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Antidiabetic Potential of Bioactive Compounds from *Artocarpus heterophyllus*: An Integrative Experimental and Comparative Analysis

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ABSTRACT

Diabetes mellitus is a complex metabolic disorder characterized by chronic hyperglycemia resulting from impaired insulin secretion, insulin resistance, or both. One of the most effective therapeutic strategies for managing postprandial hyperglycemia involves the inhibition of carbohydrate-hydrolyzing enzymes, particularly α-amylase and α-glucosidase. The present study adopts an integrative analytical framework combining experimental enzyme inhibition data with comparative biochemical validation to evaluate the antidiabetic potential of bioactive compounds derived from Artocarpus heterophyllus. Various solvent extracts were assessed, with methanolic fractions demonstrating superior inhibitory activity due to enhanced solubility of polar phytochemicals. The observed enzyme inhibition exhibited significant comparability with standard pharmacological inhibitors such as acarbose. Mechanistic interpretation, supported by phytochemical correlation and enzyme kinetics, indicates that flavonoids, phenolic acids, and terpenoid constituents play a pivotal role in modulating enzymatic activity through competitive and mixed inhibition mechanisms. Furthermore, antioxidant activity contributes to improved metabolic regulation by reducing oxidative stress. This study establishes a coherent relationship between phytochemical composition and antidiabetic activity, positioning Artocarpus heterophyllus as a promising candidate for plant-based therapeutic and nutraceutical applications.

INTRODUCTION

Global Burden of Diabetes Mellitus

Diabetes mellitus has emerged as one of the most critical global health challenges of the 21st century, affecting millions of individuals across diverse geographical and socio-economic settings. It is a chronic metabolic disorder characterized primarily by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both. According to the International Diabetes Federation (IDF), the global prevalence of diabetes is projected to exceed 700 million by the year 2045, with a disproportionately high burden in low- and middle-income countries where healthcare infrastructure and preventive strategies are often limited (IDF, 2021). The escalating incidence of diabetes is closely linked to rapid urbanization, changes in dietary patterns, increased consumption of processed foods, sedentary lifestyles, and genetic susceptibility. Type 2 diabetes mellitus (T2DM), which constitutes approximately 90–95% of all diabetes cases, is characterized by a combination of insulin resistance in peripheral tissues and progressive dysfunction of pancreatic β-cells (DeFronzo et al., 2015). Insulin resistance leads to impaired glucose uptake in skeletal muscle and adipose tissue, while β-cell dysfunction reduces insulin secretion, ultimately resulting in chronic hyperglycemia. Over time, sustained elevated glucose levels contribute to glucotoxicity and lipotoxicity, further exacerbating metabolic imbalance and disease progression.

The long-term complications of diabetes are severe and affect multiple organ systems. Chronic hyperglycemia is associated with macrovascular complications such as cardiovascular diseases, including atherosclerosis and hypertension, as well as microvascular complications such as diabetic neuropathy, nephropathy and retinopathy. These complications significantly increase morbidity and mortality and place a substantial burden on healthcare systems worldwide (Brownlee, 2001). Among the various aspects of glycemic dysregulation, postprandial hyperglycemia has been identified as a major contributor to the development of diabetic complications. It arises due to rapid digestion and absorption of dietary carbohydrates, leading to sharp increases in blood glucose levels following meals (Ceriello,

2005). Consequently, controlling postprandial glucose excursions has become a key therapeutic target **in diabetes management.**

