

## Exploring Antidiabetic Properties of Stingless Bee Pollen and Kasturi Mango (*Mangifera casturi*) Leaves: Comparative Review

Chantika Noor Khalifah<sup>1</sup> & Paula Mariana Kustiawan<sup>1\*</sup>

<sup>1</sup>Faculty of Pharmacy, Universitas Muhammadiyah Kalimantan Timur, Samarinda, Indonesia;

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\*Corresponding Author: **Paula Mariana Kustiawan**, Faculty of Pharmacy, Universitas Muhammadiyah Kalimantan Timur, Samarinda, Indonesia; Email: [pmk195@umkt.ac.id](mailto:pmk195@umkt.ac.id)

**Abstract:** The absence of a comparative biochemical analysis between stingless bee pollen and *Mangifera casturi* leaves prevents the optimization of their synergistic potential in diabetes management. This study aims to evaluate the bioactive profiles and compare the antidiabetic mechanisms of these two natural products. The investigation utilized a systematic literature review by retrieving peer reviewed articles from PubMed, Scopus, ScienceDirect, and Google Scholar. The selection process followed the PRISMA 2020 framework to ensure a transparent and reproducible screening of literature. Data analysis involved a comparative thematic synthesis to evaluate the correlation between phytochemical groups and glycemic control. Results demonstrate that both materials share homologous flavonoid compounds that improve insulin sensitivity and mitigate oxidative stress. Stingless bee pollen provides superior pancreatic  $\beta$  cell protection while *Mangifera casturi* shows higher inhibition of carbohydrate hydrolyzing enzymes. This study concludes that both materials offer significant antidiabetic efficacy through complementary molecular pathways. These findings provide a scientific foundation for the development of evidence based complementary medicine. Future research should prioritize clinical trials to determine the optimal dosage for human application.

**Keywords:** Antidiabetic; Mango; Kasturi; Stingless bee; Pollen.

### Introduction

Diabetes mellitus represents a complex metabolic pathophysiology characterized by chronic hyperglycemia. This condition results from the synergistic failure of insulin secretion and cellular insulin sensitivity. Such metabolic derangements precipitate systemic microvascular and macrovascular complications. These complications impose a critical socio-economic burden on global healthcare frameworks (American Diabetes Association, 2011; International Diabetes Federation, 2021). Despite the availability of sophisticated pharmacological agents, clinical management is often hampered by secondary drug failure. Many patients also experience adverse metabolic side effects and economic barriers to long-term adherence (American Diabetes Association, 2011). Consequently,

there is an urgent clinical imperative to explore bioactive natural products as viable adjunctive interventions.

The etiology of Type 2 Diabetes Mellitus (T2DM) is fundamentally linked to a decline in pancreatic beta cell function. This decline is often exacerbated by lifestyle induced oxidative stress (International Diabetes Federation, 2021). Within this context, stingless bee pollen and *Mangifera casturi* leaves present compelling pharmacological profiles. Stingless bee pollen contains high concentrations of flavonoids and phenolic acids. These compounds have been shown to mitigate oxidative damage in pancreatic tissues (Fadzilah et al., 2017). Concurrently, *Mangifera casturi* possesses a unique phytochemical architecture dominated by mangiferin and tannins. These specific compounds exert potent glycemic control by

modulating the activity of carbohydrate hydrolyzing enzymes (Ajabli & Eddouks, 2019).

A significant biochemical correlation exists between these two distinct biological sources. Both materials exhibit a shared presence of homologous polyphenolic and flavonoid groups. Stingless bee pollen inherently reflects the phytochemical profile of its botanical origin. Therefore, the bioactive compounds in *Mangifera casturi* may show striking similarities to the compounds found in the bee product. These shared metabolites provide a dual effect on T2DM by reducing systemic inflammation and enhancing glucose uptake. The polyphenols work by activating the signaling pathways that improve insulin receptor sensitivity. They also neutralize reactive oxygen species that typically destroy insulin producing cells.

This study aims to compare the phytochemical profiles and antidiabetic mechanisms of stingless bee pollen and *Mangifera casturi* leaves. By identifying the correlation between these two sources, the research evaluates their potential as evidence based complementary medicines and clarify the therapeutic strengths of each material in managing T2DM. This comparative data provides information for developing sustainable natural therapies and supports the

optimization in clinical management of diabetes.

