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APPLICATION OF BUTTERFLY PEA LEAVES EXTRACT ON DIABETIC PATIENT

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Abstract: Patients with Diabetes Mellitus have been expanding every year due to the population growth, urbanization, aging, and increasing prevalence of obesity. Butterfly Pea Leaf (BPL) also known as Clitoria ternatea L. has been investigated for having anti hyperglycemic activity toward the blood glucose level of alloxan-diabetic mice. The present study was conducted to produce sachets containing powder product from BPL extract through spray-drying method in order to increase convenience of storage and distribution process. Maltodextrin become a parameter in spray-drying method. Based on preliminary research, the most suitable concentration of maltodextrin was 10%. Sachets from BPL extract were distributed to 10 diabetic patients from Puskesmas Pulo Armin, Bogor. All patients were treated by sachets from BPL extract for around five months. The treatment shows the decreasing level of blood glucose from diabetic patients as well as it could keep the blood glucose level remain stable in normal range without leading to hypoglycemia.

Keywords: Diabetes Mellitus, Butterfly Pea Leaf, Maltodextrin, Blood Glucose Level, Antihyperglycaemic, Hypoglycaemia.

1. Introduction

International Diabetes Federation Western Pacific (2013) stated that there were 382 million people who lives with diabetes mellitus worldwide in 2013, with 138 million people live in western pacific area, on the condition 46% people are undiagnosed. Indonesia, as one of the countries located in western pacific, is one of the top ten countries for number of people with diabetes mellitus (20-79 years old) with total of 8.5 millions who suffers diabetes mellitus. It is predicted that there will be 55% more patients or 592 million people living with diabetes mellitus in 2035 worldwide.

Based on the facts above, researchers are trying to find the best way to find cures and also supplements to treat diabetic patients. Medicines and therapies have reduced diabetes until some extent (Grover et al., 2002; and Rajagopal and Sasikala, 2008), but besides they are expensive, they have also a lot of side effects. Therefore, an affordable and easy-to-get medicine or supplement is needed to treat diabetes mellitus.

Herbal medicine is one of the answer to attain affordable medicine or supplement nowadays in modern medicine. The utilization of herbs and plants for therapeutic or medicinal value can be done by using varieties of chemical substances coming from leaves, flowers, stems, berries, and roots of the herbs or plants. Butterfly pea (*Clitoria ternatea L.*), for instance, have been researched as a plant that has been used in many treatments for many diseases, including diabetes mellitus (Daisy et al., 2009). Butterfly pea is also easy to be cultivated because of its high adaptability skill, especially in tropical countries (Conway, 2001).

The study about extraction of Butterfly Pea Leaf has been done previously in order to find the most optimum temperature, time, and pH condition. Those aspects are truly affecting the result of extraction. It was extracted to release the active compound (flavonoids and phenols) which is believed could treat diabetes mellitus. The most optimum time of first phase of extraction was 2 hours with 50^{o}C of the solution in pH 5.5. The optimum temperature responsible for the contents within butterfly pea

leaf extract substance, which are flavonoids and phenols. Then, the extract should be centrifuged for 20 minutes in 20^{o}C to produce final result of extraction (Tunggal, 2012), Pandjaitan et.al (2014).

Furthermore, the next study done by Surya (2013), Pandjaitan et,al (2014) about the powder form of BPL extract found that there is no significant difference or loss of flavonoid and phenol content in powder form during a 4-week time span. In other words, solid state of butterfly pea extract is proven could maintain the stability of active ingredients. It other words, the powder form is better than the aqueous solution in term of stability of active ingredients and life-span. The powder form of BPL extract produced through spray-drying method. Spray-drying method could transform the extract solution into a powder form. One of the purpose of producing powder form of the extract was to improve the convenience of the storage, distribution, and consumption.

To ensure the benefits of the product, researchers have applied a medication of BPL extract to treat diabetes mice or rats. Rats that were treated with BPL extract had shown better activity than rats that were treated with butterfly pea flowers (Kumar et al., 2010). Furthermore, Pangestuti (2014) did acute toxicity study of BPL extract on mice resulted with the value of the lethal dose was 50 within 19380.7 mg/kg body weight. According to the result, researcher stated that BPL extract was classified as a non-toxic compound. In the same year, besides Pangestuti, Steven (2014) has also proved another major benefit of BPL extract which can decrease blood glucose level and increase insulin level. In addition, according to the blood hematology and kidney function tests, the consumption of BPL extract had no effect to the blood hematology and the function of kidney.