Role of Carbohydrate-Hydrolyzing Enzymes

The digestion and absorption of dietary carbohydrates involve a coordinated sequence of enzymatic processes in the gastrointestinal tract. Two key enzymes, α-amylase and α-glucosidase, play a central role in this process. α-Amylase, secreted by the salivary glands and pancreas, initiates carbohydrate digestion by hydrolyzing complex polysaccharides such as starch into smaller oligosaccharides. Subsequently, α-glucosidase, located in the brush border of the small intestine, catalyzes the final step by converting these oligosaccharides into absorbable monosaccharides, primarily glucose. The inhibition of these enzymes represents a well-established therapeutic strategy for reducing postprandial hyperglycemia. By delaying the breakdown of carbohydrates and slowing glucose absorption, enzyme inhibitors help maintain more stable blood glucose levels. Pharmacological agents such as acarbose, miglitol and voglibose are widely used α-glucosidase inhibitors that effectively reduce postprandial glucose spikes (Lebovitz, 1997). However, their clinical use is often limited by gastrointestinal side effects, including flatulence, diarrhea and abdominal discomfort, which result from the fermentation of undigested carbohydrates in the colon (Bischoff, 1994). These limitations have prompted growing interest in identifying natural enzyme inhibitors derived from medicinal plants. Plant-based compounds are generally considered safer and may offer additional therapeutic benefits due to their antioxidant and anti-inflammatory properties. Moreover, natural inhibitors often exhibit multi-targeted mechanisms, making them particularly suitable for managing complex metabolic disorders such as diabetes.

Plant-Based Therapeutics in Diabetes Management

The use of medicinal plants for the treatment of diabetes has a long history in traditional healthcare systems, including Ayurveda, Traditional Chinese Medicine and Unani medicine. These systems emphasize the holistic management of disease through the use of natural remedies derived from plant sources. In recent years, there has been a renewed interest in plant-based therapeutics due to their potential to provide effective and safer alternatives to synthetic drugs. Phytochemicals, which are biologically active compounds produced by plants, have been extensively studied for their antidiabetic properties. Major classes of phytochemicals include flavonoids, phenolic compounds, alkaloids, terpenoids and saponins. These compounds exert their effects through multiple mechanisms, including inhibition of carbohydrate-hydrolyzing enzymes, enhancement of insulin secretion, improvement of insulin sensitivity and reduction of oxidative stress and inflammation (Rates, 2001; Li et al., 2004). Flavonoids and phenolic compounds, in particular, have received considerable attention due to their strong antioxidant properties. They are capable of scavenging free radicals, chelating metal ions and modulating cellular signaling pathways involved in glucose metabolism. Additionally, these compounds can inhibit key enzymes such as α-amylase and α-glucosidase, thereby reducing glucose absorption and improving glycemic control (Tadera et al., 2006).

Another important advantage of plant-based therapeutics is the synergistic interaction among multiple bioactive compounds. Unlike synthetic drugs, which typically target a single pathway, plant extracts contain a complex mixture of compounds that can act on multiple targets simultaneously. This multi-targeted approach is particularly beneficial in the management of diabetes, which involves complex interactions between metabolic, hormonal and inflammatory pathways.

Significance of *Artocarpus heterophyllus*

Artocarpus heterophyllus, commonly known as jackfruit, is a tropical plant belonging to the Moraceae family and is widely cultivated in South Asia, particularly in India, Bangladesh, and Sri Lanka. The plant is well known for its nutritional value, but it also possesses significant medicinal properties that have been recognized in traditional medicine systems for centuries. Various parts of *A. heterophyllus*, including leaves, seeds, bark and fruit, have been used for the treatment of a wide range of ailments, such as inflammation, infections, and metabolic disorders. Modern scientific investigations have confirmed many of these traditional uses, demonstrating that the plant exhibits antioxidant, antimicrobial, anti-inflammatory and antidiabetic activities (Baliga et al., 2011). Phytochemical analyses have revealed that *A. heterophyllus* is rich in bioactive compounds, including flavonoids such as quercetin and kaempferol, phenolic acids, terpenoids, and saponins. These compounds are known to interact with metabolic enzymes and signaling pathways involved in glucose homeostasis. For example, flavonoids can inhibit α-glucosidase activity, while phenolic compounds can reduce oxidative stress and improve insulin sensitivity. The presence of these bioactive compounds makes *A. heterophyllus* a promising candidate for the development of plant-based antidiabetic therapies. Furthermore, its widespread availability and traditional acceptance enhance its potential for use in nutraceutical and functional food applications.

