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Efficacy of *Morinda citrifolia* Fruit Extract to Increase Insulin Synthesis in Wistar Rats-Induced Diabetics.

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ABSTRACT

Diabetes mellitus (DM) is a metabolic disorder characterized by hyperglycemia due to insufficiency of insulin secretion and/or insensitivity of cells towards insulin. The use of secretagogues agent as therapeutic modality has considerably frequent side effects. Hence, the use of natural materials as a new therapeutic modality is growing rapidly due to the efficacy, minimal side effects, and its economical property. *Morinda citrifolia* (Rubiaceae) is originally discovered in Asia, Australia, Polynesia and The Pacific, and identified in Indonesia as Mengkudu. This plant is common to be utilized traditionally in overcoming various health problems, one of which is diabetes mellitus. This study aimed to determine the efficacy of *Morinda citrifolia* fruit extract to increase insulin synthesis in white rats diabetic model. *Morinda citrifolia* fruits extraction process was performed with maceration technique using ethanol solvent (1:10), followed by the filtration and evaporation process. Male white rats were kept in a room that had been conditioned and acclimatized prior to be used in the study. Rats were induced to sustain diabetes mellitus with streptozotocin. Administration of studied materials was carried out for 7 days in several doses. Plasma glucose and plasma insulin measurement was performed afterward. Statistical analysis was conducted using SPSS 18 with bivariate analysis of T-test and multivariate analysis of Bonferroni post-hoc test. The administration of the extract at doses of 10, 20, 40 mg/kgBW, and glibenclamide for 7 days resulted in significant weight gain, lower fasting plasma glucose levels, and elevated insulin secretion compared to negative control. *Morinda citrifolia* fruit extract was effective in lowering plasma glucose levels by increasing insulin secretion in white rats diabetic model.

Keywords: *Morina citrifolia*, glibenclamide, diabetes.

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INTRODUCTION

Diabetes mellitus (DM) is one of the metabolic disorders characterized by occurrence of hyperglycemia, with disorders in the metabolism of carbohydrates, fats, and proteins. This metabolic disorder is caused by defects in insulin secretion and/or insulin activity. Regulation of metabolic pathways of carbohydrates, fats, and proteins is a crucial point in the physiology of the body. Insulin is a hormone produced by pancreas, serving in metabolic regulation of carbohydrates, fats, and proteins. This hormone is responsible in body energy formation by inhibiting catabolic processes such as lipolysis, gluconeogenesis, proteolysis, and glycogenolysis. Insulin holds a role in the process of glycogenesis, fatty acid synthesis, as well as elevated intake of glucose and amino acids (WHO, 1999; Nelson et al., 2004).

Insufficiency of insulin secretion and/or insensitivity of cells towards insulin are basic pathogenesis of diabetes mellitus. Optimization of insulin secretion is one of the principles in diabetes mellitus management. The use of secretagogues agent is expected to improve cells sensitivity towards insulin and inhibit intestinal absorption of glucose and reduce gastric emptying. However, the use of various agents of secretagogues has considerably frequent side effects that will diminish therapy effectiveness and may lead to the emergence of new health problems (Grahame-smith, 2002).

The use of natural materials is one of the efforts exerted in finding therapeutic modalities for the management of hyperglycemia. Presently, the use of natural materials as a new therapeutic modality is growing rapidly. This is due to the efficacy of natural ingredients on various health problems, minimal side effects, as well as its economical property (Gupta et al., 2005). *Morinda citrifolia* (Rubiaceae) is identified in Indonesia as Mengkudu. This plant is originally discovered in Asia, Australia, Polynesia and The Pacific. This plant is common to be utilized traditionally in Indonesia in overcoming various health problems, such as arthritis, skin infections, diabetes mellitus and wounds (Elkins, 1997; Hirazumi et al., 1996; Nayak et al., 2009; Wang, 2001; Partan et al., 2018). This study aimed to determine the efficacy of *Morinda citrifolia* fruit extract to increase insulin synthesis in white rats diabetic model.

METHODS

Morinda citrifolia fruits were obtained from The Research Center for Traditional Medicine (BP2OT) Tawangmangu, Karanganyar Regency, Central Java Province, Indonesia, in August-September. Furthermore, species determination was performed at Indonesian Institute of Sciences (LIPI). The process of simplisia preparation was free of various organic materials.