## Materials and Methods

### Research Design

This study employed a systematic literature review with descriptive and comparative approaches to evaluate the antidiabetic potential of stingless bee pollen and *M. casturi* leaves (*Mangifera casturi*). Relevant literature was retrieved from major electronic databases, including PubMed, Scopus, and Google Scholar (Rutkowska and Olszewska, 2023).

The search strategy utilized predefined keywords such as “stingless bee pollen” and “antidiabetic”, “Trigona” and “blood glucose”, “*Mangifera casturi*” and “antidiabetic”, and “mango leaves” and “ $\alpha$ -glucosidase inhibition”. A total of 250 records were initially identified, of which 220 were retained after removing duplicates and clearly irrelevant records

### Research Procedure

The study selection process followed the PRISMA 2020 guidelines (Chandler et al., 2019; Page et al., 2021). From the 220 screened articles, 180 were excluded during title and abstract screening due to irrelevance, absence of abstracts, or classification as review articles. Subsequently, 40 articles were sought for full-text assessment. However, 5 reports could not be retrieved (Figure 1).

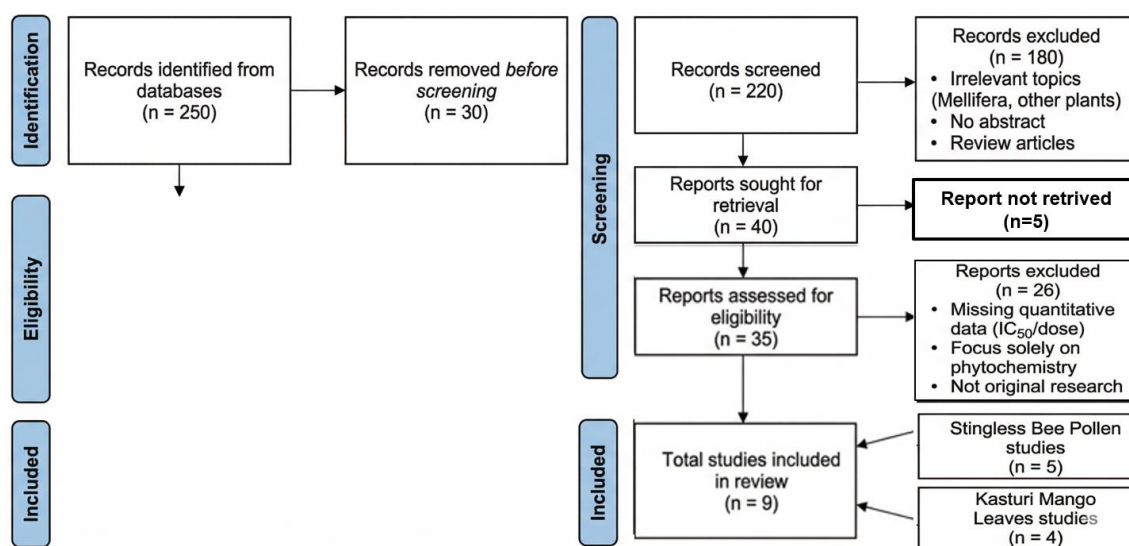


Figure 1. Flow diagram of systematic review

A total of 35 full-text articles were then assessed for eligibility, of which 26 were excluded due to incomplete quantitative data (e.g., IC<sub>50</sub> values or dosage), exclusive focus on phytochemical profiling without biological evaluation, or lack of original research design. Ultimately, 9 studies met all inclusion criteria and were included in the final analysis, comprising 5 studies on stingless bee pollen and 4 studies on kasturi mango leaves (*Mangifera casturi*).

### Data Collection

Data were systematically extracted using a standardized form to ensure consistency and accuracy. The extracted variables included study design, sample type, experimental model (in vitro, in vivo, or clinical), identified bioactive compounds, evaluated antidiabetic mechanisms, and key outcomes such as IC<sub>50</sub> values and blood glucose-lowering effects.

### Data Analysis

A qualitative approach was applied using descriptive and comparative analyses. Descriptive analysis was conducted to summarize the distribution of bioactive compounds and reported biological activities across studies. Comparative analysis was performed to identify similarities and differences in antidiabetic mechanisms, particularly with respect to  $\alpha$ -glucosidase and  $\alpha$ -amylase inhibition, antioxidant activity, and glycemic control effects. All data were organized and tabulated using Microsoft Excel to facilitate systematic comparison and synthesis.