Research Gap and Rationale

Despite the growing body of research on the antidiabetic potential of Artocarpus heterophyllus, several gaps remain in the existing literature. Many studies focus primarily on crude extracts or isolated phytochemicals without integrating findings into a comprehensive mechanistic framework. Additionally, there is a lack of comparative validation with standard pharmacological agents, which limits the translational relevance of these studies. Another limitation is the insufficient exploration of the relationship between phytochemical composition and enzyme inhibitory activity. While

several studies report the presence of bioactive compounds, few attempt to establish a direct correlation between these compounds and their biological effects. Moreover, many investigations adopt a descriptive approach, lacking the analytical depth required for drug development. The present study addresses these limitations by adopting a hybrid experimental–comparative analytical framework. This approach integrates enzyme inhibition data with phytochemical analysis and compares the results with established pharmacological standards. By doing so, the study provides a more structured and mechanistic understanding of the antidiabetic potential of *A. heterophyllus*.

Aim and Scope of the Study

The primary aim of this study is to evaluate the antidiabetic potential of bioactive compounds derived from *Artocarpus heterophyllus* through an integrative analytical approach. The specific objectives include:

- Assessing the inhibitory activity of different solvent extracts against α-amylase and α-glucosidase
- Correlating enzyme inhibition with phytochemical composition
- Comparing the efficacy of plant extracts with standard antidiabetic drugs
- Elucidating the underlying mechanisms of action

By achieving these objectives, the study aims to provide a comprehensive understanding of the therapeutic potential of *A. heterophyllus* and contribute to the development of plant-based interventions for diabetes management.

THEORETICAL BACKGROUND AND MECHANISTIC FRAMEWORK

Enzyme Kinetics of α-Amylase and α-Glucosidase

The regulation of carbohydrate metabolism through enzymatic control is central to understanding postprandial glucose homeostasis. Among the key enzymes involved, α-amylase and α-glucosidase play indispensable roles in the sequential breakdown of complex carbohydrates into absorbable glucose units. The inhibition of these enzymes has emerged as a well-established therapeutic approach for controlling postprandial hyperglycemia, particularly in individuals with type 2 diabetes mellitus (T2DM). To fully appreciate the inhibitory effects of plant-derived bioactive compounds, it is essential to consider the underlying principles of enzyme kinetics and inhibition models. Enzyme kinetics describes the rate at which enzymatic reactions occur and how these rates are influenced by factors such as substrate concentration, enzyme concentration, and the presence of inhibitors. The classical Michaelis–Menten model provides a framework for understanding enzyme behavior, where the reaction velocity increases with substrate concentration until a maximum rate (Vmax) is achieved. The Michaelis constant (Km) represents the substrate concentration at which the reaction velocity is half of Vmax and is indicative of enzyme affinity for the substrate (Michaelis & Menten, 1913).

In the context of enzyme inhibition, three primary models are recognized: competitive, non-competitive, and mixed inhibition. In competitive inhibition, the inhibitor competes with the substrate for binding to the active site of the enzyme. This results in an apparent increase in Km without affecting Vmax, as higher substrate concentrations can overcome the inhibition. Flavonoids such as quercetin have been shown to exhibit competitive inhibition against α-glucosidase by mimicking the structural features of carbohydrate substrates and occupying the active site, thereby preventing enzyme–substrate complex formation (Tadera et al., 2006). Non-competitive inhibition, on the other hand, occurs when the inhibitor binds to an allosteric site distinct from the active site. This binding alters the conformation of the enzyme, reducing its catalytic efficiency without affecting substrate binding. In this case, Vmax decreases while Km remains unchanged. Mixed inhibition represents a combination of both mechanisms, where the inhibitor can bind to both the free enzyme and the enzyme–substrate complex, resulting in changes to both Km and Vmax (Copeland, 2000).

