while the angle of repose was 34.42°. On the other hand, the mixed intermediate product has flowability properties 8.17 second. The flowability properties of dried extract still met the requirement even though it was on the upper limit. But the flowability properties of intermediate product showed better results which can support the tablets making process with direct pressing method. The better flow properties make the granules are easier to compressed into tablets.

The presence of aerosil or colloidal silicon dioxide is small particle size and large specific surface area that gives it desirable flowability that are exploited to improve the flowability of dry powders in a number of processes such as tabletting. On the other hand, grades of PEG 6000 and above are available as free-flowing powders. Polyethylene glycol grades with molecular weights of 6000 and above can be used as lubricants, particularly for soluble tablets. The lubricant action is not as good as that of magnesium stearate but the stickiness may develop to increase the compactness of tablets.

Spirulina chewable tablet critical quality attributes: Organoleptic tests performed included color, odor, taste, thickness and diameter of chewable tablets. Chewable tablets which in formulas 1 to 8 have a moss green color, a characteristic odor of spirulina, a sweet taste, with 0,5 cm thickness and 1,25 cm diameter, so that differences in the amount of aerosil 200 and PEG 6000 did not give significant differences organolepticall

The relationship between Aerosil 200 and PEG 6000 to the response of tablets weight uniformity was shown through the graphic in **FIGURE 1** which showed that the higher concentration of PEG 6000,

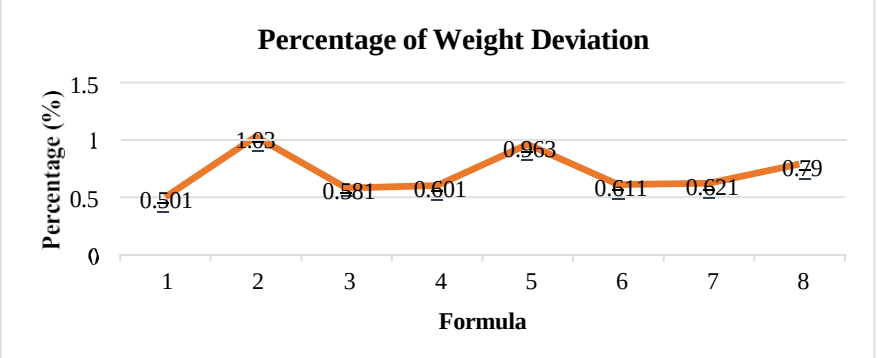


FIGURE 1. Percentage of Weight Deviation

the deviation of tablets average weight was increasing. The higher the concentration of Aerosil 200, the deviation of tablets average weight was getting decreased.

The formula with Variations in the concentration of aerosil 200 and PEG 6000 affected the tablets tensile strength **(FIGURE 2).** The formula that had the highest tensile strength was formula 1 (aerosil 200, 10 mg, PEG 6000, 20 mg), it was 11.065 kp/cm^2. The formula with the lowest tensile strength is Formula 7 (aerosil 200, 20 mg, PEG 6000, 10 mg) with an average value of 3.530 kp/cm^2. The SLD equation for the components of Aerosil 200 and PEG 6000 toward the tablet tensile strength response was equation.

$$Y = 4.89\,(A) + 7.66\,(B) - 2.38\,(A)\,(B) \quad (4)$$

Where, Y is tensile strength response, A is Aerosil 200, and B is PEG 6000.

