ISSN 2063-5346

Study of Anti-Diabetic Activities and Secondary Metabolite Production in Nyctanthes Arbor-Tristis

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Article History: Received: 15.03.2023 Revised: 20.04.2023 Accepted: 26.05.2023

ABSTRACT:

The purpose of the present investigation was to assess the antidiabetic property of Nyctanthes arbortristis leaves and flowers chloroform extract. In the present study antidiabetic properties of Nyctanthes arbortristis we investigated by hypoglycemic effect, potentiation action of exogenous insulin, oral glucose tolerance test and streptozotocin-induced diabetic rat model. The Nyctanthes arbortristis exerted hypoglycemic effect at relatively high dose 8 gm/kg of leaves and flowers chloroform extracts treated rats, significantly ($P<0.05$, $P<0.01$) lowered blood serum glucose levels, compared to 0 hrs. The maximum reduction in serum glucose levels observed at 5 hrs in flowers extract. The lower doses (50, 100 and 200 mg/kg) tested for potentiation action of exogenous insulin, oral glucose tolerance, streptozotocin-induced diabetic rat model. Oral glucose tolerance test was carried out in fasted rats by administering 2 gm/kg of glucose after administration of extract, the administration of extract significantly improved ($P<0.05$, $P<0.01$ $P<0.001$) compared to control (glucose 2 gm/kg) glucose tolerance test, which is comparable to glibenclamide 10 mg/kg treated group except 50 mg/kg of leaves extract. The potentiation action of exogenous Insulin was evaluated by administration of Insulin (1 unit/kg, i.p) after the administration of extract. The administration of extract in all dose significantly ($P<0.05$, $P<0.01$ $P<0.001$) potentiated exogenous action of Insulin, when compared to 0 hrs of treatment. The animals were made diabetic by streptozotocin (55 mg/kg, i.p) after confirming the diabetes level more than 300 mg/dl the chloroform extract from leaves and flower of Nyctanthes arbortristis (50, 100, 200 mg/kg) were used for 27 days in diabetic rats. The extract significantly ($P<0.05$, $P<0.01$, $P<0.001$) lowered serum glucose levels in treated rats when compared with control (vehicle treated diabetics). The antidiabetic activities of the leaves and flowers chloroform extract were comparable to glibeclamide at 10 mg/kg orally (positive control). In contrast, the flower extract shown more significant at 27 day of treatment, without significantly influencing on other days may be due to handling errors. This study confirms the significant antidiabetic activity of Nyctanthes arbortristis in flowers than leaves.

Keywords: Nyctanthes arbortristis, hypoglycemic, glucose tolerance test, Insulin action potentiation, and streptozotocin, diabetes, antidiabetic activity

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Introduction

Diabetes is the most common endocrine disorder in the world and causes abnormal metabolism of carbohydrates, fats, and proteins. Worldwide, 150 million people have diabetes mellitus, according to a WHO report, and this number could double by 2025. According to statistical projections, the number of diabetics will rise from 15 million in 1995 to 57 million in 2025, making India the world's highest diabetic population. In spite of the availability of numerous medications and treatments for diabetics, these are prohibitively expensive for a developing nation like India, in addition to the inherent risks they carry. As a result, new solutions to this major health issue must be sought. Skeletal muscle, the liver, and adipose tissues develop resistance to the hormonal effect of insulin as part of the pathogenesis of non-insulin-dependent diabetes mellitus (NIDDM). This decreases insulin-mediated glucose disposal, increases hepatic glucose production significantly, and increases lipolysis significantly. In addition, it has been demonstrated that hyperinsulinemia is a central pathophysiological feature of NIDDM and plays a significant role in the diagnosis of the disease as well as the development of the macrovascular complication. Multinational pharmaceutical companies are now looking for biologically active lead compounds in the plant kingdom. According to ethnobotanical data, more than 800 different plants are utilized in traditional diabetes treatments. As a result, the purpose of this study was to investigate the anti-diabetic properties of various extracts of Nyctanthes arbortristis in normal and streptozotocin-induced diabetic rats. Linn., Nyctanthes arbortristis Family: Oleaceae, also known as Night jasmine or Harsinger, is widely used by Ayurvedic practitioners as a decoction of its leaves to treat diabetes, arthritis, gout, sciatica, malaria, intestinal worms, and as a tonic, cholagogue, and laxative. Additionally, the leaves were found to have anti-inflammatory and antioxidant properties, as well as activity against Plasmodium falciparum, Leishmania donovani, and Entamoeba histolytia. Anti-inflammatory and analgesic properties were demonstrated by the isolated arbortristoside-A from the ethanolic extract of its seeds. Water-soluble ethanol extracts of Nyctanthes arbortristis have demonstrated pro- and anti-inflammatory cytokines. Encephalomyocarditis virus (EMCV) and Semliki forest virus (SFV) were tested against two pure compounds derived from the plant Nyctanthes arbortristis. The phytochemical analysis of the leaves of Nyctanthes arbortristis reveals the presence of ß-amyrin, ß-sitosterol, hentriacontane, benzoic acid, glycosides, nyctanthoside-a iridoid, nyctanthic acid, friedlin lupeol, and oleanolic acid, and 6ß-hydroxylonganin irioid glucosidesarborsides A, B and C