Glibenclamide as positive control was obtained from Dexa Medica Palembang, South Sumatra. Random Access Analyzer Bio System® and Bio System reagent were utilized to measure plasma glucose levels of diabetic rats. ELISA reader Bio Rad® and Insulin for Rat ELISA kit from Sigma Aldrich® were utilized in assessing insulin levels of diabetic rats. Streptozotocin Sigma Aldrich® was used for the induction of diabetes mellitus in rats.

Morinda citrifolia fruits were washed in advance, then were dried and mashed afterward. Furthermore, the extraction process was performed with maceration technique using ethanol solvent (1:10). Then, the filtration process was conducted, followed by the evaporation process of the extracts using rotary evaporator.

Male white rats (170-230 grams) were obtained from Eureka Research Laboratory, Palembang, South Sumatra, accompanied with the certificate of animal health. Rats were about 10 weeks old with a low average fasting plasma glucose level of 5.6 mmol/L. The rats were kept in a room that had been conditioned at 25°C temperature, with a 12-hour dark-light cycle and fed with standard feed and water, ad libitum. All rats were acclimatized prior to be used in the study for 7 days. The study was approved by the ethics committee of Mohammad Hoesin Hospital, Faculty of Medicine, Universitas Sriwijaya.

Rats were induced to sustain diabetes mellitus with streptozotocin 50 mg/kgBW, dissolved in cold citrate buffer, pH 4.5, administered intraperitoneally. After three days, white rats with plasma glucose levels greater than 11.1 mmol/L were identified as diabetics. Furthermore, diabetic white rats were divided randomly into 5 groups (6 rats/group). Group 1: negative control, group 2: positive control, glibenclamide 5

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mg/kgBW, group 3: *Morinda citrifolia* extract (ME) 10 mg/kgBW, group 4: *Morinda citrifolia* extract (ME) 20 mg/kgBW, group 5: *Morinda citrifolia* extract (ME) 40 mg/kgBW. Administration of studied materials was carried out for 7 days.

Blood sampling from the rats was performed afterward. Blood sampling was performed on the periorbital. The blood was then inserted into vacutainer with EDTA. The blood samples were centrifuged by speed of 5000 rpm for 30 minutes at 25°C temperature. Furthermore, the supernatant was separated and used for the assessment of plasma glucose and insulin levels. Plasma glucose measurement was performed using a spectrophotometer and the measurement of insulin levels was performed by ELISA method according to the manual of Insulin ELISA kit Sigma Aldrich®.

Statistical analysis was conducted using SPSS 18. Bivariate analysis with T-test was performed, followed by multivariate analysis with Bonferroni post-hoc test. Plasma glucose and insulin levels were presented as Mean ± SD.

RESULTS

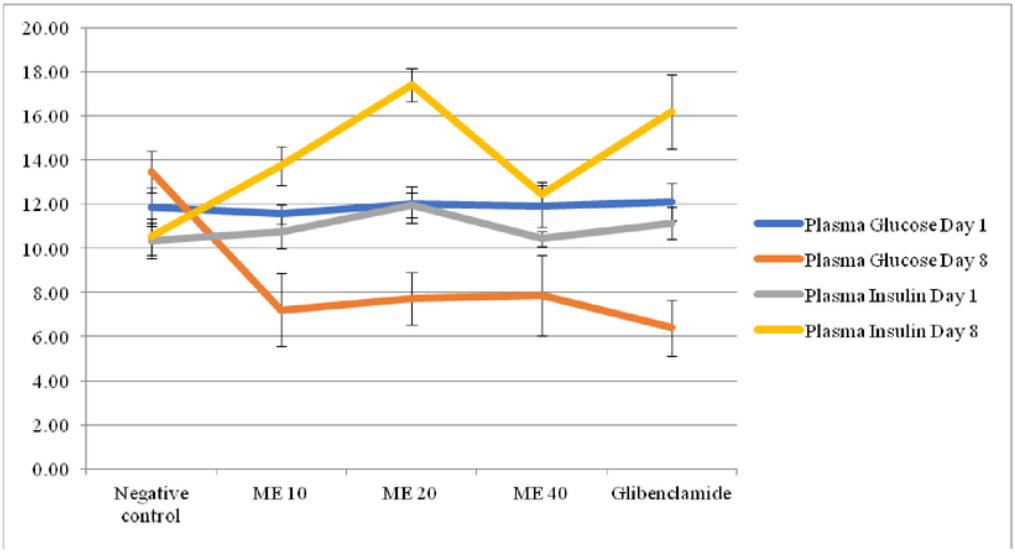

Figure 1: Fasting plasma glucose and plasma insulin levels in diabetic rats before and after the treatment of *Morinda citrifolia* extract. ME 10= *Morinda citrifolia* extract 10mg/kgBW; ME 20= *Morinda citrifolia* extract 20mg/kgBW; ME 40= *Morinda citrifolia* extract 40mg/kgBW.