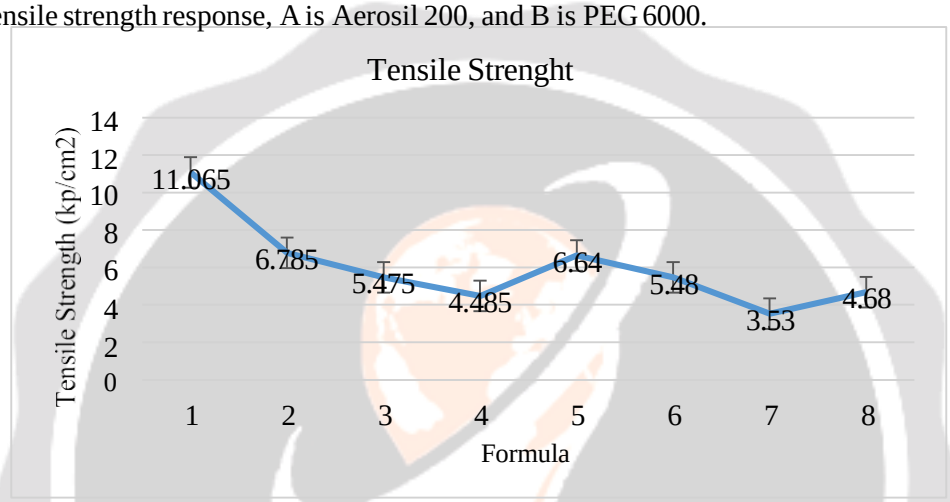


FIGURE 2. Tablet tensile strength

Equation (4) showed that aerosil 200 had smaller positive coefficient value (4,89) compared with PEG 6000 (7.66). It showed that PEG 6000 had a more positive effect in increasing tablets tensile strength compared to Aerosil 200. Aerosil 200 can provide plastic deformation that indicating increased compressibility [13]. It has amorphous properties, ductile and low density, therefore the higher the aerosil, the more difficult tablets were pressed to be compact and solid. PEG with high molecular weight can effectively function as a tablet binder. Therefore, the combination of Aerosil 200 and PEG 600 would decrease the tablets tensile strength as indicated by the negative coefficient value of Aerosil 200 and PEG 6000 (2,38). Figure 2 shows that the higher the concentration of PEG 6000, the higher the value of tablet tensile strength and the higher the concentration of Aerosil 200, then the value of tensile strength is getting decreased.

The results of tablet friability test of 8 formulas are seen in **FIGURE 3.** The formula which had the highest tablet friability was Formula 7 (aerosil 200, 20 mg, PEG 6000, 10 mg) at 1.585%. While The formula which has the lowest tablet friability was Formula 6 (aerosil 200, 25 mg, PEG 6000, 5 mg) at 0.655%. Variations in the concentration of Aerosil 200 and PEG 6000 affected the tablets friability. The SLD equation for the components of Aerosil 200 and PEG 6000 toward the tablet friability

response was equation (5).

$$Y = 0.79 (A) + 0.84 (B) + 1.65 (A) (B) \quad (5)$$

Where, Y is tablet friability response, A is Aerosil 200, and B is PEG 6000.

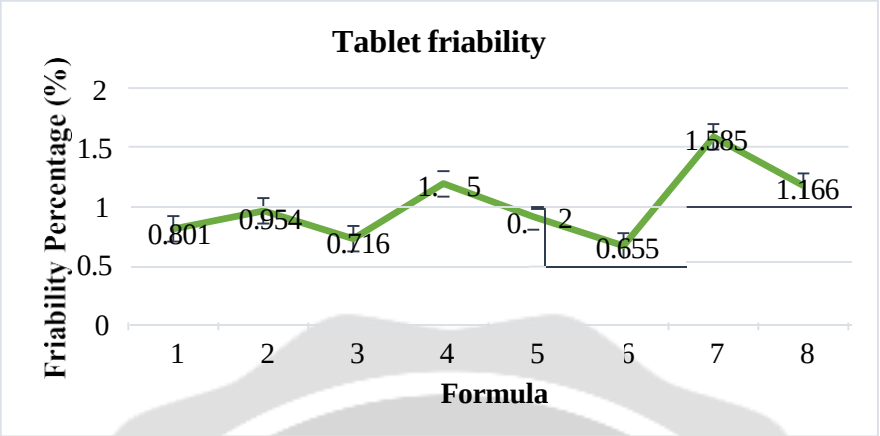


FIGURE 3. Tabletfriability

combination of aerosil 200 and PEG 6000 is able to increase the tablets friability. The relationship between Aerosil 200 and PEG 6000 on the tablet's friability response is shown in figure 3 which shows the combination of concentration of Aerosil 200 and PEG 6000 with the same amount that will increase the percentage of tablets friability.

