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RESEARCH ARTICLE

Trigona Honey as an Antihyperglycemic Agent in the Management of Type 2 Diabetes: A Scoping Review of Current Evidence

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ABSTRACT

Type 2 Diabetes Mellitus (T2DM) is a major global health challenge, influenced by urbanization, sedentary lifestyles, and poor dietary habits. While pharmacological treatments are common, their side effects, including hypoglycemia and weight gain, limit their effectiveness, driving the search for safer alternatives. Trigona honey, rich in bioactive compounds like flavonoids and polyphenols, offers promising antioxidant properties and potential to enhance insulin sensitivity, potentially improving blood glucose regulation in T2DM patients. This study aims to review the evidence on Trigona honey as a complementary therapy in managing T2DM, with a focus on blood glucose control and reducing complications. A scoping review was performed using multiple databases: PubMed, Cochrane Library, EMBASE, CINAHL, Web of Science Core Collection, DOAJ, Wiley Online, ClinicalTrials.gov, WHO ICTRP, Grey Literature (Google Scholar), ProQuest, and Garuda Websites (WHO, ADA, IDF). Relevant studies were selected based on inclusion criteria, focusing on Trigona honey in animal or human models related to blood glucose regulation. Data were analyzed descriptively to examine the effects and mechanisms of Trigona honey. Among 13 studies, Trigona honey was shown to reduce blood glucose by enhancing insulin sensitivity, protecting pancreatic beta cells, and reducing oxidative stress. While most studies were on animal models, limited human trials showed significant reductions in fasting blood glucose after 30 days. Trigona honey shows potential as a complementary therapy for T2DM, but further controlled human studies are needed to confirm its efficacy and determine optimal dosing.

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) remains a significant global health challenge, with its prevalence continuously increasing due to urbanization, sedentary lifestyles, and poor dietary habits (1)(2). (3) reported that in 2021, approximately 537 million people worldwide were affected by diabetes, and this number is expected to rise to 783 million by 2045. This trend calls for innovative approaches to manage the condition (4). T2DM, the most common form of diabetes, has a significant impact on patients' quality of life and is associated with long-term complications such as cardiovascular disease, vision impairment, neuropathy, and kidney damage (5)(6)(7). The current management of T2DM still relies on pharmacological therapies, primarily oral antidiabetic medications and insulin, which are often accompanied by adverse side effects such as hypoglycemia and weight gain (8)(9)(10).

Therefore, the search for safer and more effective therapeutic solutions for T2DM management is crucial.

Similar to the application of digital health products evaluated in previous studies, natural products such as Trigona honey may offer a holistic and integrated approach to managing T2DM. This highlights the need for therapeutic alternatives that are not only clinically effective but also align with best practices in diabetes management (4). One approach that has gained increasing attention is the use of natural products, particularly honey, which has long been used in traditional medicine. Among the various types of honey, Trigona honey (from Trigona bee species) stands out due to its high bioactive content, including flavonoids, polyphenols, and phenolic acids, which have antioxidant and anti-inflammatory properties that can influence glucose and insulin metabolism (11); (12). Research on digital health applications emphasizes the need for consistent biomarker data, such as HbA1c, to evaluate the effectiveness of interventions. A similar approach can be applied to studies on Trigona honey to ensure that research findings are widely adoptable and supported by strong evidence management (4). Several studies indicate that Trigona honey may lower blood glucose levels and improve insulin sensitivity, two key factors in T2DM management (13); (14).

However, despite the growing interest in Trigona honey's potential for managing T2DM, scientific evidence remains limited, particularly regarding the underlying mechanisms of its antidiabetic effects and its application in humans. Most of the existing research focuses on animal models, particularly diabetic rats, with only a few studies exploring the effects of Trigona honey in human blood glucose regulation. These studies have shown promising results, such as reduced blood glucose levels and improved lipid profiles (15), but the molecular mechanisms underlying the antihyperglycemic effects of Trigona honey are still not fully understood (16).

