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REVISITING LAPORTEA: QUERCETIN AS A KEY BIOACTIVE FOR NATURAL DIABETES THERAPY

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ABSTRACT
Insulin injections and oral hypoglycemic drugs are the main therapies available for the treatment of diabetes. However, side effects and dependence make many sufferers not continue treatment. The development of plant-based antidiabetic alternatives continues, one of which is the genus Laportea, which contains flavonoids and derivative compounds, such as quercetin, that are able to control blood sugar. The purpose of this literature review is to provide evidence-based information on the potential content of quercetin in Laportea. This literature review was created by searching databases such as: Pubmed, Elsevier, Science Direct, and Google Scholar. Searches on Elsevier and google Scholar were conducted using the following keywords: "quercetin AND Laportea decumana", "quercetin AND Laportea aestuans", "quercetin AND Laportea bulbifera" "Flavanoid AND quercetin AND Laportea". "quercetin AND antidiabetic". Meanwhile, the keywords to search for articles on pubmed are done by writing quercetin AND Laportea [MeSH]", "Flavanoid AND quercetin AND Laportea [MeSH]". "quercetin AND antidiabetic [MeSH]". The search was conducted on articles published in 2010-2025. The search was conducted on articles published in 2015-2025. Articles are selected and reviewed according to the theme and research questions by all researchers. Quercetin provides superior hypoglycemic effects and insulin sensitization activity by promoting pancreatic cell-β proliferation and by increasing glucose metabolism and insulin secretion. previous studied reported that the administration of 20 mmol· L-1 QE to pancreatic β cells INS-1 increases insulin secretion induced by glucose and gliclazide and protects β cells against oxidative damage. The results of this review literature have explained that the benefits of the laportea plant to overcome diabetes are the content of Quercetin which can provide a superior hypoglycemic effect.

Keywords: antidiabetes; laportea; quercetin

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INTRODUCTION

As a developing country, Indonesia is still faced with various health problems, especially non-communicable and degenerative diseases. The financing burden, morbidity, and mortality due to this disease still cannot be completely addressed. The cause of the disease is Diabetes Mellitus (DM), which is a chronic disease caused by increased blood glucose levels (hyperglycemia) caused by inadequate insulin secretion, imperfect insulin work, or both. (Ansari, 2022)

This metabolic disorder is caused by low insulin levels or insulin resistance in skeletal muscle, adipose tissue, and other target tissues. The development, pathogenesis, and complications of DM are highly correlated with high levels of oxidative stress, free radicals, and other metabolic stressors. Studies report that the majority of DM sufferers come from middle- and low-income countries. (Akhtar, et al., 2020). The prevalence of diabetes mellitus in Indonesia was around 10.7 million in 2019. WHO predicts an increase in the number of people with diabetes mellitus in Indonesia from 8.4 million in 2000 to around 21.3 million by 2030, which shows a 2-3 3-fold increase in the number of people with diabetes. (Setiawan, 2022).

Although the majority of people with type 2 diabetus mellitus (T2DM) are adults (more than 90% of the patient population), this diabetes affects people of all ages. Individuals who are over 40 years of age and have obesity problems and a family history of diseases are at higher risk of developing T2DM. Various antidiabetic drugs such as metformin, sulfonylurea, meglitinide, thiazolidinedione, GLP-1 mimetics, DPP-IV, and SGLT2 inhibitors are currently used to treat T2DM. However, many of them are expensive and have adverse side effects. (Chiang, et al., 2014) (Ansari, et al., 2022)

The development of plant-based antidiabetic alternatives continues to be carried out, one of which is the genus Laportea, which contains flavonoids and derivative compounds such as quercetin, which can control blood sugar, such as Laportea Aestuans (Adetunji, 2021)and Laportea Bulbifera. (Wang, 2024)In Indonesia, the Laportea plant group is widely distributed in the Eastern region, especially Papua and Maluku, as itch leaves (Laportea Decumana). Other special Laportea species spread across Indonesia are (Omolola EO, 2018)Laportea interrupta (L), Laportea aestuans (Linn), and Dendrocnide peltate (Safitri OM, 2018). However, information about the potential Quercetin In Laportea plants, not much has been done. The purpose of this literature review is to provide evidence-based information about the potential of the fetus Quercetin deep Laportea

