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#### ORIGINAL RESEARCH



# ALTERNATIVE COMPLEMENTARY SERVICES OF SAPONIN TOWARD REDUCTION OF FASTING BLOOD SUGAR LEVELS AND 2 HOURS POST PRANDIAL IN TYPE II DIABETES MELLITUS PATIENTS

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ABSTRACT	Keywords
Background - Diabetes mellitus (DM) is a metabolic disorder disease characterized by hyperglycemia. DM disease control aims to reduce mortality and morbidity, prevent complications and improve the quality of life of DM patients. DM treatment is carried out in a lifetime, requires large costs, causes mild to dangerous side effects, and requires a high level of medication adherence. Therefore, it is necessary to conduct an intervention that is cheap, easy to obtain and minimal risk. Objective - To prove that the administration of saponins has an effect on reducing fasting blood sugar levels and 2 hours post prandial in patients with type 2 DM. Methods - From 37,195 journals accessed full text, 18 journals were obtained from the screening results that met the inclusion criteria for a systematic literature review with the design used in this study used a randomized control trial design, quasi-experimental, and pre-clinical trial published in the 2015-2020 range. The subject of this study is related to saponins, fasting blood glucose, 2 hours pp in patients with type 2 diabetes. Results - Giving saponins to aloe vera plants with doses in the range of 300-500 mg/day is more effective in reducing fasting blood sugar levels with p value= 0.000 and effect size 1.42 (very strong) compared to other plants. Meanwhile, the saponin content in cherry plants with a dose of 15 grams was more effective in reducing fasting blood sugar levels 2 hours post prandial in patients with type 2 diabetes mellitus compared to other plants with p value= 0.000 and effect size 2.85 (very strong). Conclusion - Based on the results of the analysis of the research subjects, that the saponin intervention was very effective in reducing fasting blood sugar levels and 2 hours of PP.	Saponins, Blood sugar, Type 2 DM.

#### INTRODUCTION

Diabetes Mellitus (DM) is a chronic disease characterized by blood glucose levels exceeding normal and disturbances of carbohydrate, fat and protein metabolism caused by a relative or absolute deficiency of the hormone insulin.<sup>(1)</sup> If this is left uncontrolled, acute metabolic complications and long-term vascular complications can occur.<sup>(2-3)</sup>

Diabetes mellitus is a metabolic disorder disease characterized by

hyperglycemia, impaired carbohydrate, fat and protein metabolism caused by defects in insulin secretion or decreased receptor sensitivity. (4)

According to the American Diabetes Association (ADA), diabetes mellitus is classified into several types, type 1 diabetes mellitus and type 2 diabetes mellitus. (5-6) Approximately 90% of patients with diabetes have been diagnosed with type 2 diabetes and are associated with older age, obesity, family history of DM, history of gestational diabetes, impaired glucose physical tolerance (IGT). inactivity, impaired glucose (IGF), and fasting ethnicity.(7)

Diabetes Mellitus (DM) is one of the ten non-communicable diseases. top diabetes mellitus is the cause of mortality of 1.5 million people in the world in 2012. Chronic hyperglycemia in diabetes mellitus contributes to high mortality and morbidity due to cardiovascular disease, kidney disease chronic and cerebrovascular disease. According to data from the World Health Organization (WHO) in 2016 shows that around 150 million people suffer from DM worldwide, and this number will double by 2025.(2) In Southeast Asia, the mortality rate due to DM reaches 115.3/100,000 people in the population aged over 20 years. In Indonesia, the prevalence pattern of DM tends to increase, from 10 million DM cases in 2015 it is predicted to reach 21.3 million in 2030. In Indonesia based on diagnosis or symptoms it is 2.1% and the highest prevalence of DM is at the age of 55 to 65 years at 4,8%.(8)

The International Diabetes Federation (IDF) predicts an increase in the number of DM patients in Indonesia from 9.1 million in 2014 to 14.1 million in 2035. (9)

Factors causing diabetes mellitus include family history of diabetes, physical activity, age, gender, comorbidities, alcohol consumption, body mass index, smoking

habits, drug consumption, and food intake. Food factors as the main factor that has a significant effect on the incidence of diabetes mellitus.<sup>(10)</sup>