The administration of the extract at doses of 10, 20, 40 mg/kgBW, and glibenclamide for 7 days resulted in significant weight gain compared to negative control, with an increase of 22.5%; 6.1%; 20.1% and 40.4% respectively. Fasting plasma glucose levels in diabetic rats increased more than 11.1 mmol/L. Extract at doses of 10, 20, 40 mg/kgBW and glibenclamide for 7 days resulted in significantly lower fasting plasma glucose levels compared to negative controls, with the decrease of 35.6%, 48.3%, 37.6% and 47.3% respectively.

Along with fasting plasma glucose levels, fasting insulin levels showed a significant increase in insulin secretion in groups receiving extracts at 10, 20, 40 mg/kgBW doses and glibenclamide compared to negative control, with an increase of 30.2%, 55.6%, 20% and 45.6% respectively.

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Table 1: Efficacy of extract on body weight, fasting plasma glucose, fasting plasma insulin in diabetic rats

Group (n=6 each group)	Body weight (g)		Fasting Plasma Glucose (mmol/L)		Fasting Plasma Insulin (µU/mL)	
	Day 1	Day 8	Day 1	Day 8	Day 1	Day 8
Negative control	207±5.71	177±17.01	11.87±0.88	13.47±0.95 a	10.35±0.81	10.53±0.82 a
DM+ME 10mg/kgBW	204±11.11	250±17.19 a,c	11.55±0.44	7.21±1.67 a,c	10.76±0.76	13.75±0.87 a,c
DM+ME 20mg/kgBW	198±14.91	210±8.33 b,c	11.99±0.84	7.74±1.19 a,c	11.98±0.56	17.40±0.76 a,c
DM+ME 40mg/kgBW	209±9.49	251±18.06 a,c	11.91±0.95	7.86±1.83 a,c	10.45±0.34	12.45±0.54 a,c
Glibenclamide	192±6.78	269±12.29 a,c	12.12±0.84	6.39±1.27 a,c	11.15±0.74	16.21±1.67 a,c

DM= diabetes mellitus, ME= *Morinda citrifolia* extract; Paired T-test, a $p<0.05$; Unpaired T-test, b $p<0.05$ VS metformin; c $p<0.05$ VS negative control; Significance level was determined by one-way ANOVA followed by Bonferroni post-hoc test

DISCUSSION

The results exhibited that the effects of *Morinda citrifolia* fruit extract (ME) were equivalent to oral hypoglycemic drug, glibenclamide. ME was capable of lowering plasma glucose levels by inducing pancreatic secretion as the effects of oral hypoglycemic drug, sulfonylureas. These results were similar to studies of the hypoglycemic effects from *Argania spinosa* and *C. dactylon* extracts (Singh et al., 2008; Samane et al., 2006).

Morinda citrifolia comprises various bioactive compounds such as flavonoids, triterpenoids, triterpenes, and saponins (Scortichini, 1991; Tsuchiya et al., 1996). Saponins are believed to reduce gastric emptying (Matsuda et al., 1999; Yoshikawa et al., 1997). Saponins are able to inhibit gastric emptying by initiating the secretion of glucagon-like peptide 1 (GLP-1), thereby reducing nutrient absorption to the bloodstream. In addition, saponins are competent to initiate glucagon activation, responsible in increasing glucose utilization and insulin secretion to achieve lower plasma glucose levels (Norberg et al., 2004). Flavonoids are capable in elevating insulin secretion so as to lower plasma glucose levels. Triterpenoids are able to improve glycosuria in diabetic white rats induced by alloxan (Chen et al., 2008). With a variety of modalities from bioactive compounds comprised in ME, it is effective in lowering plasma glucose levels through elevated insulin secretion.

CONCLUSION

Morinda citrifolia fruit extract was effective in lowering plasma glucose levels by increasing insulin secretion in white rats diabetic model.

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Conflict of Interests: The authors declared there was no conflict of interests in this study.

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REFERENCES

[1] World Health Organization, *Department of Non-Communi- cable Disease Surveillance. Definition, Diagnosis and Classifica- tion of Diabetes Mellitus and its Complications*, WHO, Geneva, Switzerland, 1999.

[2] L. D. Nelson and M. M. Cox, *Lehninger's Principles of Biochemistry*, W.H Freeman, New York, NY, USA, 4th edition, 2004.

