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From Lipids to Signalling: Herbal Formulation Strategies in Type 2 Diabetes Mellitus with Emphasis on Andrographis paniculata Hard Gelatin Capsules

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ABSTRACT:

Insulin resistance and relative insulin insufficiency are the main causes of type 2 diabetes mellitus (T2DM), a chronic metabolic disease marked by persistent hyperglycemia. T2DM is becoming more and more common worldwide, which presents a serious public health concern. Chronic low-grade inflammation, oxidative stress, disrupted insulin signalling pathways, and altered lipid metabolism are all strongly associated with insulin resistance. The fundamental pathophysiology of insulin resistance is not sufficiently addressed by traditional antidiabetic medications, despite their effectiveness in glycaemic management and frequent side effects. Due to their long history of traditional usage, improved tolerability, and multitargeted activities, herbal medications have drawn more attention in recent years. The well-known medicinal herb Andrographis paniculata has shown notable antihyperlipidemic, antidiabetic, antioxidant, and insulin-sensitizing effects. This article offers a thorough analysis of type 2 diabetes, including its etiology, contemporary treatment modalities, and the function of herbal remedies in antidiabetic treatment. With particular reference to hard gelatin capsules, special attention is paid to Andrographis paniculata, its phytochemistry, pharmacological activity, and formulation issues. The improvement of insulin sensitivity in diabetes is highlighted in the essential discussion of the molecular relationship among lipid metabolism, insulin signalling, and glycaemic control. Lastly, a summary of current research gaps and potential directions for herbal antidiabetic formulations is provided.

Keywords: Type 2 diabetes mellitus, insulin resistance, insulin sensitivity, lipid metabolism, *Andrographis paniculata*, herbal formulations, hard gelatin capsules.

INTRODUCTION:

A class of metabolic diseases known as diabetes mellitus is typified by persistently high blood sugar levels brought on by deficiencies in either insulin production, insulin action, or both (1). Type 2 diabetes mellitus makes up between 90 and 95 percent of all cases of diabetes globally. Obesity, a sedentary lifestyle, dyslipidemia, and genetic risk are all closely linked to the condition (2). A defining feature of type 2 diabetes, insulin resistance is essential to the advancement of the illness and the emergence of chronic complications. (3)

Recent scientific attention has shifted from mere glycaemic control to improving insulin sensitivity and correcting metabolic dysfunctions at the cellular level. (4) Altered lipid metabolism and impaired insulin signalling pathways are now recognized as key contributors to insulin resistance. (5) Herbal medicines, with their complex mixture of bioactive compounds, offer a promising approach to target multiple pathways simultaneously (6).

Traditional medical systems have made extensive use of Andrographis paniculata, sometimes referred to as "Kalmegh," to treat diabetes and other metabolic diseases (7). Its main bioactive component, andrographolide, has demonstrated promise in regulating lipid metabolism, boosting insulin sensitivity, and promoting glycaemic management (8). Using a formulation-oriented viewpoint, this study critically examines A. paniculata's therapeutic potential in T2DM.

TYPE 2 DIABETES MELLITUS: DEFINITION, CLASSIFICATION AND EPIDEMIOLOGY

Chronic hyperglycemia brought on by insulin resistance and insufficient compensatory insulin production is the hallmark of type 2 diabetes mellitus, a metabolic disease (9). Unlike type 1 diabetes, type 2 diabetes develops gradually over time rather than being largely caused by the autoimmune loss of pancreatic β-cells.(10) Type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes mellitus, and other distinct forms linked to genetic flaws, pancreatic disorders, or drug-induced illnesses are the main categories of diabetes mellitus. The most common of them is type 2 diabetes, which is greatly impacted by lifestyle choice (11).

The prevalence of type 2 diabetes is rapidly rising, according to epidemiological data, especially in emerging nations. This tendency has been greatly influenced by urbanization, dietary changes, physical inactivity, and rising obesity rates (12). With a significant percentage of people acquiring diabetes at an earlier age, India is regarded as one of the world's epicenters for the condition. The growing prevalence of type 2 diabetes highlights the pressing need for more comprehensive, affordable, and safe treatment approaches (13).