METHOD

Search Strategy

This literature review was created by browsing databases such as: PubMed, Elsevier, Science Direct, and Google Scholar. Searches on Elsevier and Google Scholar were conducted using the following keywords: "quercetin AND Laportea decumana", "quercetin AND Laportea aestuans", "quercetin AND Laportea bulbifera", "Flavanoid AND quercetin AND Laportea", "quercetin AND antidiabetic". Meanwhile, the keywords to search for articles on PubMed are done by writing quercetin AND Laportea [MeSH], "Flavanoid AND quercetin AND Laportea [MeSH]", "quercetin AND antidiabetic [MeSH]" “ The search was conducted on articles published in 2010-2025.

Inclusion and Exclusion Criteria

All primary articles that discuss and report on the content of quercetin in the Laportea plant. Articles that report the results of laboratory analysis with various extraction methods, the results of primary analysis with cross-sectional, observational, and even experimental designs are included in this review. Articles with secondary data, such as systematic review and meta-analysis are also included in this review. Articles that are letters to the editors and unpublished articles have not been included due to limited evidence and the ability of researchers to conduct searches.

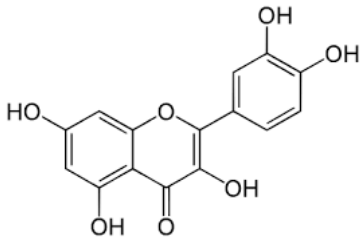
Data Analysis and Presentation

The results of the article search will be unified and grouped according to subtitles and similarities in content using design mapping review. Starting from information about quercetin, potential benefits, doses that have been tested, and its mechanism in overcoming diabetes. Articles are selected and reviewed according to the theme and research questions by all researchers.

RESULT

Quercetin *Content* in Flavonoids of the Laportea Plant

Quercetin (QE) is the main member of the flavonoid family, which can be extracted from a variety of vegetables and fruits, such as onions, apples, berries, many nuts, seeds, bark, flowers, tea, brassica vegetables, and leaves. Quercetin (3,5,7- (C. Chen, 2010)*trihydroxy-2-(3,4-dihydroxyphenyl)-4Hchromen-4-one*) is a typical flavonoid, found in many plants and is an active ingredient in many Chinese herbal medicines [22]. The basic parent nucleus of QE is the phenyl benzoyl ketone, which consists of 2 benzene rings (A and B) and is connected by an oxygen-containing pyrenal ring (C ring). The basic skeleton has a C6-C3-C6 structure, the three rings are planar, and the molecules are relatively polarized. (Shi, 2019)



Source: (Shi, 2019)

Modern pharmacological studies have shown that QE has versatile biological functions on human health, including anti-diabetes. QE has two main forms of existence, namely glycosides and non-glycosides, which have been studied in cell-based trials and experimental animal models in recent years and are gaining popularity as a natural therapy for diabetes and its complications. (A. Gupta, 2016) (Chiang, et al., 2014)

The different positions of the hydroxyl groups in QE cause different acid-base and oxidizing properties, resulting in the diversity of their derivatives. QE is stable in human urine, human plasma, acetonitrile, and water at temperatures of 4°C, 20°C, and -80°C. Analysis of the relationship between the structure of activity shows that the physical properties of QE are determined by its chemical structure. The molecular structure of QE crystals is very dense, and its intermolecular gravity is large, which is not easily dispersed by solvents or solutes and severely limits their bioavailability in animals (Zupanets, 2019)

One of the compounds in Itchy Leaves (Laportea) is Quercetin, where the compound significantly inhibits the activity of the DPP-IV enzyme at a level comparable to diprotein-A inhibitors. In obtaining quercetin compounds requires the right extraction method is required (Singh, 2020)The extraction method plays an important role in obtaining quercetin compounds from itchy leaves.