## Result and Discussion

### Study Characteristics and Evidence Profile

A total of nine studies met the inclusion criteria in this review, consisting of five studies on stingless bee pollen and four studies on *Mangifera casturi* leaves. Most studies employed in vitro and in vivo experimental designs, with only one clinical study identified. This distribution indicates that current scientific evidence is predominantly preclinical, with variations in experimental models and measured biological parameters. Furthermore, stingless bee pollen studies mainly focus on glycemic control,

while *M. casturi* studies emphasize antioxidant activity and enzyme inhibition.

The predominance of preclinical studies suggests that although the mechanistic basis of both natural materials is relatively well established, clinical validation remains limited. This represents a critical gap, as findings from in vitro and animal models cannot always be directly translated into human outcomes. Recent studies highlight that clinical trials are essential to confirm the efficacy and safety of plant-based antidiabetic agents (Willcox et al., 2021; Uti et al., 2025). In addition, the difference in research focus reflects distinct therapeutic pathways. Stingless bee pollen primarily targets metabolic regulation, particularly glucose reduction and insulin sensitivity. Whereas *M. casturi* leaves are more associated with oxidative stress reduction and digestive enzyme inhibition. This distinction aligns with the multifactorial nature of diabetes mellitus, which involves insulin resistance, oxidative stress, and impaired glucose metabolism (Davies et al., 2026; Firdous et al., 2025). Therefore, both materials demonstrate potential within a multi-target therapeutic framework. However, the limited number of clinical studies and lack of standardized methodologies remain key limitations. These findings imply the need for further clinical validation and standardized experimental approaches.

### Bioactive Compounds and Their Functional Significance

The data in Table 1 demonstrated that both stingless bee pollen and *M. casturi* leaves contain diverse bioactive compounds with significant antidiabetic potential. Flavonoids are the most dominant compounds identified in both materials, while mangiferin is a characteristic compound of *M. casturi*. In addition, phenolics, alkaloids, and tannins contribute to the observed biological activities. This diversity suggests a potential synergistic interaction among compounds in exerting antidiabetic effects.

Flavonoids, identified in both pollen and *M. casturi*, play a central role in improving glycemic control. These compounds enhance insulin sensitivity by activating key signaling pathways such as the PI3K/Akt pathway, which promotes glucose uptake in peripheral tissues. Additionally, flavonoids exhibit strong

antioxidant properties that protect pancreatic  $\beta$ -cells from oxidative damage. This dual function is supported by previous studies indicating that flavonoid-rich extracts significantly reduce blood glucose levels and improve insulin response in diabetic models (Huang et al., 2021).

Phenolic compounds, predominantly found in pollen, contribute primarily through their free radical scavenging activity. Oxidative stress is a major contributor to the progression of diabetes and its complications, and phenolics

help mitigate this by neutralizing reactive oxygen species. Although the antioxidant activity reported by Syafrizal et al. (2016) falls into a moderate category ( $IC_{50} > 75$  ppm), even moderate antioxidant capacity can play a protective role when acting synergistically with other compounds. Similar findings have been reported by Pannucci et al. (2023), who emphasized the importance of dietary phenolics in reducing oxidative stress-related metabolic disorders.

**Table 1.** Bioactive Compounds and Their Antidiabetic Roles

Compound	Source	Mechanism	Supporting Evidence	Reference
Flavonoids	Pollen & <i>M. casturi</i>	Enhance insulin sensitivity, antioxidant	Improve glycemic status in vivo	Mohamed et al. (2018); Yuliawati et al. (2022)
Phenolics	Pollen	Free radical scavenging	Moderate antioxidant activity ( $IC_{50} > 75$ ppm)	Syafrizal et al. (2016)
Mangiferin	<i>M. casturi</i>	Antihyperglycemic, enzyme inhibition	Comparable to glibenclamide	Yuliawati et al. (2022)
Alkaloids	Both	Metabolic regulation	Present in phytochemical screening	Lestari et al. (2021)
Tannins	<i>M. casturi</i>	$\alpha$ -amylase inhibition	Strong antioxidant activity	Dwiatun (2018)

Mangiferin, a xanthonoid compound characteristic of *Mangifera* species, is a key contributor to the antidiabetic activity of *M. casturi*. Its mechanism involves inhibition of carbohydrate-hydrolyzing enzymes such as  $\alpha$ -glucosidase and  $\alpha$ -amylase, thereby delaying glucose absorption in the intestine. Furthermore, mangiferin has been shown to improve glucose metabolism and lipid profiles, as well as reduce insulin resistance. Studies by Vesnina et al. (2025) and Mistry et al. (2023) have demonstrated that mangiferin exhibits potent antihyperglycemic effects comparable to standard antidiabetic drugs, supporting the findings in Table 2.