DM disease if not properly managed would contribute greatly to the emergence of heart disease and blood vessels. The results of the study concluded that hypertension in diabetes in Indonesia increased from 15% to 25% and 40-50% of heart disease patients were diabetic. Patients with diabetes mellitus have a 2 times greater risk of developing coronary heart disease and cerebral vascular disease, are 5 times more likely to suffer from diabetic ulcers, 7 times more likely to develop terminal renal failure, and 12 times more likely to experience blindness due to retinal damage than patients with diabetes mellitus. non-diabetic.(11) Thus, in addition to DM affects the quality of life also increase mortality in diabetic patients, the health care costs for patients with diabetes mellitus on average three times higher than other patients.<sup>(8)</sup>

DM disease control aims to reduce mortality, morbidity due to Diabetes Mellitus and also prevent complications of diabetes and which is no less important is to improve the quality of life of DM patients. This is also in accordance with the latest guidelines from the American Diabetes Association (ADA) which emphasize the need for "patient-centered" DM management with a quality of life approach, blood sugar control and prevention of complications. (6)

The five main pillars in the management of Type 2 Diabetes Mellitus are education, medical nutrition therapy, physical exercise, and pharmacological interventions. Management of Diabetes Mellitus begins with non-pharmacologic therapy, namely the regulation of eating and physical exercise. (12-13) If blood glucose levels are not on target, pharmacological intervention with oral hypoglycemic drugs

(OHO) and or insulin injections is carried out. (14)

Treatment of diabetes mellitus is divided into pharmacological and nonpharmacological treatment. Pharmacological treatment consists of antidiabetic drugs which are divided into several groups, such as sulfonylureas (glibenclamide) which have a mechanism of stimulating insulin release. The treatment of diabetes mellitus is carried out for a long period of time, namely for life and requires sufficient cost. (6, 15) In addition, public concerns about the side effects of drugs taken for a long time can affect the level of medication adherence, such as side effects caused by taking metformin, namely gastrointestinal disturbances, such diarrhea, nausea, and vomiting. In addition, serious effects of metformin in the form of lactic acidosis which can accumulate in the blood vessels which eventually causes muscle pain, decreased blood pressure, fast heart rate, difficulty breathing and even death. (16-17) This problem can trigger potential difficulties in controlling the increase in the incidence of diabetes mellitus, therefore it is necessary to conduct cheap and easily available interventions.

The use of traditional complementary medicine is generally considered safer than the use of modern medicine. One of the plants that can be used as a complementary treatment for diabetes a plant mellitus is that contains phytochemicals, one of which is saponins, such as binahong, moringa, cherry, aloe vera and various kinds of plants that are easy to use. obtained. In these plants there are various phytochemical compounds that have been used, one of which is in lowering blood sugar levels, but in these plants the content of saponins is more in number than other compounds. The content of saponins in these plants can be used to treat burns, typhoid, intestinal inflammation, canker sores,

vaginal discharge, swelling of the liver, swelling of the heart, increase vitality and endurance and lower blood sugar levels.<sup>(18)</sup>

The decrease in blood sugar levels by saponin compounds because saponins are a natural glycoside bound to steroids or triterpenes. Saponins have insulin-like activity, can inhibit lipolysis, increase glucose uptake by adipose cells. A study shows that saponin compounds can improve insulin resistance. (19)

Saponins are efficacious as antidiabetic because they act as inhibitors of the -glucosidase enzyme. -glucosidase is an enzyme that plays a role in converting carbohydrates into glucose. Thus, if the -glucosidase enzyme is inhibited, the blood glucose level will decrease, causing a hypoglycemic effect (decreased blood sugar levels). (20)

In addition, saponins increase the permeability of the small intestine, thereby increasing the uptake of substances that are actually poorly absorbed and causing loss of normal intestinal function. The effect of saponins on the composition of cell membranes can inhibit the absorption of smaller nutrient molecules, which should be absorbed quickly, such as blood glucose. Disrupted cell membrane structure is thought to also cause disturbances in the glucose transport system so that there will be obstacles to glucose absorption. (21)

Several studies related to the benefits of saponins to reduce blood sugar levels, such as the study conducted by Leone (2018) using a 20 gr moringa leaf powder supplement containing saponins in type 2 diabetes mellitus patients obtained results showing that the administration of moringa leaf supplements decreased blood glucose higher than the control group who only received drug therapy. with p value = 0.001. (22)