Material and Method

In the months of September and October of 2005, the flowers and leaves of Nyctanthes arbortristis were gathered from widely cultivated plants in the Delhi region. The plant material was shade-dried, coarsely ground, and then solvent-extracted for 24 hours per cycle using benzene, chloroform, ethyl acetate, and methanol at temperatures ranging from 40 to 600 degrees Celsius. A rotary evaporator was used to concentrate the extract, and a lyophilizer (Mini Lyotrap, Serial No. J8199/5, LET Logical LTD, UK). Using 5% Tween-80 as a suspending agent, the extracts were prepared as a suspension in distilled water (15). Both sexes of Wistar albino rats (150-200 gm) were obtained from the central animal house at Delhi. After being acclimatized to the conditions of the laboratory for a week, the rats were fed the same diet (Food-pellet). The Institutional Animals Ethics Committee approved the study design. The chloroform extract was found to be active (the dose was chosen based on a previous study (4, 6)), while other extracts were found to be inactive when tested for hypoglycemic activity on normal rats. Subsequently chloroform extricate was chosen for the review. The chloroform extract of the plant's leaves and flowers contained alkaloids and

flavonoids, as determined by the qualitative test.

Evaluation of Hypoglycemic Activity (16, 18, 20)

The acclimatized animals were divided into three groups of six rats and kept on a 24-hour fast with free access to water. The control group received 0.5 milliliters of 5% Tween 80. The flower and leaf chloroform extracts of Nyctanthes arbortristis were given to Groups 2 and 3 at a dose of 8 gm/kg, respectively, following the withdrawal of the initial (0 h) blood sample and at intervals of 11, 2, 3, and 5 h after the flower and leaf extract administration. Under anesthesia, blood samples were collected from the retro-orbital plexus, centrifuged at 1000 g for 15 minutes to obtain serum, and the Glucose kit and the star-21plus semiautoanalyser were used to estimate glucose.

Potentiation action of exogenous insulin (16)

The accustomed creatures were abstained for 24 hrs with water not obligatory, abstained creatures were isolated into eight gatherings of six rodents. As a control, Group 1 received 0.5 milliliters of 5% Tween 80. Group. No. Group No. 2 received insulin intravenously (1 Unit/kg), and After withdrawing the initial (0 hrs) and 30 min of extract administration, the groups were treated with insulin (1 Unit/kg) and blood samples were collected 30 min, 1, and 2 hrs later. Serum glucose was estimated by repeating the previous procedure. 3-8 received leaves and flower chloroform extract (50, 100, and 200 mg/kg) to rats.

Glucose tolerance test (17-18)

The acclimatized animals were divided into seven groups of six rats and kept on a 24-hour fast with free access to water. No. of Groups 1 who was the control got distilled water. No. of Groups After withdrawing the initial 0 hours of blood samples and after 30 minutes of extract administration, the rats of all groups were orally treated with 2 g/kg glucose. Group 2 received Glibenclamide at an oral dose of 10 mg/kg, and Groups 3 through 7 received Chloroform extract leaves and flowers at doses of 50, 100, and 200 mg/kg, respectively. Under general anesthesia, blood samples were taken from the retro-orbital plexus at intervals of 30, 90, and 180 minutes following the loading of glucose. These blood samples were then centrifuged at 1000 g for 15 minutes to obtain serum. The OGENT Glucose kit, which was manufactured by Span diagnostic LTD, and the star-21plus semiautoanalyser were used to estimate glucose.

Evaluation of anti-diabetic activity (2, 16, 19)

Before administering streptozotocin, the acclimated animals were kept on a 24-hour fast with unlimited water supply. On the first day, blood serum glucose levels were measured. By injecting a single dose of 55 mg/kg intraperitoneally, the streptozotocin (Sigma chemical Co., U.S.A.) that was freshly dissolved in citrate buffer (pH 4.5) made diabetics. For the first 24 hours, rats treated with streptozotocin were given 5% glucose in water to avoid any initial hypoglycemia. The animals were randomly divided into nine groups of six rats on the third day and tested for serum glucose levels of more than 300 mg/dl for the experiments. No. of Groups 1 filled in as diabetic control got refined water in 5% Tween-80. No. of Groups 2 received 10 mg/kg of Glibenclamide as a positive control, and groups 3 through 8 received 50, 100, and 200 mg/kg, respectively, of chloroform leaves and flower extract. Group No. 9 Normal received 5 percent Tween-80 in distilled water. After one hour of treatment on days 1, 7, 14, 21, and 27, blood samples were centrifuged at 1000 g for 15 minutes to obtain serum, which was then used for glucose estimation with the OGENT Glucose kit (manufactured by Span diagnostic LTD) and the star-21plus semi-autoanalyser. The treatment was continued daily for the remaining 27 days.