Alkaloids, detected in both pollen and *M. casturi*, are known to contribute to metabolic regulation, although their exact mechanisms in antidiabetic activity. Previous studies suggest that alkaloids may influence glucose homeostasis by modulating enzymatic activity and enhancing insulin secretion (Amssayef & Eddouks, 2023). Their presence in phytochemical screening, as reported by Martin & Ramos (2021), indicates a potential supportive role in the overall antidiabetic effect.

Tannins, primarily found in *M. casturi*, contribute through the inhibition of  $\alpha$ -amylase, which reduces the breakdown of complex carbohydrates into glucose. This mechanism helps control postprandial blood glucose levels. In addition, tannins possess strong antioxidant properties, further enhancing their protective effects against oxidative stress-induced cellular damage. Comparable findings have been reported by Laddha et al. (2025), who highlighted the enzyme inhibitory potential of tannin-rich plant extracts.

These antidiabetic potential of stingless bee pollen and *M. casturi* is not attributed to a single compound but rather to a synergistic interaction among multiple bioactive constituents. Pollen appears to be more prominent in antioxidant and insulin-sensitizing activities, whereas *M. casturi* demonstrates stronger enzyme inhibitory effects. This complementary mechanism supports the potential development of combined or functional formulations targeting multiple pathways in diabetes management. Interestingly, the phytochemical profile of stingless bee pollen is influenced by regional flora, supporting the idea

that its bioactivity is partly derived from plant sources collected by bees (Kustiawan et al., 2017). However, this also introduces variability, which may affect reproducibility and standardization.

### Antidiabetic Activity and Dose–Effect Relationship

Table 2 presents the relationship between dosage and antidiabetic effectiveness of stingless bee pollen and *M. casturi*. The data indicate that stingless bee pollen exhibits significant glucose-lowering effects at relatively low doses, whereas

*M. casturi* requires higher doses to achieve comparable outcomes. This difference highlights variations in biological potency and pharmacological efficiency.

The high potency of stingless bee pollen at low doses suggests the presence of synergistic interactions among its bioactive compounds. Such synergy is commonly observed in natural products, where multiple compounds act together to enhance biological effects. Recent research supports that combined phytochemicals often produce stronger antidiabetic effects than isolated compounds (Chen et al., 2022).

**Table 2.** Antidiabetic Activity and Effectiveness

Sample	Dose	Model	Outcome	Reference
<i>T. incisa</i> pollen	0.25 mg	In vivo	↓ glucose 24.50%	Kurniati et al. (2024)
<i>A. mellifera</i> pollen	100 mg/kg BW	In vivo	Improved glycemic status	Mohamed et al. (2018)
Bee pollen	250 mg/kg BW	Clinical	Improved T2DM parameters	Senyuk et al. (2016)
<i>M. casturi</i> leaves	150 mg/kg BW	In vivo	Comparable to glibenclamide	Yuliawati et al. (2022)

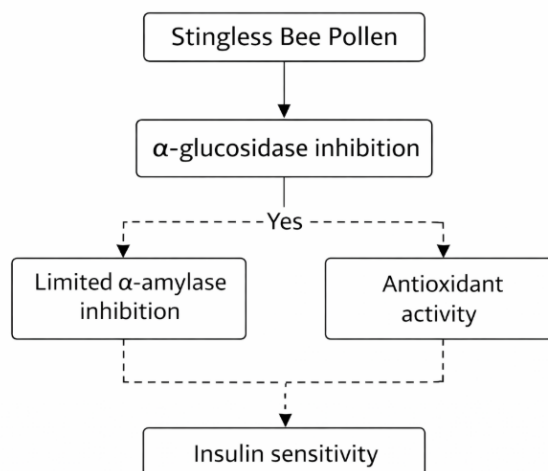
In contrast, *M. casturi* demonstrates a dose-dependent effect, where higher concentrations are required to achieve optimal pharmacological activity. This pattern indicates that dominant compounds such as mangiferin act through specific mechanisms that require sufficient bioavailability. Despite requiring higher doses, its efficacy comparable to standard drugs such as glibenclamide highlights its therapeutic potential. These findings suggest different functional roles. Stingless bee pollen as a high potency, low dose agent, and *M. casturi* as a stable, dose dependent phytotherapeutic agent. This distinction has important implications for formulation and clinical application.