Based on the description above, it is necessary to study literature review on

interventions saponin in lowering fasting blood sugar levels and postprandial blood sugar levels in people with type 2 diabetes Study literature review is very important as a basis for new drug research with the potential to determine or analyze the types of plants with the highest content of saponins or the most effective in lowering blood sugar levels. Saponins were chosen as an alternative intervention because saponins are known as -glucosidase inhibitors which can be included in one of six classes of antidiabetic drugs. Saponins which are included in this class of antidiabetic drugs make saponins have advantages over other phytopharmaceuticals in their position as antidiabetic drugs. Due to the identification of saponins in this group, the saponin intervention has a strong basis to be carried out for people with diabetes mellitus. In addition, other phytopharmaceuticals are not in the antidiabetic drug class, so they do not have a base as strong as saponins as an alternative to antidiabetic treatment.

Although saponins are known as glucosidase inhibitors, there are several aspects that are not well known about saponins. These aspects are the effectiveness, mechanism and dose in reducing fasting and postprandial blood sugar levels in type 2 DM patients. Therefore, this literature review study is also important as a scientific effort to explore the gap between what is known and what is not known in the treatment of type 2 Diabetes Mellitus using saponin intervention.

#### **METHODS**

#### **Desain**

Data or literature collection was carried out manually and through electronic media in the form of research results regarding saponin intervention on reducing fasting blood sugar levels and 2 hours PP in patients with type II diabetes mellitus. The literature search through electronic media is

carried out online with an assessment of appropriate journal data sources with the following criteria: Peer Reviewer, indexed by citeSocre, Journal Impact Factors (JIF), Source Normalized Impact Per Paper (SNIP) for Elsevier Scopus journal, Scimago Journal Rank (SJR). Some of the keywords used are saponins, fasting blood glucose, 2 hours post prandial in type 2 diabetes mellitus patients.

#### **Data Bases**

Determination of keywords in the search based on predetermined criteria, namely health journals with the keywords used are saponins, fasting blood glucose, 2 hours post prandial in patients with type 2 diabetes mellitus and spanning the last 5 years published in journals starting from 2015-2020. The data is obtained through journal portal websites which can be accessed freely by searching such as MEDLINE, ABI/Inform Complete, ACM Library, Elsevier (SCOPUS), Digital Emerald, IEE Xplore, Science Direct and IGI Global, Garuda Portal, Google Scholar, Libraries.

#### **Inclusion and Exclusion Criteria**

Table 1. List of criteria in the literature review articles

No	Inclusion criteria	Exclusion
		criteria
1	The maximum	The exclusion
	period of journal	criteria in this
	publication is the	study were: a
	last 5 years starting	journal in the
	from 2015 - 2020	form of a
2	The language used is	literature
	Indonesian and	review,
	English	descriptive.
3	The research	Does not have
	subjects are adult	statistical
	humans	results, and
4	Types of journals	journals that are
	with original	not related to
	research articles, not	research
	research reviews	variables

5 The theme of the journal content is alternative services Complementary administration of saponins to decrease fasting blood sugar levels and 2 hours postprandial in patients with type II diabetes mellitus

#### **PICO Process**

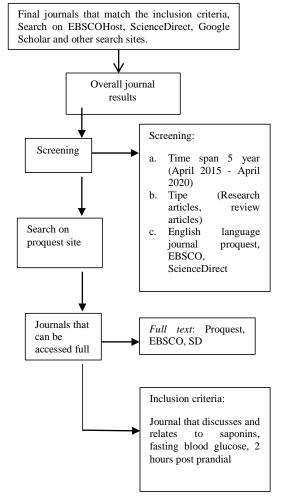


Figure 2 Diagram flow of Searching Literature Study of Saponin Intervention on Fasting Blood Sugar and 2 Hours Post Prandial Blood Sugar in Diabetes Mellitus Patients

#### RESULTS

#### 1. Results Search Process

Results search process that displayed as many as 37,195 journals that can be accessed in full text and identified in the initial search. After screening of titles and abstracts, 281 complete journal articles were taken for full text assessment. A total of 18 studies met the inclusion criteria requirements.

## 2. Selection results of inclusion and exclusion criteria

The results of the search process will be selected based on inclusion and exclusion criteria. This process obtained 281 journals study literature and 18 studies that met the inclusion criteria requirements which would then be scanned for data.

Based on all the studies summarized, almost all studies showed significant results of data analysis and testing, although there were some that were not significant regarding the intervention given. A total of 3 journals were assessed as low risk for bias with selective results reporting due to a comprehensive presentation of all results provided including statistically significant and non-significant differences.