PATHOPHYSIOLOGY OF TYPE 2 DIABETES MELLITUS

T2DM has a complicated and diverse etiology. A major problem is insulin resistance in peripheral tissues such the liver, adipose tissue, and skeletal muscle. Pancreatic β-cells make up for this in the early stages of the illness by secreting more insulin. Prolonged metabolic stress, however, ultimately results in β cell failure and malfunction (14).

The development of insulin resistance is significantly influenced by altered lipid metabolism. Impaired glucose uptake results from disruptions in insulin signalling pathways caused by elevated free fatty acids and ectopic lipid buildup (15). Oxidative stress and persistent inflammation also make insulin resistance worse.

Reduced phosphorylation of insulin receptor substrates, malfunctions in insulin receptor signalling, and poor activation of downstream pathways like PI3K/Akt are some of the biochemical causes of diminished insulin sensitivity. These alterations result in reduced glucose transporter translocation and increased hepatic glucose production, culminating in persistent hyperglycaemia (16).

CURRENT THERAPEUTIC APPROACHES FOR TYPE 2 DIABETES MELLITUS

The management of T2DM primarily aims at achieving and maintaining optimal glycaemic control while preventing complications. Lifestyle modification, including dietary regulation and physical activity, forms the cornerstone of therapy (17). Pharmacological treatment includes oral hypoglycaemic agents and injectable therapies.

Biguanides, sulfonylureas, thiazolidinediones, DPP 4 inhibitors, SGLT-2 inhibitors, and GLP-1 receptor agonists are among the frequently utilized medication classes (18). Despite the fact that these medications effectively lower blood glucose levels, many of them have negative side effects, including weight gain, hypoglycemia, gastrointestinal issues, and cardiovascular

Moreover, most conventional therapies focus on symptomatic control rather than addressing the underlying insulin resistance. This limitation has led to growing interest in alternative and complementary therapies, particularly herbal medicines with insulin sensitizing properties. (20)

HERBAL MEDICINES IN ANTIDIABETIC THERAPY

In management of diabetes Herbal medicines are used in the centuries. Numerous medicinal plants possess antihyperglycaemic, antihyperlipidaemic, antioxidant, and anti-inflammatory activities (21). The multitargeted nature of herbal drugs makes them particularly suitable for complex metabolic disorders like T2DM.

Among the many ways that herbal antidiabetic medicines work is by promoting insulin production, improving insulin sensitivity, blocking enzymes that break down carbohydrates, modifying lipid metabolism, and shielding pancreatic β-cells (22). Additionally, their relatively lower toxicity and better patient compliance make them attractive alternatives or adjuncts to conventional therapy (23).

However, lack of standardization, variability in phytochemical content, and limited clinical evidence remain major challenges in the widespread acceptance of herbal medicines (24).

Andrographis paniculata: Botanical and Phytochemical Profile

The annual herb Andrographis paniculata is a member of the Acanthaceae family. It is widely distributed in tropical and subtropical regions and is extensively used in traditional medicine systems (25).

Diterpenoid lactones, flavonoids, polyphenols, and sterols have all been found through phytochemical analyses. The primary bioactive substance in charge of the majority of the plant's pharmacological actions is andrographolide (26). Other important constituents include deoxyandrographolide and neoandrographolide (27).

PHARMACOLOGICAL ACTIVITIES RELEVANT TO DIABETES

A. paniculata has been shown to have antidiabetic properties in a number of preclinical investigations (28). It has been demonstrated that the plant extracts and isolated components increase insulin sensitivity, improve glucose tolerance, and lower fasting blood glucose levels (29).

Improving insulin resistance is largely dependent on A. paniculata's antihyperlipidaemic action. Improved insulin signalling is a result of lower levels of total cholesterol, free fatty acids, and serum triglycerides (30).