[3] D. G. Grahame-Smith and J. K. Aronson, *Clinical Pharmacol- ogy and Drug Therapy*, Oxford University Press, New York, NY, USA, 3rd edition, 2002.

[4] R. K. Gupta, A. N. Kesari, P. S. Murthy, R. Chandra, V. Tandon, and G. Watal, "Hypoglycemic and antidiabetic effect of ethanolic extract of leaves of *Annona squamosa* L. in experimental animals," *Journal of Ethnopharmacology*, vol. 99, no. 1, pp. 75–81, 2005.

[5] R. Elkins, *Hawaiian Noni (Morinda citrofolia)*, Woodland, Pleasant grove, Utah, USA, 1997.

[6] Hirazumi, E. Furusawa, S. C. Chou, and Y. Hokama, "Immunomodulation contributes to the anticancer activity of Morinda citrifolia (Noni) fruit juice," *Proceedings of the Western Pharmacology Society*, vol. 39, pp. 7–9, 1996.

[7] S. Nayak, S. Sandiford, and A. Maxwell, "Evaluation of the wound-healing activity of ethanolic extract of *Morinda citri- folia* L. leaf," *Evidence-Based Complementary and Alternative Medicine*, vol. 6, no. 3, pp. 351–356, 2009.

[8] M. Y. Wang and C. Su, "Cancer preventive effect of Morinda citrifolia (Noni)," *Annals of the New York Academy of Sciences*, vol. 952, pp. 161–168, 2001.

[9] S. K. Singh, P. K. Rai, D. Jaiswal, and G. Watal, "Evidence- based critical evaluation of glycemic potential of Cynodon dactylon," *Evidence-Based Complementary and Alternative Medicine*, vol. 5, no. 4, pp. 415–420, 2008.

[10] S. Samane, J. Noe¨l, Z. Charrouf, H. Amarouch, and P. S. Haddad, "Insulin-sensitizing and anti-proliferative effects of *Argania spinosa* seed extracts," *Evidence-Based Complementary and Alternative Medicine*, vol. 3, no. 3, pp. 317–327, 2006.

[11] M. Scortichini and M. P. Rossi, "Preliminary in vitro evalua- tion of the antimicrobial activity of terpenes and terpenoids towards *Erwinia amylovora* (Burrill) Winslow et al," *Journal of Applied Bacteriology*, vol. 71, no. 2, pp. 109–112, 1991.

[12] H. Tsuchiya, M. Sato, T. Miyazaki et al., "Comparative study on the antibacterial activity of phytochemical flavanones against methicillin-resistant *Staphylococcus aureus*," *Journal of Ethnopharmacology*, vol. 50, no. 1, pp. 27–34, 1996.

[13] H. Matsuda, Y. Li, J. Yamahara, and M. Yoshikawa, "Inhibition of gastric emptying by triterpene saponin, momordin Ic, in rats: roles of plasma glucose, capsaicinsensitive sensory nerves, and central nervous system," *Journal of Pharmacology and Experimental Therapeutics*, vol. 289, no. 2, pp. 729–734, 1999.

[14] M. Yoshikawa, T. Murakami, and H. Matsuda, "Medici- nal foodstuffs. X. Structures of new triterpene glycosides, gymnemosides-c, -d, -e, and -f, from the leaves of Gymnema sylvestre R. BR.: influence of gymnema glycosides on glucose uptake in rat small intestinal fragments," *Chemical and Pharmaceutical Bulletin*, vol. 45, no. 12, pp. 2034–2038, 1997.

[15] A Norberg, K. H. Nguyen, E. Liepinsh et al., "A novel insulin- releasing substance, phanoside, from the plant Gynostemma pentaphyllum," *Journal of Biological Chemistry*, vol. 279, no. 40, pp. 41361–41367, 2004.

[16] J.Chen,W.L.Li,J.L.Wu,B.R.Ren,andH.Q.Zhang, "Hypoglycemic effects of a sesquiterpene glycoside isolated from leaves of loquat (Eriobotrya japonica (Thunb.) Lindl.)," *Phytomedicine*, vol. 15, no. 1-2, pp. 98–102, 2008.

[17] Partan RU, Hidayat R, Saleh I, Parisa N, Tanzil N. Effect of Supplementation Kayu Manis (Cinnamomum burmanii) in Neuronal Cell Death Protection in Wistar Rats Lir-Psychotics on Haloperidol Therapy. *Asian J Pharm Clin Res, Vol 11, Issue 2, 2018, 363-365*

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