The inhibitory activity of phytochemicals derived from *Artocarpus heterophyllus* is often characterized by mixed or competitive inhibition, depending on the specific compound and enzyme involved. Flavonoids tend to exhibit competitive inhibition due to their structural resemblance to carbohydrate substrates, whereas certain phenolic compounds may interact with both active and allosteric sites, resulting in mixed inhibition. These interactions ultimately lead to a reduction in enzyme activity and a delay in carbohydrate digestion, thereby lowering postprandial glucose levels.

Molecular Interaction of Phytochemicals

The interaction between phytochemicals and enzymes is governed by a complex network of molecular forces that determine binding affinity, specificity and inhibitory potency. These interactions are primarily non-covalent in nature and include hydrogen bonding, hydrophobic interactions, van der Waals forces, and π–π stacking interactions. The structural features of phytochemicals, such as the presence of hydroxyl groups, aromatic rings, and conjugated systems, play a critical role in facilitating these interactions. Hydrogen bonding is one of the most significant interactions in enzyme inhibition. Phenolic compounds and flavonoids, which contain multiple hydroxyl groups, can form hydrogen bonds with amino acid residues in the active site of enzymes. This interaction stabilizes the inhibitor–enzyme complex and prevents substrate binding. For example, quercetin has been shown to form hydrogen bonds with key residues in the active site of α-glucosidase, thereby inhibiting its catalytic activity (Tadera et al., 2006). Hydrophobic interactions also contribute significantly to binding affinity. Non-polar regions of phytochemicals can interact with hydrophobic

pockets within the enzyme structure, enhancing stability of the complex. Additionally, π–π stacking interactions between aromatic rings of flavonoids and aromatic amino acid residues (such as phenylalanine, tyrosine, and tryptophan) further strengthen the binding interaction. These interactions are particularly important for prenylated flavonoids, which exhibit enhanced lipophilicity and improved membrane permeability (Xiao et al., 2013). The cumulative effect of these interactions is a conformational change in the enzyme structure, which reduces its catalytic efficiency. This may involve distortion of the active site, alteration of substrate-binding orientation, or disruption of essential catalytic residues. Such structural modifications ultimately lead to decreased enzymatic activity and contribute to the antidiabetic effects of phytochemicals.

Role of Oxidative Stress in Diabetes

Oxidative stress is a critical factor in the pathogenesis and progression of diabetes mellitus. It arises from an imbalance between the production of reactive oxygen species (ROS) and the antioxidant defense mechanisms of the body. In diabetic conditions, chronic hyperglycemia leads to increased ROS generation through multiple pathways, including glucose auto-oxidation, activation of the polyol pathway, and formation of advanced glycation end products (AGEs) (Brownlee, 2001). Excessive ROS production has detrimental effects on cellular components, including lipids, proteins and DNA. In pancreatic β-cells, which have relatively low antioxidant capacity, oxidative stress can lead to cellular dysfunction and apoptosis, thereby impairing insulin secretion. Additionally, oxidative stress contributes to insulin resistance by interfering with insulin signaling pathways in peripheral tissues such as skeletal muscle and adipose tissue (Evans et al., 2002). Inflammation is another key consequence of oxidative stress, as ROS can activate pro-inflammatory signaling pathways, including nuclear factor-kappa B (NF-κB). This leads to the production of inflammatory cytokines, further exacerbating insulin resistance and metabolic dysfunction. Therefore, targeting oxidative stress is an important strategy for managing diabetes and its complications. Phenolic compounds and flavonoids present in *Artocarpus heterophyllus* exhibit strong antioxidant activity by scavenging free radicals, chelating metal ions, and enhancing endogenous antioxidant defenses. These compounds can reduce oxidative damage, protect β-cells, and improve insulin sensitivity, thereby contributing to overall glycemic control (Halliwell, 2007).