Anti-inflammatory effects further support the role of A. paniculata in improving metabolic health, as chronic inflammation is a key contributor to insulin resistance in T2DM (31).

ENHANCEMENT OF INSULIN SENSITIVITY IN DIABETES

Enhancement of insulin sensitivity is a primary therapeutic goal in the management of T2DM. Increased insulin sensitivity lowers hepatic glucose production and promotes effective glucose absorption by peripheral tissues (32).

Herbal agents such as A. paniculata enhance insulin sensitivity by modulating insulin receptor signalling pathways, activating AMP-activated protein kinase, and improving lipid metabolism. By reducing lipid-induced insulin resistance and oxidative stress, these agents restore insulin responsiveness at the cellular level (33).

In addition to helping with glycaemic management, increased insulin sensitivity lowers the risk of cardiovascular problems linked to type 2 diabetes.

MECHANISTIC LINK: LIPID METABOLISM, INSULIN SIGNALLING AND GLYCAEMIC CONTROL

Lipid metabolism and insulin signalling are intricately connected. Excess circulating lipids impair insulin signalling through lipotoxicity, leading to reduced glucose uptake. Dysregulated lipid metabolism also promotes inflammation and oxidative stress, further worsening insulin resistance (34).

Herbal compounds that modulate lipid metabolism can indirectly improve insulin signalling and glycaemic control. It has been demonstrated that A. paniculata improves insulin receptor activity, increases fatty acid oxidation, and decreases lipid buildup (35).

By targeting the lipid-insulin axis, herbal formulations offer a comprehensive approach to managing T2DM beyond conventional glucose-lowering strategies (36).

FORMULATION ASPECTS OF HERBAL ANTIDIABETIC PRODUCTS

Formulation plays as an Important part in the efficacy and stability of herbal medicines. Challenges such as poor solubility, low bioavailability, and variability in phytochemical content must be addressed to ensure therapeutic effectiveness (37)

Hard gelatin capsules are widely used for herbal formulations due to their convenience, accurate dosing, and patient acceptability (38). They provide protection to active constituents from environmental factors and allow incorporation of standardized extracts.

For A. paniculata, formulation into hard gelatin capsules ensures uniform distribution of andrographolide, improved stability, and enhanced bioavailability. Excipients such as diluents, disintegrants, and glidants are selected to optimize release characteristics (39).

Andrographis paniculata Hard Gelatin Capsules: Therapeutic Rationale

The use of A. paniculata in hard gelatin capsule form offers several advantages. Standardization of extracts ensures consistent therapeutic outcomes, while encapsulation improves patient compliance (40).

Such formulations can be developed as standalone therapies or as adjuncts to conventional antidiabetic drugs (41). The combination of insulin-sensitizing, lipid lowering, and antioxidant effects makes A. paniculata capsules particularly suitable for long-term management of T2DM (42).

RESEARCH GAPS AND FUTURE PERSPECTIVES

Despite promising preclinical evidence, clinical validation of A. paniculata formulations remains limited. Large-scale, well-designed clinical trials are required to establish efficacy, safety, and optimal dosing (43).

Standardization of herbal extracts, quality control, and regulatory approval are critical challenges. Future research should focus on advanced drug delivery systems, pharmacokinetic studies, and mechanistic investigations to full exploit the therapeutic potential of A. paniculata (44).

CONCLUSION

Insulin resistance and dysregulated lipid metabolism are the main causes of type 2 diabetes mellitus, a complicated metabolic disease. Enhancing insulin sensitivity represents a rational and effective therapeutic strategy. Herbal medicines, particularly Andrographis paniculata, offer a promising multitargeted approach to T2DM management.

Formulation of A. paniculata into hard gelatin capsules provides a practical and effective dosage form with improved stability and patient compliance. By modulating lipid metabolism, insulin signalling, and glycaemic control, such herbal formulations hold significant potential as adjunct or alternative therapies in T2DM. To incorporate these advantages into standard therapeutic practice, more study and clinical confirmation are required.

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