In vitro and vivo experiments have been done, thus continuously in vivo experiment is needed to be carried out. The target is to treat 10 diabetic patients from one of the clinic (Puskesmas) in Bogor. The effect of BPL extract on diabetic patient will be observed for 20 Weeks.

2. Literature Review

2.1. Diabetes Mellitus

Diabetes mellitus is a metabolic disease with a condition of hyperglycaemia – a condition where blood glucose level is elevated which resulted at a high level. It is usually associated with the deficiency in the secretion insulin or the insulin does not properly function. Diabetes could lead to severe complications in the body, making a very serious health threat. Common symptoms are: frequent urination, increased thirst, blurry vision, weight loss, and infections (Ekoe et al., 2008).

2.2. Butterfly Pea Leaf

Butterfly pea leaf contains lots of flavonoids, phenols, and other substances, such as 3 monoglucoside, 3-rutinoside, 3-neohisperidoside, 3-o-rhamnosyl Glycoside, kaempferol-3-o-rhamnosyl, aparajitin, beta-sitosterol, and essential oil (Morita et al., 1997). Medicinal values can be gained from butterfly pea leaf extract. It has been used for some treatment for instance body aches, infections, urinogenital disorders such as burning sensation in urinary tract, and as antidote to animal stings or snake bites (Patil and Patil, 2011).

Leaf extract also showed strong antibacterial activity, antimicrobial activity. Daisy et al. (2009), Tunggal (2012) and Pandjaitan et.al (2014) also reported that butterfly pea leaf extract exhibits anti hyperglycemic effect in mice. Moreover, aqueous leaf extract of butterfly pea has antioxidant potential (Rao et al., 2009).

2.3. Flavonoids

Flavonoids are categorized into subclasses based on its chemical structure or characteristic. Only one or more individual flavonoids within the subclasses predominate in a specific food. All compounds do not occur together.

Flavonoids are infamous for anti diabetic efficacy (Brahmachari and Gorai, 2006). Numerous studies have been carried out to explore the hypoglycaemia effect of butterfly pea leaf as a treatment for diabetes (Matsui et al., 2006; and Daisy et al., 2009). The studies showed that the utilization of flavonoid could avoid the glucose absorption or to improve glucose tolerance, so beneficial effects against the disease manifestation are exerted.

Flavonoids also act as insulin secretagogues or insulin mimetic. It influences pleitropic mechanism to decrease diabetic complications. It increases the uptake of glucose in peripheral tissue and regulates the activity rate-limiting enzymes that involved in carbohydrate metabolism pathway (Brachmachari, 2011). Flavonoids have the ability to preserve β-cell function by reducing oxidative stress-induced tissue damage and against the insulin resistance progression to type 2 diabetes.

2.4. Spray-Dried Butterfly Pea leaf Powder and Its Stability

Spray drying process was evaluated by Surya (2013) to produce powder from Butterfly Pea Leaf extract. Carrier agent was added to the Butterfly pea leaf extract. The most suitable carrier agent for spray drying was 10% of concentration from maltodextrin. It results percentage of 66.8%, flavonoid percentage and phenol percentage were about 80%. After 4 weeks storage the content of the extract was remain stable.

2.5. Maltodextrin

Maltodextrin is a starch hydolysates, a non-sweet saccharide polymer that consist of α-D-glucose units linked primarily by (1→4) glycosidic linkages with dextrose equivalent (DE) of less than 20. The general formula of maltodextrin is $[(C_6H_{10}O_5)_nH_2O]$. Maltodextrin is fully soluble carbohydrates of low bulk density in general, it is similar to starch in their metabolic pathway, and therefore in some application it is suitable for diabetics (Kennedy et al., 1995).