### Mechanisms of Action and Comparative Analysis

The mechanism of stingless bee pollen is primarily associated with improving insulin sensitivity and enhancing glucose uptake, making it particularly effective in addressing insulin resistance, a hallmark of type 2 diabetes. Figure 1 summarizes the antidiabetic mechanisms of stingless bee pollen. Stingless bee pollen exhibit  $\alpha$ -glucosidase inhibitory activity,

but differ in the strength of other mechanisms. Stingless bee pollen shows stronger effects on insulin sensitivity, whereas *M. casturi* demonstrates more potent  $\alpha$ -amylase inhibition and antioxidant activity (Bakti et al., 2017; El-Nashar et al., 2023).

This effect is largely attributed to its flavonoid content, which modulates insulin signaling pathways. Conversely, *M. casturi* exerts its antidiabetic effect mainly through inhibition of carbohydrate-digesting enzymes, thereby reducing postprandial glucose spikes. The presence of mangiferin further enhances antioxidant activity, which plays a crucial role in protecting pancreatic  $\beta$ -cells from oxidative damage. Recent studies highlight that targeting multiple pathways simultaneously is more effective in managing diabetes (Wang et al., 2022). These findings indicate that the two materials have act through distinct yet complementary mechanisms. Rather than serving as substitutes, they have the potential to be used synergistically in a multi-target therapeutic strategy.



**Figure 1.** Mechanisms of Antidiabetic Action in Stingless Bee Pollen

### Integrated Implications, Limitations, and Future Directions

The findings of this review suggest that both stingless bee pollen and *M. casturi* leaves have strong potential as complementary antidiabetic agents. From an application perspective, stingless bee pollen may be more suitable as a functional supplement, while *M. casturi* leaves have potential for phytopharmaceutical development due to the presence of a dominant active compound (mangiferin).

However, several limitations must be considered. First, the number of studies is limited ( $n = 9$ ), and most are preclinical, reducing the strength of clinical recommendations. Second, variability in extraction methods and experimental conditions may affect consistency. Third, the lack of standardized dosage and formulation remains a major barrier to practical application.

Future research should prioritize clinical trials, standardization of extracts, and bioavailability studies. Additionally, investigating the synergistic effects of combining both materials may provide a promising strategy for developing more effective and holistic antidiabetic therapies.

Based on the literature review, the antidiabetic activity of stingless bee pollen and *M. casturi* leaves is closely associated with their bioactive compound profiles. Stingless bee pollen (*Trigona* sp.) is known to contain flavonoids, phenolic compounds, alkaloids, essential amino acids, and various biological enzymes. The presence of flavonoids and phenolic derivatives typically

associated with the *Mangifera* genus has also been documented in stingless bee products from East Kalimantan, supporting the hypothesis that phytochemical signatures of regional flora are partially transferred into bee-derived matrices through nectar and pollen collection (Kustiawan et al., 2017)

Flavonoids and phenolic compounds play a crucial role in lowering blood glucose levels by enhancing insulin sensitivity and protecting pancreatic  $\beta$ -cells from oxidative damage. Studies conducted in mice have demonstrated that stingless bee pollen significantly reduces blood glucose levels even at low doses, indicating the high biological potency of its active constituents (Mohamed et al., 2018; Kurniati et al., 2024). In addition, several studies have reported that stingless bee pollen exhibits considerable antioxidant activity, as indicated by  $IC_{50}$  values in DPPH assays ranging from moderate to strong categories. This antioxidant activity is particularly important in the context of diabetes mellitus, as oxidative stress plays a major role in disease progression and pancreatic tissue damage (Al-Hatamleh et al., 2020).

Meanwhile, *M. casturi* leaves (*Mangifera casturi*) contain key bioactive compounds such as mangiferin, flavonoids, tannins, alkaloids, and quinones. Mangiferin, a xanthone compound, is widely recognized for its antidiabetic properties through strong antihyperglycemic and antioxidant effects. In vivo studies have shown that ethanol extracts of *M. casturi* leaves at a dose of 150 mg/kg body weight significantly reduce blood glucose levels in alloxan-induced mice, with effectiveness comparable to that of glibenclamide (Yulawati et

al, 2022). Furthermore, in vitro assays have demonstrated strong antioxidant activity with low IC<sub>50</sub> values, particularly in the ethyl acetate fraction of *M. casturi* leaves (Lestari, 2021).

