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### RESEARCH ARTICLE

# $\alpha$ -Glucosidase and $\alpha$ -Amylase Inhibitory Activity of Senna surattensis

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#### Abstract

In this study, we investigated the inhibitory effects of ethanolic extract of the leaves of Senna surattensis (EESS) on  $\alpha$ -glucosidase and  $\alpha$ -amylase. We also studied the in vitro antidiabetic activity of S. surattensis using the glucose uptake by isolated rat hemidiaphragm model. In vitro studies using mammalian  $\alpha$ -glucosidase extracted from the small intestine homogenate of mouse showed that the extract was found to be more effective in inhibiting the activities of maltase [half maximal inhibitory concentration  $(IC_{50})$ : 209.15  $\mu$ g/mL] and sucrase (IC<sub>50</sub>: 366.44  $\mu$ g/mL) when compared with the control group (acarbose). The extract of S. surattensis were further quantified with respect to porcine pancreatic  $\alpha$ -amylase inhibition using the chromogenic 3.5-dinitrosalicylic acid method. Interestingly, S. surattensis was also found to exhibit  $\alpha$ -amylase (IC<sub>50</sub>: 123.95 µg/mL) inhibitory activity. The glucose uptake in the rat hemidiaphragm was significantly (p < 0.01) increased by EESS (220.95  $\pm$  5.4 mg/g/30 minute) when compared with the control group. The total polyphenolic content of EESS was found to be 98  $\mu$ g pyrocatechol/mg of the extract. These results suggest that EESS inhibited carbohydrate digestive enzymes and increased the peripheral uptake of glucose. This study endorses the use of this plant for further studies to determine their potential for managing type II diabetes.

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<sup>†</sup> Authors' contributions: B.P., E.T., and S.C.M. designed the experiments. C.K. and E.T. conducted the experiments. All authors have read, reviewed, and approved the final version of the manuscript. The authors declare that they have no competing interest.

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#### 1. Introduction

Noninsulin-dependent diabetes mellitus (NIDDM) is a common disease of the endocrine system caused by the decreased secretion of insulin by the pancreatic Langerhans  $\beta$  cell or by the lowering of insulin resistance due to excessive absorption of glucose [1]. A number of pharmacological approaches are used to control diabetes by different modes of action such as stimulation of insulin release, increase in the number of glucose transporters, inhibition of gluconeogenesis, and reducing absorption of glucose from the intestine [2]. Diabetes is a multifactorial disease leading to several complications and, therefore, it demands multiple therapeutic approaches. In the prediabetic state of insulin resistance, glycemic control can be achieved using oral agents that either interfere with the absorption of glucose ( $\alpha$ -glycosidase and/or pancreatic  $\alpha$ amylase inhibitors) or facilitate glucose disposal in peripheral tissues (insulin-sensitizing agents). One of the most beneficial therapies for NIDDM is said to be the control of postprandial hyperglycemia after a meal [3]. In patients with diabetes, postprandial hyperglycemia is most pronounced following a meal due to the absorption of glucose from the gastrointestinal tract. Inhibiting glucose uptake in the intestines and/or promoting glucose disposal in the tissues may be beneficial for these patients to control the blood glucose level in the postprandial state.

Acting as a key enzyme for carbohydrate digestion is intestinal  $\alpha$ -glucosidase, a glucosidase secreted in the epithelium of the small intestine.  $\alpha$ -Glucosidase has been recognized as a therapeutic target for the modulation of postprandial hyperglycemia, which is the earliest metabolic abnormality that occurs in NIDDM [4]. The major source of blood glucose is dietary carbohydrates such as starch, which are hydrolyzed by  $\alpha$ -glucosidases and pancreatic  $\alpha$ amylase, so as to be absorbed by the small intestine. Therefore, an effective treatment option for NIDDM is to inhibit the activity of  $\alpha$ -glucosidases and pancreatic  $\alpha$ -amylase [5]. In this regard, inhibitors can retard the uptake of dietary carbohydrates, suppress postprandial hyperglycemia, and could be useful for treating patients with diabetes and/or obesity [6].  $\alpha$ -Glucosidase inhibitors such as acarbose, miglitol, and voglibose are known to reduce postprandial hyperglycemia primarily by interfering with the activity of carbohydrate-digesting enzymes and delaying glucose absorption. In addition, numerous  $\alpha$ glucosidase inhibitors have been extracted from plants, which are of clinical importance [7,8].

