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Anti-diabetic potential of fruit extracts of *Flacourtia indica* (Burm. F.) Merr-An *in-vitro* study

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Diabetes mellitus is one of the biggest global health problems requiring preventive and new therapeutic interventions. There is a need for safe, reliable, and cost-effective anti-diabetic drugs, and investigating medicinal plants for new anti-diabetic medications is an exciting research field. Thus, the present study examined the *in-vitro* anti-diabetic activity of ethanolic and aqueous extracts of *Flacourtia indica* (Burm. F.) Merr (Flacourtiaceae) fruits by different enzyme inhibition assay methods. Alpha-amylase and Alpha-glucosidase are the principal enzymes present in the human body which helps in the digestion of carbohydrates. Inhibition of these enzymes slows down the absorption of glucose and lowers the sugar level in the blood. Both extracts showed potent inhibitory activity against these enzymes in a dose-dependent manner. The highest percentage of inhibition is exhibited by ethanolic extract at a concentration of 100 µg/mL with an IC_{50} value of 84.02. The results were compared with the standard drug Acarbose, a competitive inhibitor of both enzymes. The ethanolic extract was subjected to preliminary phytochemical analysis to find out different chemical constituents. It revealed the presence of reducing sugars, flavonoids, phenolic compounds, terpenoids, fatty acids, and steroids. Therefore, the current study proved that both ethanolic and aqueous extracts of *F. indica* fruits possess bioactive constituents that could be responsible for the anti-diabetic activity.

Keywords: Acarbose, Alpha-amylase, Alpha-glucosidase, Anti-diabetic, *Flacourtia indica*.

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Introduction

Medicinal plants play an important role in the development of modern herbal medicines. The bioactive constituents present in the medicinal plants are used as anti-diabetic, chemotherapeutic, anti-inflammatory, and anti-arthritic agents, whereas modern medicines fail to provide a satisfactory cure. Medicinal plants have been used as dietary supplements and for treatment purposes without proper knowledge about their medicinal values. Traditional medicine makes extensive use of secondary metabolites found in plants, which could lead to the discovery of new medications[1]. WHO developed its first comprehensive traditional medicine strategy in 2002 to support efforts to promote the use of traditional medicine and complementary alternative medicine that is inexpensive, effective, and safe for the treatment of various ailments.

Diabetes mellitus is a complex multifactorial condition defined by hyperglycemia (very high blood glucose levels) and glucose intolerance, which can be caused by a lack of insulin or an ineffective insulin action to improve glucose uptake. Over recent years the population suffering from diabetes mellitus has been increasing dramatically[2]. It is also expected that by 2030, India, China, and the United States will have the highest number of diabetic patients[3]. Diabetic patients experience oxidative stress, which causes lipid peroxidation and tissue damage, such as retinopathy, nephropathy, and coronary heart disease[4]. The control of blood glucose levels is a critical strategy as many anti-diabetic therapies with conventional drugs are frequently not a single-dose programme, as most drugs require frequent injections, sometimes for the rest of the diabetic patient's life. However, many of these conventional medicines are ineffective and have significant negative side effects. One therapeutic way to prevent postprandial hyperglycaemia is to retard the digestion and absorption of carbohydrates in the gastrointestinal tract through the

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Fig. 2 — Correlation between fruit extracts concentration and percentage of α-glucosidase inhibition.

between standard drugs and fruit extracts is represented in Fig. 2.

Discussion

Diabetes mellitus is a life-threatening problem that is exponentially increasing in both developed and developing countries. Both men and women can have diabetes at any stage of life. Among the two types of diabetes (type 1 or insulin-dependent diabetes mellitus and type 2 or non-insulin-dependent diabetes mellitus), type 2 is the most common form and occurs in about 90-95% of all diabetic cases. In the early stages of diabetes, lowering post-prandial hyperglycaemia is a therapeutic strategy. This is achieved by inhibiting carbohydrate hydrolysing enzymes such as alpha-amylase and alpha-glucosidase in the digestive tract, which slows glucose absorption[21]. Acarbose is a complex oligosaccharide that synthetically inhibits alpha-glucosidase and alpha-amylase enzymes by reducing glucose absorption and thereby decreasing the blood glucose level. However, these synthetic medications cause side effects and fail to cure diabetic complications. Therefore, currently, medicinal plants are considered to be an important source of most potent hypoglycaemic properties as they produce fewer side effects and are less expensive compared to synthetic drugs. As a result, using a drug extracted from plants is a different way to treat diabetes[22].

The phytochemicals present in medicinal herbs are well known for their various pharmacological activities. Plant-derived phytoconstituents influenced metabolic glucose by inhibiting apoptosis, increasing translocated and expressed glucose transporters, decreasing gluconeogenesis, enhancing pancreatic beta-cell proliferation, and protecting pancreatic beta cells from oxidative stress and inflammation. These phytocompound mechanisms aided in the development of anti-diabetic drugs[23]. As per the literature survey, glycosides, terpenoids, and alkaloids can control the conversion of starch into sugar in the event of excess glucose production and act as alpha-amylase inhibitor[24]. Plant phenols serve as key antioxidants and scavengers of free radicals[25]. Rusasinghe *et al.*[26], reported that saponins possess hypocholesterolemic and anti-diabetic properties. Plant polyphenols and flavonoids are some of the naturally occurring anti-diabetic agents known to have an inhibitory effect on the inhibition of carbohydrate hydrolyzing enzymes by their ability to bind to proteins. In the present study, fruit extract shows the presence of these secondary metabolites which may be accountable for its anti-diabetic activity.

Regarding the *In vitro* anti-diabetic activity, both extracts of *F. Indica* fruits had an enormous inhibitory effect on alpha-amylase and alpha-glucosidase in a dose-dependent manner. Previous literature evidenced the phytoconstituents present in the extracts were responsible for the enzyme inhibition. Here the ethanolic extract reveals the highest percentage inhibition of 62.96±1.82% against alpha-amylase and 72.44±0.70% against alpha-glucosidase when compared to the reference standard drug Acarbose. In comparison to manufactured medications with multiple adverse effects such as gastrointestinal discomfort, bloating, flatulence, and diarrhoea, these active extracts could be employed as anti-diabetic agents. Natural alpha-amylase and alpha-glucosidase inhibitors from plant sources offer an attractive therapeutic approach to the treatment of postprandial hyperglycaemia by decreasing glucose release from starch and delaying carbohydrate absorption by inhibiting the activity of the carbohydrate hydrolyzing enzymes in the small intestine and may have the potential for use in the treatment of diabetes mellitus.

Conclusion

In our findings, we conclude that both ethanolic and aqueous extracts of *F. indica* possess anti-diabetic potential against alpha-amylase and alpha-glucosidase enzymes. However, ethanolic extract showed highest percentage of inhibition when compared to the aqueous extract. The phytoconstituents present in the extract were responsible for this anti-diabetic activity. Therefore, this study gives an idea that fruit extracts of the plant *F. indica* can be used as a lead compound for designing a potent anti-diabetic drug which can be used

for the treatment of hyperglycaemia. In future the current work can be extended to identify more chemical constituents through GC-MS analysis and NMR based techniques. Similarly, a functional food formulation could be produced with societal economic and nutritional benefits.

Conflicts of interest

The authors declare no conflicts of interest.

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