Maltodextrin usually serves as coating agent as the particle crust in drying methods. The addition of maltodextrin results in high soluble product (Desai and Park, 2004). The solubility depends on the DE and the hydrolysis method. High DE value gives similar solubility, bulking and body characteristic to corn syrup. While low DE values have binding properties of starch and more effective as fat binders. Moreover, it is flavourless, thus it does not mask the flavour of the product (Morris, 1984). Thus, maltodextrin has been used in various processed foods due to its unique properties.

2.6. Blood Glucose Test

Weekly fasting blood glucose tests were proved the effect from Butterfly Pea leaf extract to the blood glucose levels of diabetic patients. The treatment was success fully decreased the majority of blood glucose levels of diabetic patients including patients who served as healthy control. Their blood glucose level were remained stable in the normal range. It did not lead to hypoglycaemia. The consumption of flavonoid in sachet from Butterfly Pea Leaf extract is believed could avoid the glucose absorption or to improve glucose tolerance. The increase of insulin levels of diabetic patients justify the statement.

3. Methods

This research consist of two methods which are experimental procedure and medical application. The experimental procedure aims to produce good quality of powder product from BPL extract. It is divided into two phases; extraction and spray drying. The second step which is medical application aims to observe the effect of BPL extract consumption to blood glucose level of diabetic patients. The figure below shows the main procedure of the research.

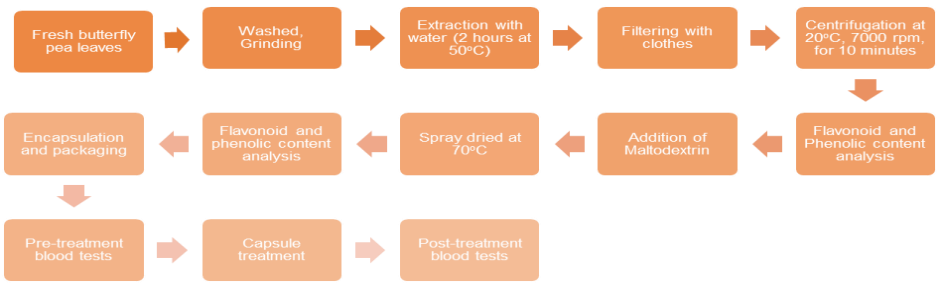

Figure 1. Main procedure of the research

3.1. Experimental Procedure

Consideration in selecting raw material is an important thing to produce good quality product. To initiate the experiment, first good quality of fresh BPL were chosen and removed from the stalks. After being removed, BPL were washed thoroughly with water to ensure the hygiene. BPL were cut into smaller pieces and grounded using a blender with water in ratio 1:3. The next step is extraction.

The extraction process was conducted for 2 hours at 50^{o}C and homogenized with homogenizer to keep the temperature in the range as well as to produce homogenous solution. If the temperature went to high, it would break down the content of BPL and affect the result of end product. After 2 hours, the solution was filtered with clothes to separate the liquid with supernatant. The extraction process does not finish yet. Centrifugation was conducted in a certain time and speed in order to obtain pure extract from BPL. In this research, centrifugation was done at 20^{o}C, 7000 rpm, for 10 minutes. The extract of BPL was then tested for its phenolic and flavonoid compounds. The second phase of experimental procedure is spray drying. Spray drying was conducted to produce powder product of BPL extract. Before the process has begun, 10% of maltodextrin was added to the extract.

3.2. Treatment program

The treatment will be done in 20 weeks.

1. Before the treatment begins, blood glucose test is done and body weight is measured.
2. Each patient will be given sachet of butterfly pea leaves extract powder twice a day: before lunch and before dinner. The powder is diluted in 200cc water. A supervisor for daily taking will check whether the patient has consumed the extract.
3. The treatment is divided into 4 parts:
   a. Part I (Week 1 – week 3) : Extract powder (2 sachet) + medicine
   b. Part II (Week 4 – week 6) : Extract powder with higher dosage than part I (3 sachet) + ½ dosage of the medicine
   c. Part III (Week 7 – week 20) : Extract powder with higher dosage than part II (4 sachet)
   d. Part IV (Week 21 – week 25) : no extract powder or medicine is given

3.3. Flavonoid content analysis

This test was conducted in the chemistry laboratory in Swiss German University and divided into several steps which are:

1. There were two kind of sample must be analysed on this research which are liquid and powder extract. The Butterfly Pea Leaf liquid extract was diluted in distilled water with a ratio 1:24. As for measuring total flavonoid content in the powder sample, 1 gram of powder was first dissolved in 100 ml of distilled water and homogenized with magnetic stirrer for 10 minutes, then followed the same steps as the measurement of liquid samples.
2. In a test tube, 0.5 ml of sample were mixed with 1.5 ml of methanol and then brought to a vortex. For the blank sample, 0.5 ml of sample was substituted with 0.5 ml of distilled water.
3. 0.1 ml of aluminium chloride 10% added and mixed using a vortex.
4. 0.1 ml of 1 M potassium acetate added followed by the addition of 2.8 ml of distilled water, and put into a vortex to make homogenous solution.
5. The mixtures will be incubated for 30 minutes at room temperature and measured at 415 nm using a UV-Vis Spectrophotometer.

4. Results And Discussion

4.1. Fasting Blood Glucose Levels Analysis

People with high level of blood sugar are diagnosed with Diabetes Mellitus. The defficiency of pancreas in producing insulin or the condition where insulin does not properly function are the cause of Diabetes Mellitus. Normal fasting blood glucose level ranging from 70-120 mg/dL. All patients were treated with sachet from Butterfly Pea Leaf extract and fasting blood glucose test were done every 2 weeks with glucometer to see the effect of the sachet . Fasting blood gluoce test considered as an simple way to

complete the observation of patients blood glucose levels during the treatment. Patients were asked to fasting at least 5 hours before the test to maximize the result. Blood glucose levels of each patient can be seen in Figure 2.

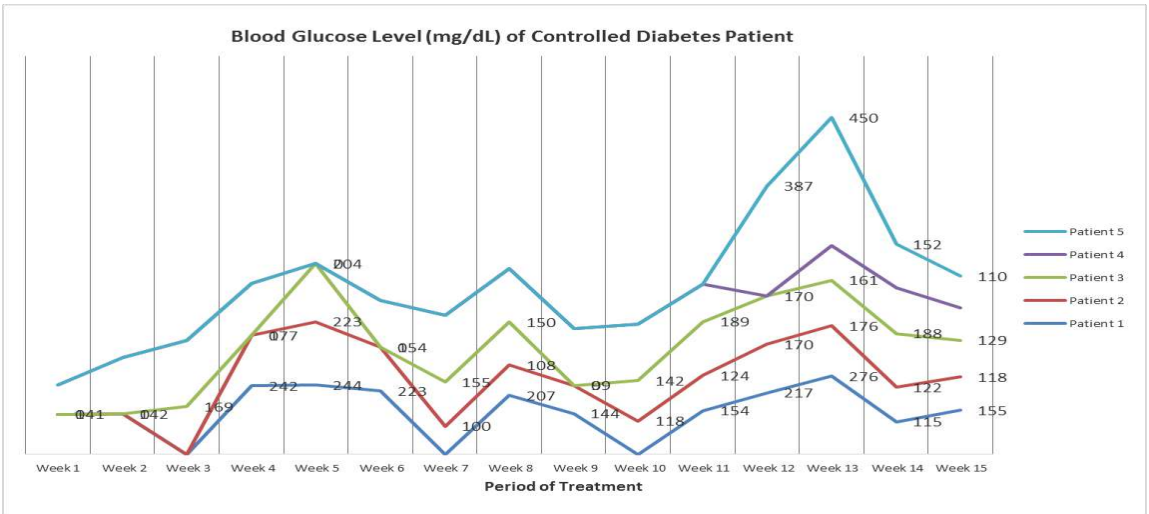

Figure 2. Controlled Diabetes Patient

The graph above illustrates the blood glucose level of controlled diabetic patient (5 People) within 15 weeks. It can be clearly seen that the level of blood glucose is remaining stable without any consumption of medicine including the Butterfly Pea Leaf extract. The result of blood glucose test authenticates the total recovery of patients from diabetes.