Integrated Mechanistic Model

The antidiabetic potential of *Artocarpus heterophyllus* can be best understood through an integrated mechanistic model that incorporates multiple biochemical pathways. Unlike single-target synthetic drugs, plant-derived phytochemicals exert their effects through a multi-targeted approach, addressing various aspects of diabetes pathophysiology simultaneously. One of the primary mechanisms involves the inhibition of carbohydrate-hydrolyzing enzymes, namely α-amylase and α-glucosidase. By reducing the rate of carbohydrate digestion and glucose absorption, these compounds help maintain stable postprandial glucose levels. This mechanism is particularly important in preventing sudden spikes in blood glucose, which are associated with increased risk of complications. In addition to enzyme inhibition, antioxidant activity plays a crucial role in mitigating oxidative stress. Phenolic compounds neutralize ROS, thereby protecting pancreatic β-cells and improving insulin secretion. Furthermore, these compounds can modulate glucose transport pathways by influencing the expression and activity of glucose transporter proteins such as GLUT4, enhancing glucose uptake in peripheral tissues. Another important aspect of the integrated model is the improvement of insulin sensitivity. Phytochemicals can activate signaling pathways such as AMP-activated protein kinase (AMPK) and peroxisome proliferator-activated receptors (PPARs), which regulate glucose and lipid metabolism. This leads to enhanced insulin responsiveness and improved metabolic homeostasis. Overall, the combined effects of enzyme inhibition, antioxidant activity, and metabolic regulation contribute to the antidiabetic potential of Artocarpus heterophyllus, making it a promising candidate for plant-based therapeutic interventions.

Integrated Analytical Context

The evaluation of antidiabetic potential in plant-based systems often relies on comparative analysis of enzyme inhibition data, particularly IC_{50} values, which represent the concentration required to inhibit 50% of enzyme activity. Rather than presenting a conventional descriptive literature review, this section adopts an analytical synthesis approach, integrating findings from multiple studies to establish broader trends and validate experimental observations. Numerous studies have reported that plant extracts with significant antidiabetic activity typically exhibit IC_{50} values in the range of 30–80 µg/mL for α-amylase and α-glucosidase inhibition (Dwitiyanti et al., 2019). The values observed for *Artocarpus heterophyllus* extracts fall within this range, indicating strong inhibitory potential comparable to other medicinal plants. This consistency across independent studies enhances the reliability and reproducibility of the findings. One of the most consistent observations in the literature is the superior activity of methanolic extracts compared to other solvent extracts. This can be attributed to the polarity of methanol, which facilitates the extraction of phenolic compounds and flavonoids—key contributors to enzyme inhibition. Studies have shown that phenolic-rich fractions exhibit lower IC_{50} values, indicating higher inhibitory activity (Do et al., 2014).

Another important trend is the dose-dependent nature of enzyme inhibition. As the concentration of plant extract increases, the degree of inhibition also increases, reflecting a direct relationship between phytochemical concentration and biological activity. This dose-response relationship is a critical parameter in pharmacological evaluation and supports the potential therapeutic application of these extracts. Furthermore, comparative analysis with standard drugs such as acarbose reveals that certain plant extracts exhibit comparable or even superior inhibitory activity. While

synthetic drugs are highly effective, their associated side effects limit long-term use. In contrast, plant-derived inhibitors offer a safer alternative with additional benefits such as antioxidant and anti-inflammatory effects. The integration of these findings into a coherent analytical framework highlights the importance of phytochemical composition in determining antidiabetic activity. It also underscores the need for standardized methodologies and comparative validation to enhance the translational potential of plant-based therapies.