Table 3 presents a comparative overview of the antidiabetic potential of stingless bee pollen and *Mangifera casturi* leaves. It summarizes their main

bioactive compounds, mechanisms of action, effectiveness based on experimental studies, advantages, limitations, and overall relevance in diabetes therapy. The comparison highlights the distinct yet complementary roles of both natural products in regulating blood glucose through different biochemical pathways.

**Table 3.** Overview of Antidiabetic Potential of Stingless Bee Pollen and *Mangifera casturi* Leaves

Aspect	Stingless Bee Pollen	<i>M. casturi</i> Leaves
<b>Main Bioactive Compounds</b>	Flavonoids (quercetin, kaempferol), high total phenolics, alkaloids	Mangiferin (dominant compound), flavonoids (quercetin, rutin), tannins
<b>Antidiabetic Mechanism</b>	$\alpha$ -glucosidase inhibition, increased insulin sensitivity, antioxidant activity protects pancreatic $\beta$ cells	$\alpha$ -amylase and $\alpha$ -glucosidase inhibition, strong antioxidant activity (mangiferin), antihyperglycemic effects similar to glibenclamide in some studies
<b>Effectiveness Based on Research</b>	Blood glucose reduction up to $\pm$ 24.5% at very low dose (0.25 mg/kg BW), rapidly enhances insulin response	Strong antioxidant activity (IC <sub>50</sub> 83.61 ppm; ethyl acetate fraction 68.63 ppm), significant blood glucose reduction in various animal models
<b>Advantages</b>	Effective at low doses, combination of antioxidant activity, insulin enhancement	High antioxidant content (mangiferin), dual mechanism on carbohydrate digestive enzymes
<b>Limitations</b>	Composition variability depending on bee colony and environment, limited human clinical trials	Endemic plant (limited availability), dosage standardization not yet clear
<b>Relevance for Diabetes Therapy</b>	Potential as a supportive agent for diabetes therapy via increased insulin sensitivity and pancreatic cell protection	Potential as an alternative plant-based therapy with enzymatic and antioxidant mechanisms

A comparative analysis of the mechanisms of action indicates that stingless bee pollen and *M. casturi* leaves exert antidiabetic effects through different yet complementary pathways. Stingless bee pollen primarily acts by inhibiting the  $\alpha$ -glucosidase enzyme, thereby slowing the breakdown of complex carbohydrates into glucose in the digestive tract. This mechanism contributes to the reduction of postprandial glucose spikes. In addition, stingless bee pollen enhances insulin sensitivity, particularly in peripheral tissues, leading to increased cellular glucose uptake (Ganogpichayagrai et al., 2017; Setyawan et al., 2023).

The antioxidant activity of stingless bee pollen further contributes to its antidiabetic mechanism by reducing oxidative stress that can damage pancreatic  $\beta$ -cells. Protection of pancreatic cells is important for preserving endogenous insulin function and slowing the progression of type 2 diabetes mellitus.

*M. casturi* leaves exhibit a more pronounced mechanism of action by inhibiting carbohydrate-digesting enzymes, namely  $\alpha$ -amylase and  $\alpha$ -

glucosidase. Inhibition of these enzymes reduces the rate of intestinal glucose absorption, allowing for more stable regulation of blood glucose levels. Additionally, mangiferin and flavonoids present in *M. casturi* leaves exhibit high antioxidant activity by acting as free radical scavengers, thereby protecting pancreatic tissue and improving overall glycemic control (Wang et al., 2022; Yuliawati et al., 2022).

Comparatively, stingless bee pollen appears to be more efficient in terms of dosage and insulin sensitivity enhancement, whereas *M. casturi* leaves show greater strength in antioxidant activity and more potent  $\alpha$ -amylase inhibition. These mechanistic differences indicate that both natural materials possess distinct pharmacological characteristics while remaining effective in reducing blood glucose levels.

## Conclusion

Based on the results of the systematic literature review, it can be concluded that stingless bee pollen and *M. casturi* leaves possess potential antidiabetic activity associated with

their bioactive compound content. Stingless bee pollen contributes to enhanced insulin sensitivity and inhibition of the  $\alpha$ -glucosidase enzyme, while *M. casturi* leaves exhibit antihyperglycemic effects through the inhibition of  $\alpha$ -amylase and  $\alpha$ -glucosidase enzymes, supported by significant antioxidant activity. Comparative analysis of previous studies indicates that these natural materials act through different mechanisms and may complement each other as adjunctive therapies for type 2 diabetes mellitus. Therefore, their clinical application should be approached with caution and supported by further research.

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