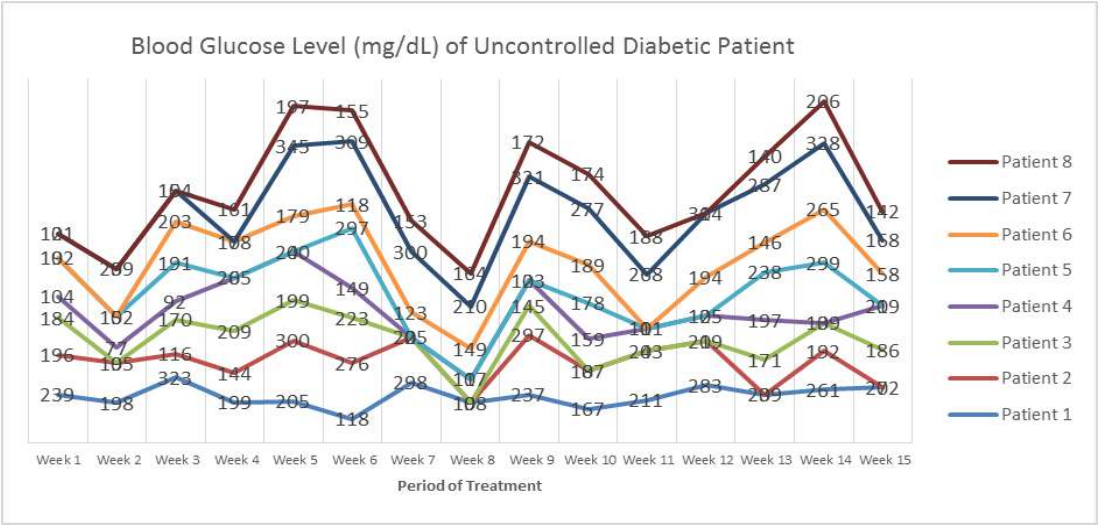

Figure 3. Uncontrolled Diabetes Patient

Uncontrolled Diabetic Patient (8 People) grouped as a patient who is regularly consumed a medicine from the doctor, but the blood glucose level remains out of the normal range (70 – 120 mg/dl). Treatment with Butterfly Pea Leaf extract apparently also did not show the decrease of blood glucose level. From this case, it can be concluded that the patient needs another kind of treatment that can lower the blood glucose level, furthermore could repair and optimizing the work of the pancreas.

From Figure above, it can be clearly seen that blood glucose level of each patient from the first week until last week of the treatment are fluctuative. It proves that the treatment of sachet from Butterfly Pea Leaf extract affect their blood glucose level and did not cause hypoglycaemia. After the treatment, fasting blood glucose level of 5 patients remained stable in thenormal range. The

consumption of sachet from BPL extract can be assumed could replace the medicine that the patients already consumed.

Figure 2 and 3 shows the average of fasting blood glucose levels of diabetic patients during the treatment. It reflects the consumption of flavonoid in capsules from Butterfly Pea Leaf extract succesfuly decreased blood glucose levels. Flavonoid is believed could avoid the glucose absorption or to improve glucose tolerance.

Flavonoids also act as insulin secretagogue or insulin mimetic. It influences pleiotropic mechanism to decrease diabetic complications. It increases the uptake of glucose in peripheral tissue and regulates the activity rate-limiting enzymes that involved in carbohydrate metabolism pathway. Flavonoids have the ability to preserve β-cell function by reducing oxidative stress-induced tissue damage and against the insulin resistance progression .

5. Conclusion

The used of sachet as the end product of BPL extract is believed could maximize the convenience of distribution, storage, and consumption. Those products from BPL extract were distributed to 10 diabetic patients in Puskesmas Pulo Armin, Bogor. All patients were treated for 20 weeks and their blood glucose level were tested every two weeks in order to observe the blood glucose between before, during, and after the treatment. As a result, the consumption of sachets from BPL extract affect the blood glucose level of diabetic patients. It successfully decreased the majority of diabetic patients. Besides, it also keep the blood glucose level remain stable in normal range without leading to hypoglycemia even though patients consume it continuously. Different with some patients who still have blood glucose level higher than the normal range but during the treatment, the blood glucose level gradually decreased to the normal range. Every person has a different way and a different period of time to react with foreign materials in this case BPL extract. Thus, some people might needed a longer period to adapt to BPL extract until it can successfully fall the blood glucose level into the normal range.

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