Diabetes mellitus is also characterized by a diminished reaction of insulin-sensitive peripheral tissues and a marked decrease in glucose uptake and metabolism in response to insulin. The defective glucose transport system may play an important role in the pathogenesis of peripheral insulin resistance, and glucose uptake in target tissues is a critical step in maintaining glucose homeostasis and in clearing the postprandial glucose load [9]. To enhance the glucose uptake by peripheral cells, biguanides such as metformin are used to control postprandial hyperglycemia in patients with NIDDM. This has been attributed to increased glucose disposal by peripheral tissues, as observed in euglycemic clamp studies in rats and patients with NIDDM [10,11]. Direct stimulation of basal glucose transport, disposal, and metabolism in muscle and fat cells would explain increased glucose utilization. Therefore, cellular assays are used to determine the mechanism of action of natural or synthetic compounds from isolated rat diaphragms, as well as isolated and cultured rat 3T3 adipocytes. For this reason, it is highly desirable to find new antidiabetic agents from natural resources that stimulate glucose uptake/disposal by peripheral tissues such as adipose tissue or muscle cells.

Recent interests in the study of plant polyphenols have focused on their potential benefits to human health. The polyphenols are capable not only of reducing oxidative stress but also of inhibiting carbohydrate-hydrolyzing enzymes to prevent hyperglycemia [12,13]. Senna surattensis Burm. f./Cassia surattensis Burm. f. (syn: C. glauca Lam., Family: Caesalpiniaceae) is commonly known as Glaucous cassia. It is a small tree or a large shrub, distributed throughout India. The tender leaves are consumed as a vegetable with rice [14]. Bark and leaves are useful for treating diabetes and gonorrhea, and the aerial parts are used for treating diabetes [15,16]. The plant is described as a medication for diabetes, gonorrhea, and blennorrhea [17]. The beads made from its wood are worn around the neck to cure jaundice [18]. A phytoconstituent reported in this plant contains anthraquinone, flavonol glycosides, chrysophanol, kaempferol, and guercetin [19-21]. This plant has been used as traditional medicine for the treatment of diabetes, but scientific evaluation is still lacking in this regard. To clarify its mechanism of action, we evaluated the inhibitory effect of ethanolic extract of S. surattensis (EESS) on postprandial blood glucose levels in vitro. Therefore, this study was aimed at establishing the potential therapeutic value of EESS by evaluating its *in vitro* inhibitory activities against  $\alpha$ -glucosidase,  $\alpha$ -amylase, and by calculating the glucose uptake by the isolated rat hemidiaphragm.

#### 2. Materials and methods

#### 2.1. Plant materials

Fresh leaves of S. surattensis were collected from Tiruchirappalli (Tamil Nadu, India) in December 2006 and authenticated by the Botanical Survey of India (Coimbatore, Tamil Nadu, India; Ref. No.: BSI/SC/5/23/06-07/Tech-1638). An authentic voucher specimen was deposited in the Herbarium of Division of Pharmacognosy, Department of Pharmaceutical Technology, Jadavpur University, Kolkata, India.

#### 2.2. Preparation of plant extract

The collected leaves were air dried at room temperature without exposure to sunlight, coarsely powdered (300 g), and then extracted with ethanol (95%) in a Soxhlet apparatus. The solvent was then evaporated under reduced pressure in a rotary evaporator (Superfit, India) at <40°C to obtain a dry extract (yield 24.25% w/w) that was stored at  $-20^{\circ}$ C in a refrigerator until further use.

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