These limitations underscore the need for further exploration of the therapeutic potential of Trigona honey in T2DM management, as well as a deeper understanding of the mechanisms involved in glucose metabolism regulation. Therefore, this study aims to summarize the available evidence on the effects of Trigona honey in managing blood glucose levels in T2DM. By integrating the existing research findings, this study is expected to provide a clearer understanding of Trigona honey's potential as an alternative or complementary therapy in diabetes management, while also identifying gaps in the literature.

The results of this study are expected to offer a better understanding of the application of Trigona honey in managing type 2 diabetes and provide a stronger foundation for the development of natural product-based therapies. These findings could also serve as a valuable reference for healthcare practitioners and therapy developers when considering Trigona honey as a safer and more affordable alternative for managing T2DM.c

MATERIALS AND METHODS

Study Design

This study adopts a scoping review design to explore and summarize the existing evidence on the use of Trigona honey in managing Type 2 Diabetes Mellitus (T2DM). The scoping review approach was chosen as it allows for the inclusion of various study types, such as randomized controlled trials, observational studies, and in vitro research, providing a comprehensive overview of the topic (17)(18)(19)(20). With this design, we aim to identify diverse forms of relevant evidence and explore how Trigona honey impacts glucose metabolism, as well as its potential in T2DM therapy. The reporting of this study follows the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) framework to maintain clarity and uniformity throughout the reporting process (21)(22).

Study Protocol

The protocol for this scoping review is registered in PRISMA for Scoping Reviews, available at http://prisma-statement.org/Extensions/ScopingReviews. This protocol adheres to PRISMA guidelines to ensure transparency and reproducibility in the search process, study selection, and data extraction.

Search Strategies

Literature searches were conducted using multiple databases, including PubMed, Cochrane Library, EMBASE, CINAHL, Web of Science Core Collection, DOAJ, Wiley Online, ClinicalTrials.gov, WHO ICTRP, Grey Literature (Google Scholar), ProQuest, Garuda Websites (WHO, ADA, IDF), and other relevant organizations (American Diabetes Association, International Diabetes Federation), as well as citation searching. The search strategy combined relevant keywords and MeSH terms using Boolean logic, based on the PCC model (Population: patients with Type 2 diabetes, Concept: diabetes care, Context: Trigona honey therapy) **(Table 1).** This strategy was developed in collaboration with an Information Scientist and follows the guidelines of (23). The reference lists of included studies were also checked to complement the search. If full-text articles were unavailable, authors were contacted.

Eligibility Criteria

The articles selected for this scoping review must meet the following inclusion criteria: studies involving patients with Type 2 Diabetes Mellitus (T2DM) or animal populations (mice/rodents), focusing on the use of Trigona honey in diabetes management. Included studies must specify the type of honey, administration protocols and dosages, as well as blood glucose measurements as the primary indicator. Articles published in English and Indonesian between 2014 and 2024 will be considered.

Exclusion criteria include articles that are unavailable in full text, irrelevant to the topic, duplicates, or those not meeting the inclusion criteria (e.g., studies not involving the use of Trigona honey for diabetes). These criteria ensure that only relevant, high-quality studies are included in the review.

Study Selection

The flowchart below illustrates the article selection process used in this review. It started with the identification of records from various sources, yielding a total of 1,254 records found across multiple databases and registers, including: PubMed (n = 187), Cochrane Library (n = 145), EMBASE (n = 193), CINAHL (n = 112), Web of Science Core Collection (n = 155), DOAJ (n = 98), Wiley Online (n = 102), Grey Literature from Google Scholar (n = 135), ProQuest (n = 45), and Garuda (n = 35). Additional records were identified through registers such as ClinicalTrials.gov (n = 29) and WHO ICTRP (n = 18). After the initial screening, duplicates (200 records) were removed, followed by records flagged as not meeting the criteria by the inventory tool (100 records), and records removed for other reasons (50 records). After this cleaning process, 904 records remained for further screening. Of these, 700 records were excluded for not meeting the inclusion criteria, such as being irrelevant to diabetes care or not aligning with the study focus.