Most studies mention the need for further research, especially regarding the time, dose and number of samples in the study, so that the results of the effectiveness of the interventions provided will be more visible. The assessment of bias in a research study shows that the results of articles specified in a systematic review are considered to be at high risk of selection bias because most of the sample determination is using non-probability

techniques so that there is a lack of selection random procedures research samples. In addition, most of the studies were pre-experimental, so the intervention was less in-depth. It is necessary to do further research on the effect of giving saponins to lower blood sugar levels. This can be biased because respondents only feel that intervention is of a short duration, so the results of each respondent will be different and cause bias. In addition, other confounding variables are also not considered properly, so that they will participate and affect the results of the study.

A total of 18 studies that became the sample of this study involved 741 respondents. A total of 16 studies (64%) were conducted in Indonesia, 2 studies (8%) in the UK, 1 study (4%) in Thailand, 2 studies (8%) in Iran, 1 study (4%) in Italy, 1 study (4%) in Korea, 1 study (4%) in Africa, and 1 study (4%) in the United States. Respondents in these studies are 40-65 years old on average. The gender characteristics of the respondents are almost the same between men and women.

Of the 18 research studies that met the inclusion criteria, there were 5 journals discussing saponins in aloe vera, 4 journals discussing saponins in cherry leaves, 3 journals discussing saponins in cinnamon, 2 journals discussing saponins in insulin leaves, 2 journals that discuss saponins in Moringa oleifera/ Moringa, 2 journals that discuss saponins in soursop, 1 journal that discusses saponins in ginseng, 1 journal that discusses saponins in fenugreek / fenugreek, 1 journal that discusses saponins in Citrullus colocynthis/ handhalah, 1 journal that discusses saponins in

starfruit, 1 journal that discusses saponins in Balanites aegyptiaca/ desert dates, 1 journal that discusses saponins in betel leaves, 1 journal that discusses saponins in dragon fruit and 1 journal that discusses about saponins in Tribulus terestris/ nutmeg salad.

#### **DISCUSSION**

# 1. Intervention of Giving Saponins on Fasting Blood Sugar Levels

There are 11 studies that measure the effectiveness of the intervention of giving plants containing saponins specifically on fasting blood sugar levels. Of the 11 studies, there were 3 studies that obtained non-significant intervention both statistically results, clinically, in reducing fasting blood sugar levels. The research is research conducted by Zarrintan, Taweerutchana and Najdi. Meanwhile, 8 other studies that obtained significant results were those Ariska, Hidayati, conducted by Mofrad, Rashad, Samani, Ariska, Choi, Barghamdi, and Najdi.

All studies were conducted with the intervention of giving plants containing saponins. The intervention was in the form of giving juices, extracts, gels, powders, juices and decoctions from plants containing saponins in different amounts. All of these studies had a duration of at least 8 days and a maximum of 8 weeks. All of them were randomized control trials with a pretest-posttest design. This means that each pretest result will seem to be a control group over itself in the posttest. The existence of a control group that received a placebo or 0 calorie sugar syrup is expected to have a effect blind on the respondents.

The statistically significant decrease in fasting blood sugar levels in the five studies in this sub-chapter has a range of 2-42 mg/dL. Based on the results of the study, almost all interventions with plants containing saponins can reduce fasting blood sugar levels even though in a narrow range. More than half of all studies showed that the intervention of giving plants containing saponins had a moderate to very strong effect on reducing fasting blood sugar levels. is corroborated This bv comparison of the decrease in fasting sugar levels in the control group which was very different statistically and clinically after the intervention when compared to the intervention group. That is, the intervention of giving saponins is effective in reducing fasting blood sugar levels.

### 2. Intervention of Giving Plants Containing Saponins on 2 Hours Post Prandial Blood Sugar Levels

There were 19 studies examining the effect of intervention giving plants containing saponins on postprandial reduction in blood sugar levels. Some are randomized control trials, while others are quasiexperimental. This means that each of the pretest results will seem to be a control group over itself against the posttest. Almost all studies that examine blood sugar 2 hours postprandial use a separate control group in addition to using a pretestposttest control group design. The existence of a control group that received an identical intervention, placebo or 0 calorie sugar syrup was expected to have a effect blind on the respondents. In addition, the control group is also useful as a comparison

of postprandial sugar levels in the and continuous comprehensive intervention group. If there is no control group, it will be difficult for researchers to determine the effect of metabolites on changes in postprandial sugar levels before 2 hours. This means that the presence of a control group can help researchers describe changes in postprandial blood sugar levels in the intervention group.