Quercetin *dosage has n*ever tested.

Quercetin is found in many fruits, vegetables, and more than twenty species of plants. Due to its extensive pharmacological activity, quercetin is widely used as a dietary supplement in powder and capsule form. Some countries report different dietary intake according to fruit, vegetable, and tea consumption, which ranges from 50 to 800 mg/day. The average consumption of quercetin in countries such as China, Japan, Spain, and the U.S. was reported to be 18, 16.2, 18.48, and 9.75 mg/day. Table 1 shows the amount of quercetin present in food sources (Azeem, 2023) (Li, 2016)

Ethyl acetate extract from the leaves was taken, and at doses of 100 and 200 mg/kg orally administered to a model of diabetic induced mice *streptozotocin* (STZ), alloxan-induced diabetic rats, and STZ-nicotinamide-induced rat models, oral administration of various doses of QE was able to reduce levels of glucose, hemoglobin (Hb), and glycosylated hemoglobin (HbA1C) in the blood and prevent weight loss *in vivo* (Sharma, 2018). A significant decrease in hyperglycemia levels was reported at a dose of 200 mg/kg, concomitant with an increase in body weight and lipid profile. The extract also exhibits an antioxidant profile that confirms the role of quercetin in the management of blood glucose and lipid levels in diabetes mellitus. (Azeem, 2023)

Oxidative stress due to hyperglycemia is a common complication associated with diabetes. Mina Hemmati et al. investigated two enzyme expressions in glucose metabolism, namely glucokinase and glucose-6-phosphatase. For this, twenty-four adult Wistar rats were divided into three groups, namely control, streptozotocin-induced diabetic mice, and quercetin-treated group (15 mg/kg, intraperitoneally). At the end of the 21-day treatment period, quercetin showed a significant decrease in blood glucose and malondialdehyde levels. Levels of HSP70, HSP27, HSF-1, and glucose 6 phosphatase mRNA decreased significantly, while glucokinase expression increased in

response to quercetin ($p<0.05$). These findings are beneficial for healthcare professionals to use quercetin as a nutritional supplement. (Hemmati, 2018)

Commonly used doses and treatment cycles of QE derived from the literature include: 30 mg/kg body weight (bb) for 14 days; 10 and 15 mg/kg.bb for 2 weeks[39] and 8 weeks; 50 and 80 mg/kgbb for 45 days; 100 mg/kg.bb for 49 days; 25, 50, and 75 mg/kg for 28 days; 100 and 200 mg/kg BB for 6 weeks. (D.K. Yang, 2018) (M.M. Alam, 2014) (Shi, 2019) (P. Srinivasan, 2018) (Sharma, 2018)

In addition, QE in food (0.5% in food) was also effective in correcting increased fasting blood glucose, urinary sugar, and urine volume levels in STZ-induced diabetic rats [41]. In general, administration of oral QE (15–100) for 14–70 days resulted in a significant decrease in blood glucose by regenerating pancreatic islets, increasing serum insulin levels, and promoting insulin release in a model of diabetic mice. In insulin resistance induced by a high-fat diet (HFD) and a mouse model of type 2 diabetes, C57BL/KsJ-db/db (H.H. Gaballah, 2017)

DISCUSSION

Commonly used hypoglycemic drugs can be classified as insulin and its analogues, sulfonylurea secretion enhancers, metformin, alpha-glucosidase inhibitors, and others used as monotherapy or combinations. In addition, insulin is used for patients with ketoacidosis, hyperosmolar coma, and lactic acidosis or other secondary diabetes. Insulin is an irreplaceable drug in the treatment of diabetes, but insulin therapy also has many problems in clinical medicine, such as psychological and biological side effects. Generally, this situation can subside on its own by following a low-salt diet for a few days. In addition, some patients will experience blurred vision after receiving insulin treatment, which is caused by changes in the refractive lens. These changes are temporary and do not need to be corrected. (A.M. Stolf, 2017)