A total of 204 reports were then processed for extraction, but 30 reports could not be accessed. Of the 174 reports assessed for eligibility, 164 were excluded with the following details: irrelevant to diabetes management (n = 54), low study quality (n = 67), and incomplete data (n = 43). This process resulted in 10 relevant articles that were eligible for inclusion in the review.

Additionally, further records were identified through other methods, including websites like WHO (n = 10), ADA (n = 10), and IDF (n = 10), as well as organizations such as the American Diabetes Association (n = 5) and International Diabetes Federation (n = 5). Citation searching resulted in 20

additional records. Of the 10 reports requested for extraction, 7 were assessed for eligibility, and 4 were excluded for the following reasons: irrelevant to diabetes care (n = 1), low study quality (n = 2), and incomplete data (n = 1). This resulted in 3 additional relevant articles for inclusion in the review.

Overall, through various sources and identification methods, 13 articles were finally included in the review, providing a comprehensive perspective on the use of Trigona honey in managing Type 2 Diabetes Mellitus. The selection process followed PRISMA guidelines and is illustrated in **(Figure 1)**.

Data Extraction

Data were extracted from full-text journal articles that met the inclusion criteria using a data extraction form developed by the (24). Information extracted included study characteristics such as authors, year, country, title, research design, sample size, type of Trigona honey used, dosages and administration protocols, as well as mechanisms of blood glucose control (Table 2). Key findings regarding the effects of Trigona honey on blood glucose levels, including fasting blood glucose and HbA1c, were recorded. All data were entered into an Excel spreadsheet and reported in a narrative form, highlighting key findings related to the effectiveness of Trigona honey in managing Type 2 Diabetes Mellitus.

RESULTS

General Characteristics

Of the 13 studies analyzed, nine were conducted in Indonesia, using various types of honey, including *Trigona laeviceps* (25), *Tetragonula* sp. (26), *Tetragonula biroi* and *T. laeviceps* (27), klanceng honey from Kuningan (28), *Heterotrigona itama* (29), and *Trigona* sp. used in other studies (30); (31). In Malaysia, four studies used honey from *Geniotrigona thoracica* (32) and *Kelulut* honey (*Trigona* sp.) in various combinations and concentrations (33); (34) **(Figure 2).** All the types of honey studied in this review are *Trigona* honey, although the names used to refer to it differ across regions. In each area, this honey has shown significant potential in lowering blood glucose levels through mechanisms such as antioxidant activity, inhibition of oxidative stress, and increased insulin sensitivity.

Types of Honey and Their Characteristics

Trigona honey, produced by stingless bees from the Trigona genus, contains very high levels of bioactive compounds, including flavonoids, polyphenols, and phenolic acids. These compounds provide Trigona honey with powerful antioxidant effects, which help neutralize free radicals and alleviate oxidative stress in the body. This is particularly beneficial for health, especially in reducing inflammation that can worsen diabetes. For example, Trigona laeviceps honey is known to increase glucose solubility, facilitate its excretion through urine, and protect pancreatic beta cells, which play a crucial role in insulin production. A study by (25) demonstrated that Trigona laeviceps honey can lower blood sugar levels in male rats at a specific dosage.

Additionally, honey from *Geniotrigona thoracica* has similar characteristics, with flavonoids and polyphenols that can enhance insulin sensitivity and protect the pancreas from oxidative stress damage. Research by (32) revealed that this honey has a pancreatic protective effect, improving lipid profiles and increasing serum insulin levels in diabetic rats. Honey from *Tetragonula sp.*, used in the study by (26), also contains high levels of flavonoids and phenolic compounds, which help reduce oxidative stress, improve insulin sensitivity, and regulate glucose metabolism. *Kelulut* honey (*Trigona* sp.), used in studies by (33) and (34), shows similar potential by reducing inflammation, improving hormonal profiles, and addressing oxidative stress in metabolic syndrome and PCOS.

Overall, Trigona honey from various species offers a range of remarkable health benefits, particularly in managing blood glucose levels and protecting organs involved in glucose metabolism. With its high

antioxidant content, Trigona honey can be an effective natural choice to help prevent and manage diabetes.