The tablet disintegration time of the eight formulas has met the requirements, that the tablet is completely dissolved without leaving the tablet core on the disintration tester. When the tablet is not completely chewed by the patient, that can cause gastrointestinal obstruction. To prevent that matter, the tablet disintegration time should be as short as possible. Optimum formula verification: The optimum formula of *spirulina* chewable tablet was obtained using the *simplex lattice design* method from *Design Expert* with optimized physical response test parameters which were tablet weight uniformity, tablet hardness, tablet friability and tablet disintegration time. The independent variables used were concentration of aerosil 200 and PEG 6000. The optimum formula was determined based on the target response which wanted to be achieved and the degree of importance. There were several options of target determination; *minimize, maximize, target, in range and equal to* and also *lower* and *upper limit*. The degrees of *importance* were determined from the very unimportant (+) to the most important (+++++). The most important degree showed the most important response that most influenced the optimum formula thus the results were close to expectation.

The predicted results of the SLD method provi ded a solution of 1formula consisting of a combination of 25 mg Aerosil 200 and 5 mg PEG 6000. The optimum formula of produced spirulina chewable tablets from the SLD method expert design program 7.1.5 were

Table V. The significant level of differences between SLD optimum formula prediction against actual result

Responce	SLD prediction	Actual result	Sig. (2 tailed)
Weight uniformity (%)	0.619	0.581	0.659
Tensile strength (kp/cm^2)	4.89	4.52	0.142
Tablet friability (%)	0.795	0.738	0.089

Formulated and tested for physical properties

The results of the actual physical properties test conducted by the researcher were verified by comparing them with the value of predicted SLD response using *one-sample t-test* version 15.0 with 95% confidence level. The significant results of the *one-sample t-test* showed the comparison between the predicted and experimental results can be seen in table V

Table V shows the comparison of experiment and predicted SLD responses, the response data were all normally distributed. The value of weight uniformity, tensile strength, friability had a significance value that is greater than 0.05, thus the data are not significantly different. Based on the obtained results, it could be concluded that there is no significant difference between the predicted parameter values and the results of the validation therefore the developed SLD equation can be used to prepare the valid tablet formula.

Hedonic test: Hedonic test of tablet appearance, taste and, aroma was conducted to the optimal formula aerosil 200, 25 mg and PEG 6000, 5 mg. The test results of the tablets appearance showed as much as 65% of respondents expressed like slightly and 35% expressed likes. Some respondents expressed like slightly was due to the lack of attractive colors of chewable tablets that there is no additional coating material. Another result showed that 100% respondent expressed that they liked the taste of chewable tablet. The sweet flavor of the saccharine fitted well and made the taste easily acceptable for the respondents when it was chewed. The last result of hedonic test was about the aroma of chewable spirulina tablets. Fifteen percent of respondents expressed dislikes, 75% expressed like slightly and 10% expressed likes. This were caused by the tablet has not added a mask odor to the formula, so that the distinctive smell of spirulina was still being smelled. Based on the result, it is necessary to add mask odor to minimize the characteristic aroma and the coating material to beautify physical appearance of spirulina the chewable tablet.

CONCLUSION

The SLD predicted results provide a solution of an optimum formula consisting of a combination of 25 mg aerosil 200 and 5 mg PEG 6000. The value of weight uniformity, tensile strength, friability and tablets disintegration time have a significance value that is greater than 0.05 thus the data are not significantly different so the results of SLD equation can be used to prepare the valid formula.

Spirulina is generally considered safe for human consumption supported by its long history of use and its favorable safety profile in animal studies. However, rare cases of side effects have been reported. Additional preclinical and clinical studies should also be taken into consideration. Finally, quality control in the growth and processing of *Spirulina* to avoid contamination is mandatory to guarantee the safety of *Spirulina* products.

In addition, our understanding of the underlying mechanisms for *Spirulina*'s activities is still limited. Future studies to identify the active ingredients in *Spirulina* and uncover the mechanistic insights into its therapeutic effects will provide the basis for developing new drugs for preventing or treating diseases, such as cardiovascular diseases and hypercholesterolemia.

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