The decrease in postprandial blood sugar levels has a very wide range, which is -29 to 166 mg/dL. Like the results of research on fasting blood sugar levels, the results of research on postprandial blood sugar levels are polar. More than half of all studies showed that the intervention of giving plants containing saponins had a moderate to strong effect on lowering postprandial blood sugar levels. This is corroborated by the comparison of the postprandial reduction in sugar levels in the control group which was very different statistically and clinically at 30-90 minutes after the intervention when compared to the intervention group. That is, the intervention of giving plants containing saponins was effective in reducing peak postprandial blood sugar levels.

In contrast to the effectiveness of the intervention giving plants containing saponins to changes in fasting blood sugar levels, the effectiveness of the intervention giving plants containing saponins to postprandial blood sugar levels does not seem to be related to time. Almost all of the studies in Table 4.6 are cross-sectional studies. This means that the intervention and taking postprandial sugar levels were carried

out on the same day and only 2 hours apart. Only research by Rashad, Taweerutchana, Svafriani, Choi, Arini, Gusti, Khasanah, Samani, Hidayati and Sari alone maintained the intervention for several days in all subjects. Rashad intervened for 8 weeks, Syafriani for 1 week, Choi provided intervention for 12 weeks, Taweerutchana for 4 weeks, Arini for 2 weeks, Gusti for 1 week, Khasanah for 1 week, Samani for 12 weeks, Hidayati for 10 days and Sari for 4 weeks. The difference in changes in postprandial sugar levels seems to be only influenced by the subject's blood sugar history and the dose of the intervention.

Blood glucose levels will rise after eating for the first two hours with levels of 50-80 mg/dL, and right at minute 120 blood sugar levels will be relatively the same as blood glucose levels at minute 0 (when consuming food). Whereas in subjects with type 2 diabetes, postprandial blood glucose levels were not at normal levels at 120 minutes.

#### **CONCLUSION**

Based on a literature review study, 11 literature review journals related to fasting blood sugar were obtained, 9 of them had significant results in reducing blood sugar levels and 2 of them were not significant, with the results of several studies showing that the administration of saponins in aloe vera plants with doses at the range of 300-500 mg/day has an effect on reducing fasting blood sugar levels in patients with type 2 diabetes mellitus compared to other plants with p value = 0.000 and effect size 1.42 (very strong) compared to other plants that have values effect size in the weak and moderate categories. The difference in the values effect size in these various studies

could be due to the amount of saponin content from various plants and the length of the intervention time.

Based on a literature review study from 7 journals of literature review studies related to blood sugar 2 hours post prandial which was significant, with the results of several studies showing the administration of saponins in cherry plants at a dose of 15 grams had an effect on lowering blood sugar levels 2 hours postprandial in people with type 2 diabetes mellitus compared to other plants with p value = 0.000 and effect size 2.85. The difference in the value is effect size also caused by other factors that can be a support in reducing blood glucose levels such as diet, drugs and exercise that affect the value effect size.

#### REFERENCES

- Holt Ri, Cockram C, Flyvbjerg A And Goldstein Bj. Textbook Of Diabetes. John Wiley & Sons, 2017.
- 2. Sri Wahyuni, Yesi Hasneli & Juniar Ernawaty. Hubungan Kadar Gula Darah Dengan Terjadinya Gangren Pada Pasiendiabetes Mellitus. Program Studi Ilmu Keperawatan Universitas Riau. 2018.
- Defronzo Ra, Ferrannini E, Zimmet P And Alberti G. International Textbook Of Diabetes Mellitus. John Wiley & Sons, 2015.
- 4. Buraerah, Hakim. Analisis Faktor Risiko Diabetes Melitus tipe 2 di Puskesmas Tanrutedong, Sidenreg Rappan,. Jurnal Ilmiah Nasional;(2010) [diakses 2018 Mei 25]. Dari :http://lib.atmajaya.ac.id/default.aspx ?tabID= 61&src=a&id=186192
- Dupre Me, Silberberg M, Willis Jm And Feinglos Mn. Education, Glucose Control, And Mortality Risks Among Us Older Adults With