Dosage and Duration of Trigona Honey Administration

The dosage and duration of Trigona honey administration vary across studies. (25) used doses of 0.27 ml/200 mg body weight and 0.54 ml/200 mg body weight for 21 days in *Trigona laeviceps* rats. (32) administered doses of 1 g/kg and 2 g/kg body weight of *Geniotrigona thoracica* honey for 28 days in diabetic rats. (26) used *Tetragonula sp.* honey without specifying the exact dosage, but it was shown to effectively lower blood glucose levels in rats. (27) used doses ranging from 0.5 g/kg to 2 g/kg of *Tetragonula biroi* honey over 35 days. (34) administered *Kelulut* honey (KH) at a dose of 1 g/kg/day for 35 days. (35) used a dose of 10.40 g/kg body weight of *Trigona* sp. honey for 3 weeks in mice. (31) gave *Trigona* honey at a dose of 40 ml per day for 30 days to type 2 diabetes patients **(Table 3).** All of these studies show that Trigona honey is effective in managing blood glucose levels at various dosages and durations.

Mechanisms of Blood Glucose Control

Several studies show that Trigona honey is effective in controlling blood glucose levels. (25) found that *Trigona laeviceps* honey increased insulin sensitivity and protected pancreatic beta cells. (32) demonstrated that *Geniotrigona thoracica* honey could reduce blood glucose levels and increase serum insulin. The study by (26) on *Tetragonula sp.* honey also showed increased insulin sensitivity and reduced oxidative stress, which helped lower blood glucose. (27) found that *Tetragonula biroi* honey prevented increases in fasting blood glucose levels. *Kelulut* honey (KH), studied by (33) and (34), proved to reduce fasting blood glucose levels and improve metabolic regulation. These studies suggest that Trigona honey works through mechanisms such as increasing insulin sensitivity, protecting pancreatic beta cells, and reducing oxidative stress.

Effectiveness of Trigona Honey in Humans

Some studies demonstrate the effectiveness of Trigona honey in controlling blood glucose levels in humans, although most research has been conducted on animal models. A study by (31) in Indonesia tested *Trigona* honey on type 2 diabetes patients at Puskesmas Labibia, Kendari. In this study, *Trigona* honey was administered at a dose of 40 ml per day (20 ml in the morning and evening) for 30 days. The results showed a significant reduction in fasting blood glucose levels, although there was no significant difference between *Trigona* honey and forest honey in terms of effectiveness.

Additionally, research by (30) also suggests that *Trigona* honey can serve as a complementary therapy for managing type 2 diabetes, although the exact dosage and duration were not specified. This study indicates that natural products like *Trigona* honey can significantly lower blood glucose levels in individuals with type 2 diabetes.

Overall, while most studies have been conducted on animals, the findings in humans suggest that *Trigona* honey has potential as a natural alternative to help control blood glucose levels in people with diabetes. However, further human studies with rigorous controls are needed to confirm its broader effectiveness.

Blood Glucose Reduction Levels

Research on Trigona honey has demonstrated notable reductions in blood glucose levels in both animal models and humans. In the study by (25), Trigona laeviceps honey was shown to significantly decrease blood glucose levels in Wistar rats, with a clear distinction between the control and treatment groups ($p<0.005$). Similarly, (32) observed that honey from Geniotrigona thoracica prevented increases in fasting blood glucose levels in diabetic rats. According to (26), blood glucose levels in Balb/c rats were reduced, although the exact dosage was not specified.

In (27)'s research, rats treated with Trigona honey maintained stable fasting blood glucose levels over a 35-day period. A decrease in blood glucose was also reported in type 2 diabetes patients in the study by (31), with the Trigona honey group showing an average reduction of 40.58 mg/dL after 30 days of treatment. In conclusion, various studies have consistently shown that Trigona honey is effective in lowering blood glucose levels in both animal and human models.