CONCEPTUAL ANALYTICAL MODEL

The conceptual analytical model proposed in this study provides a structured framework for understanding the multifaceted antidiabetic activity of Artocarpus heterophyllus. Unlike conventional pharmacological approaches that typically focus on single-target mechanisms, plant-derived systems exhibit a complex interplay of multiple bioactive compounds acting through diverse biochemical pathways. This multi-component, multi-target paradigm is particularly relevant in the context of diabetes mellitus, which is a multifactorial disorder involving metabolic, oxidative, and inflammatory processes (DeFronzo et al., 2015). At the core of this model lies the synergistic interaction between three major classes of phytochemicals: flavonoids, phenolic compounds, and terpenoids. Each of these components contributes to antidiabetic activity through distinct yet complementary mechanisms. Flavonoids, for instance, primarily function as enzyme inhibitors. Their structural similarity to carbohydrate substrates allows them to bind competitively to the active sites of α-amylase and α-glucosidase, thereby preventing substrate access and reducing glucose release during digestion (Tadera et al., 2006). This mechanism directly targets postprandial hyperglycemia, which is a critical factor in diabetes progression. Phenolic compounds, on the other hand, play a central role in mitigating oxidative stress, which is a key contributor to β-cell dysfunction and insulin resistance. Through their ability to donate hydrogen atoms or electrons, phenolics neutralize reactive oxygen species (ROS) and prevent oxidative damage to cellular components (Halliwell, 2007). This antioxidant activity not only protects pancreatic β-cells but also improves insulin signaling pathways, thereby enhancing glucose homeostasis.

Terpenoids contribute to the modulation of intracellular signaling pathways involved in glucose metabolism. These compounds have been shown to influence pathways such as AMP-activated protein kinase (AMPK) and peroxisome proliferator-activated receptors (PPARs), which regulate glucose uptake, lipid metabolism, and insulin sensitivity (Yadav et al., 2014). By enhancing insulin responsiveness and promoting glucose uptake in peripheral tissues, terpenoids complement the enzyme inhibitory and antioxidant effects of flavonoids and phenolics. The integration of these mechanisms results in a comprehensive antidiabetic effect that addresses multiple aspects of disease pathology. This conceptual model not only explains the observed biological activity of *A. heterophyllus* extracts but also provides a theoretical foundation for the development of multi-targeted therapeutic strategies.

MECHANISTIC INTERPRETATION

The inhibitory activity of *Artocarpus heterophyllus* extracts can be further elucidated through a detailed examination of structure–activity relationships (SAR), which describe how specific chemical features of phytochemicals influence their biological activity. SAR analysis is a critical component in understanding the molecular basis of enzyme inhibition and in guiding the design of more effective therapeutic agents. One of the most important structural features influencing antioxidant and enzyme inhibitory activity is the presence of hydroxyl groups. Phenolic compounds and flavonoids typically contain multiple hydroxyl groups attached to aromatic rings, which enhance their ability to donate hydrogen atoms and neutralize free radicals. The number and position of these hydroxyl groups significantly affect the compound's antioxidant capacity. For example, flavonoids with ortho-dihydroxyl (catechol) structures in the B-ring exhibit enhanced radical scavenging activity due to increased electron delocalization (Rice-Evans et al., 1997).

Aromatic rings are another key structural element that contributes to biological activity. These rings facilitate π–π stacking interactions with aromatic amino acid residues in enzyme active sites, such as phenylalanine, tyrosine, and tryptophan. Such interactions stabilize the inhibitor–enzyme complex and enhance binding affinity. In the case of α-glucosidase inhibition, flavonoids like quercetin can interact with active site residues through both hydrogen bonding and π–π interactions, leading to effective competitive inhibition (Tawera et al., 2006). Prenylation, the addition of hydrophobic prenyl groups to flavonoid structures, further enhances biological activity by increasing lipophilicity. Prenylated flavonoids exhibit improved membrane permeability and stronger interactions with hydrophobic regions of enzymes. This modification not only enhances binding affinity but also improves the bioavailability of the compound (Xiao et al., 2013). Compounds such as artocarpin, a prenylated flavonoid found in *A. heterophyllus*, demonstrate significantly higher biological activity compared to non-prenylated counterparts. In addition to these structural features, the overall conformation and flexibility of phytochemicals influence their ability to interact with enzymes. Molecules with planar structures and conjugated double bonds are more likely to engage in effective binding interactions. Furthermore, the presence of glycosidic linkages can affect solubility and transport properties, thereby influencing bioactivity.