- Diabetes. Diabetes Research And Clinical Practice. 2015: 107: 392-9.
- 6. Buyukkaya E, Karakas M, Karakas Ejijocp And Laboratory M. American Diabetes Association,(2009). Diagnosis Dan Klasifikasi Diabetes Mellitus, Buku Ajar Ilmu Penyakit Dalam Ed. 5 Vol. 3. Jakarta: Fk Ui. Anonim,(2007). Kontrol Hba1c. Diakses 20 Mei 2017, Dari. 16: 97-101.
- 7. Nuari Na. Pengembangan Model Peningkatan Pemberdayaan Diri Dan Kualitas Hidup Pasien Diabetes Mellitus Tipe 2. Jurnal Ners Lentera. 2016; 4: 152-65.
- 8. Melmed S, Polonsky Ks, Larsen Pr And Kronenberg Hm. Williams Textbook Of Endocrinology E-Book. Elsevier Health Sciences, 2015.
- 9. Atlas D. International Diabetes Federation. Idf Diabetes Atlas, 7th Edn Brussels, Belgium: International Diabetes Federation. 2015.
- Tripathi K And Saboo B. Sadikot's International Textbook Of Diabetes.
  Jaypee Brothers Medical Publishers, 2019.
- Indonesia Pe. Pengelolaan Dan Pencegahan Diabetes Melitus Tipe 2 Di Indonesia. Pb Perkeni. 2015.
- Indonesia Pejpp. Pengelolaan Dan Pencegahan Diabetes Melitus Tipe 2 Di Indonesia. 2015.
- 13. Putri Nhk And Isfandiari Ma. Hubungan Empat Pilar Pengendalian Dm Tipe 2 Dengan Rerata Kadar Gula Darah. Jurnal Berkala Epidemiologi. 2013; 1: 234-43.
- Rossi G. Association Ad. Diagnosis And Classification Of Diabetes Mellitus. Diabetes Care. 2018; 33: S62-S9.
- Muflih Fla. Efek Teh Binahong (Anredera Cordifolia (Ten.) Stennis)
  Terhadap Penurunan Gula Darah.

- Prosiding Seminar Nasional Multidisiplin Ilmu. 2019, P. 445-50.
- Tjokroprawiro A. Buku Ajar Ilmu Penyakit Dalam. Ed. 2: Fakultas Kedokteran Universitas Airlangga Rumah Sakit Pendidikan Dr. Soetomo Surabaya. Airlangga University Press, 2015.
- 17. Nurtika N And Aisyah R. Uji Antidiabetik Daun Binahong (Anredera Cordifolia (Ten.) Steenis) Pada Tikus Putih Jantan Galur Wistar (Rattus Norvegicus) Yang Diinduksi Aloksan. Universitas Muhammadiyah Surakarta, 2017.
- 18. Siskaningrum A. Efektifitas Hidrogel Binahong (Anredera Cordifolia (Ten.) Steenis) Terhadap Luas Luka Pada Tikus Hiperglikemia (Rattus Norvegicus) Galur Wistar. Journal Keperawatan Stikes Icme Jombang. 2019; 17: 50-9.
- 19. Fatmala Ut, Apriyanto Dr And Nurbaiti N. Efektivitas Kombinasi Ekstrak Daun Annona Muricata L. Dan Anredera Cordifolia (Ten.) Steenis Terhadap Kadar Glukosa Darah Tikus Putih Jantan Galur Wistar. Tunas Medika Jurnal Kedokteran & Kesehatan. 2018; 4.
- 20. Fiana N And Oktaria D. Pengaruh Kandungan Saponin Dalam Daging Buah Mahkota Dewa (Phaleria Macrocarpa) Terhadap Penurunan Kadar Glukosa Darah. Jurnal Majority. 2016; 5: 128-32.
- 21. Rotblatt M And Zimet I. Evidence-Based Herbal Medicine. London: Haney & Belfus. Inc, 2002.
- 22. Leone A, Bertoli S, Di Lello S, Et Al. Effect Of Moringa Oleifera Leaf Powder On Postprandial Blood Glucose Response: In Vivo Study On Saharawi People Living In Refugee Camps. Nutrients. 2018; 10: 1494.

23. Crofts C, Schofield G, Zinn C, Wheldon M, Kraft JJDr and practice c. Identifying hyperinsulinaemia in the absence of impaired glucose tolerance: An examination of the Kraft database. 2016; 118: 50-7.