DISCUSSION

From the analysis of the 13 studies reviewed, *Trigona* honey demonstrates significant potential in lowering blood glucose levels in both animal models and humans. Most studies reveal that *Trigona* honey, derived from species such as *Trigona laeviceps*, *Geniotrigona thoracica*, and *Tetragonula sp.*, contains bioactive compounds like flavonoids and polyphenols, which help reduce oxidative stress, enhance insulin sensitivity, and protect pancreatic beta cells from oxidative damage (25); (32); (34) (36).

A study by (29) further confirms these findings, showing that *Heterotrigona itama* and *Geniotrigona thoracica* honey improve glucose metabolism regulation and lipid profiles in diabetic rats. This suggests that, in addition to honey from more well-known *Trigona* species, honey from other species within the same genus may also offer similar benefits. These results are consistent with research by (37), who reported that *Heterotrigona itama* honey exhibits significant antioxidant activity and can reduce blood glucose levels in diabetic animal models by alleviating oxidative stress.

Moreover, (38), in their study on *Kelulut* honey (Trigona sp.), also found that this honey can lower blood glucose levels in type 2 diabetic rats through similar mechanisms, such as reducing inflammation and inhibiting enzymes that regulate glucose metabolism. These findings strengthen the argument that *Trigona* honey, particularly honey from *Trigona sp.* and *Tetragonula* species, has exceptional potential in diabetes management, although the doses used in different studies still vary.

Further research by (39), also demonstrated that *Kelulut* honey (Trigona sp.) can increase insulin levels and reduce insulin resistance in rats on a high-glucose diet. This study suggests that *Trigona* honey, rich in antioxidant compounds, works by reducing systemic inflammation and enhancing glucose metabolism, ultimately contributing to the reduction of blood glucose levels.

Human studies conducted by (31) in Indonesia on type 2 diabetes patients also provide evidence that *Trigona* honey can serve as a complementary therapy. In this study, administering 40 ml of *Trigona* honey per day for 30 days resulted in a significant reduction in fasting blood glucose levels, although no significant difference was found between *Trigona* honey and forest honey in terms of effectiveness. This indicates that *Trigona* honey holds potential as a natural option for controlling blood glucose levels, although further studies with more rigorous designs are still required.

Overall, while most studies have been conducted in animal models, the existing findings suggest that *Trigona* honey, including honey from various species such as *Trigona laeviceps*, *Geniotrigona thoracica*, *Tetragonula sp.*, and *Kelulut* (Trigona sp.), has great potential in managing blood glucose levels. This honey works through mechanisms that involve improving insulin sensitivity, protecting pancreatic beta cells, and reducing oxidative stress, which can exacerbate diabetes. Research by (39) and (37) further underscores that *Trigona* honey is not only effective in animal models but also provides indications that it could be used as a complementary therapy in managing diabetes in humans, although more human studies with tighter controls and larger samples are needed.

Therefore, despite the positive results from existing studies, further research is required, particularly large-scale and controlled human trials, to confirm the effectiveness and optimal dosage of *Trigona* honey in blood glucose management.

CONCLUSION

Based on the analysis of 13 studies, *Trigona* honey from various species has been proven effective in lowering blood glucose levels. This reduction occurs through mechanisms such as improved insulin sensitivity, protection of pancreatic beta cells, and reduction of oxidative stress. Although the majority of the studies were conducted in animal models, some human studies also show significant reductions in blood glucose levels.

Overall, *Trigona* honey demonstrates potential as a natural complementary therapy for diabetes management. However, further research, particularly in humans, is needed with more controlled designs and larger sample sizes to confirm its effectiveness and determine the appropriate dosage.

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AUTHOR CONTRIBUTIONS

Ns. Junaidin, S.Kep., M.Kep: Responsible for the primary research concept, data collection, analysis, and drafting the initial manuscript.

Prof. Dr. dr. Abdurachman, M.Kes., PA(K): Supervised the research methodology, data analysis, and provided critical revisions of the manuscript.

Prof. Dr. Drs. I Ketut Sudiana, M.Si.: Provided technical guidance, data validation, and contributed to the final revision of the manuscript.

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