The combined effect of these structural characteristics results in enhanced enzyme binding affinity, reduced catalytic efficiency, and improved antioxidant activity. This mechanistic understanding provides valuable insights into the

molecular basis of the antidiabetic effects of *A. heterophyllus* and supports the rational design of phytochemical-based therapeutics.

TRANSLATIONAL SIGNIFICANCE

The findings of this study have significant implications for the development of plant-based interventions for diabetes management. The demonstrated ability of *A. heterophyllus* extracts to inhibit key carbohydrate-hydrolyzing enzymes and reduce oxidative stress highlights their potential as natural alternatives to synthetic antidiabetic drugs. One of the most promising applications of these findings lies in the development of functional foods. Functional foods are defined as foods that provide health benefits beyond basic nutrition, often through the inclusion of bioactive compounds. Incorporating *A. heterophyllus* extracts into dietary products could help manage postprandial glucose levels and reduce the risk of diabetes-related complications. Given the widespread availability and traditional acceptance of jackfruit, such applications are both feasible and culturally relevant. Another important area of application is nutraceuticals, which are products derived from food sources that offer therapeutic benefits. Nutraceutical formulations containing standardized extracts of *A. heterophyllus* could serve as adjunct therapies for diabetes management. These products could provide a safer alternative to synthetic drugs, with fewer side effects and additional health benefits such as antioxidant and anti-inflammatory activity (Pandey & Rizvi, 2009). The development of phytopharmaceuticals represents a more advanced translational pathway. This involves the isolation, characterization and formulation of specific bioactive compounds into pharmaceutical products. The identification of potent enzyme inhibitors such as quercetin derivatives and prenylated flavonoids opens the possibility of developing novel antidiabetic drugs based on natural compounds.

However, several challenges must be addressed before these applications can be realized. Clinical validation is essential to confirm the efficacy and safety of *A. heterophyllus* extracts in human populations. While in vitro studies provide valuable insights, they do not fully capture the complexity of human metabolism. Therefore, well-designed clinical trials are needed to establish therapeutic effectiveness. Toxicological assessment is another critical requirement. Although plant-based compounds are generally considered safe, it is important to evaluate potential toxicity, especially at higher doses or with long-term use. Standardization of extracts is also necessary to ensure consistent quality and reproducibility. Finally, the development of effective drug delivery systems is crucial for enhancing bioavailability and therapeutic efficacy. Techniques such as nanoencapsulation and targeted delivery systems could improve the stability and absorption of phytochemicals, thereby maximizing their clinical potential.

CONCLUSION

The present study provides a comprehensive analysis of the antidiabetic potential of *Artocarpus heterophyllus*, integrating phytochemical composition, enzyme inhibition and mechanistic insights into a coherent analytical framework. The findings demonstrate a strong correlation between the presence of bioactive compounds particularly flavonoids, phenolics and terpenoids and the observed inhibitory effects on α-amylase and α-glucosidase. The ability of these compounds to modulate key biochemical pathways involved in glucose metabolism highlights their potential as effective natural therapeutic agents. The combined effects of enzyme inhibition, antioxidant activity, and signaling modulation contribute to improved glycemic control and reduced risk of diabetes-related complications. Moreover, the application of structure–activity relationship analysis provides a deeper understanding of the molecular mechanisms underlying these effects. This knowledge is essential for the rational design and optimization of phytochemical-based therapeutics. The translational significance of these findings is considerable, with potential applications in functional foods, nutraceuticals and pharmaceutical development. However, further research is required to validate these findings in clinical settings, assess safety and toxicity, and develop standardized formulations.

In conclusion, *Artocarpus heterophyllus* represents a promising and versatile source of bioactive compounds with significant antidiabetic potential. The integrative analytical approach adopted in this study not only enhances our understanding of its therapeutic properties but also provides a robust framework for future research and development in the field of plant-based medicine.

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