Flavonoids have received more attention by the scientific community due to their structural diversity, their abundance in nature, strong pharmacological activity with low adverse reactions. More and more flavonoids are confirmed to have potential antihyperglycemic effects such as QE, iso-quercetin, rutin, hypericum, and others. QE, a flavonol-type typical flavonoid, is a type of monomer or low-molecular-weight drug that has prominent anti-diabetic activity in a safe way. Many studies have elucidated its potential functional mechanisms. The detailed action of QE in diabetes and its complications of diabetes has been studied in the entire process of carbohydrate metabolism and in the signaling network of insulin action complexes. Therefore, flavonoids, especially QE, have been well studied as promising and interesting herbal monomers to enrich diabetes-related function in releasing insulin. (H.N. Choi, 2016)

Insulin is released by the cells β the pancreas and controls glucose levels in the bloodstream when blood sugar concentrations rise. Complications of diabetes are usually associated with decreased viability and cell-β dysfunction of the pancreas. Experts have proposed flavonoids as potential anti-diabetic agents because flavonoids exert many actions on the cells β pancreatic isles. Among all flavonoids, QE provides superior hypoglycemic effects and insulin sensitization activity by promoting pancreatic cell-β proliferation and by increasing glucose metabolism and insulin secretion. Youl et al. reported that the administration of 20 mmol· L-1 QE to pancreatic β cells INS-1 increases insulin secretion induced by glucose and glibenclamide and protects β cells against oxidative damage. (S.O. Adewole, 2007) (Shi, 2019)

In addition, ERK1/2 plays a major role in this effect. The potential of QE in preventing β-cell dysfunction associated with diabetes should be investigated further. Oral treatment of 120 mg/kg/day of QE for 8 weeks significantly lowered plasma triglyceride concentrations and weight in diabetic rats. Furthermore, QE significantly lowered plasma cholesterol, fasting plasma insulin,

and postprandial glucose levels and significantly improved insulin sensitivity index at 30 minutes during oral glucose tolerance tests in diabetic rats. In this case, the protective effect of QE on islet cells can be categorized into three aspects, namely, increased insulin secretion, β cell protection, and increased islet β cell proliferation. (E. Youl, 2010)

Extracts Laportea ovalifolia and Laportea Bulbifera have a hypoglycemic effect. Laportea leaf decoction is widely used to treat diabetes mellitus (Momo et al., 2006). Extract Laportea. It is reported to increase glucose homeostasis in vivo. (Dhouibi et al., 2020) It has also been reported that the total coumarin content of Urtica dentata shows significant defense against the increase in autoimmune diabetes, lowers blood glucose levels, inhibits the proliferation and hypertrophy of HBZY-1 cells, lowers the regulation of transforming growth factor-β1, and activates the tol-like receptor 4 (Cao et al., 2015).

Laportea extract can improve glycemic control in T2DM patients requiring insulin therapy (Kianbakht et al., 2013) providing a protective effect on diabetes recovery by controlling serum insulin, blood glucose, pancreatic islet, and β cells in diabetic mice. It has been proven that Laportea extract treats hyperglycemic mice

CONCLUSION

The results of this review literature have explained that the benefits of the laportea plant to overcome diabetes are the content of Quercetin which can provide a superior hypoglycemic effect and insulin sensitization activity by encouraging the proliferation of pancreatic β cells and by increasing glucose metabolism and insulin secretion. Youl et al. reported that the administration of 20 mmol· L-1 QE to pancreatic β cells INS-1 increases insulin secretion induced by glucose and glibenclamide and protects β cells against oxidative damage.

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