Results and Discussions

It is claimed to be beneficial for diabetes

treatment in light of the preceding reports (3). It was decided to evaluate the experimental design of hypoglycemic activity, insulin potentiation, glucose tolerance test, and streptozotocin-induced diabetes rats in order to establish a scientific basis for the plant's use in the treatment of diabetes. The present study's findings are depicted in figure No. When compared to the initial blood serum glucose levels (0 hours), the chloroform extract of Nyctanthes arbortristis leaves and flowers significantly (P0.05, P0.01) decreased fasting blood serum glucose in normal rats at 11, 2, and 5 hours. However, flowers extract reduces blood serum glucose levels more rapidly than leaves at a dose of 8 gm/kg. In addition, the results showed that flowers had a greater potential for glucose suppression than leaves extracts did after 5 hours of treatment. Table No. shows the potential activation of Nyctanthes arbortristis leaves and flower chloroform extract at various doses (50, 100, and 200 mg/kg) when challenged with insulin (1 Unit/kg). II received insulin (1 unit/kg) in all three doses of flower and leaf extracts after 30 minutes of extract administration, resulting in significantly (P 0.05, P 0.01, P 0.001) lower serum glucose levels than the initial glucose levels (0 hrs). Flower and leaf extracts at concentrations of 100 and 200 mg/kg showed the greatest reduction. These doses also resulted in a significant (P0.05, P0.01, P0.001) drop in serum glucose at 30 minutes, 1, and 2 hours. On the other hand, administering insulin on its own resulted in a significant (P0.05, P0.01) drop in serum glucose, albeit a smaller one when compared to extract treated with insulin (1 Unit/kg). These outcomes demonstrate that concentrate potentiates exogenous Insulin. The chloroform extract of the leaves and flowers at various doses (50, 100, and 200 mg/kg) and the positive control on serum glucose levels are challenged with a glucose load in Table No. III The three doses of leaves and flowers extract significantly (P0.05, P0.01, P0.001) reduced serum glucose levels in comparison to the control at 90-180 minutes after the glucose load, when all animals' serum glucose levels reached their highest. With 100 and 200 mg/kg of flower extract, the maximum reduction was observed. At 90 and 180 minutes, these doses also led to a significant drop in serum glucose. The results are not shown in the table, but the extract of 50 mg/kg of leaves did not significantly (P>0.05) reduce serum glucose levels in these rats when compared to the control. When compared to the control, serum glucose levels decreased significantly (P 0.001) at 30, 90, and 180 minutes when the reference drug glibenclamide was administered orally (10 mg/kg). Serum glucose levels significantly decreased in streptozotocin-induced diabetic rats after oral administration of chloroform extract from Nyctanthes arbortristis leaves and flowers for up to 27 days. The outcomes are listed in the Table. No. IV. When compared to the control, streptozotocin-treated rats' fasting blood serum glucose was significantly (P0.05, P0.01, P0.001) lower on the leaves and flowers of Nyctanthes arbortristis than on any other day. However, compared to other doses, the reduction in blood serum glucose levels at 14, 21, and 27 in flower extract at 50 mg/kg is more significant (P 0.001). The results also showed that on the 27th day of treatment, the maximum glucose suppression occurred in the flower, which was found to have more potential than leaves extracts. In contrast, the flower extracts showed a more marked decrease in blood glucose levels. When compared to a control, serum glucose levels were significantly (P 0.001) lower on the 1, 7, 14, 21, and 27th days of treatment when the reference drug Glibenclamide was administered orally (10 mg/kg). The relative higher LD50 of 16g/kg (21) of Nyctanthes arbortristis extract suggests probably that the plant extract is safe for rats. Sulphonylureas, biguanides, thazolidinediones, and alphaglucosidase inhibitors are the main classes of synthetic oral hypoglycemic agents that are currently available for the management or control of adults-onset type 2 Non-Insulin-Dependent Mellitus (NIDDM). As a class, sulphonylureas stimulate and increase the release of endogenous insulin from pancreatic Z-cell The Nyctanthes Arbortristis plant extracts were found to have analgesic, anti-inflammatory, tranquilizing, antihistamine, and purgative properties in laboratory animals (4, 6, 7, 21), as well as in vitro and in vivo antitrypanosomal, antihistamine, and purgative properties. The antitrypanosomal activity was either due to the presence of iridoid glucosides, most notably Z-Sitoste Therefore, the streptozotocin-induced diabetic and normal rats' blood glucose levels were significantly reduced by the chloroform extract used in this study. At this time, the underlying mechanism of the plant

extract's hypoglycemic effect is unknown. Nyctanthes arbortristis has been accounted for to contain iridoid glucosides, fundamentally Z-Sitosterol, 6-ZHydroxyloganin 1 and 2 from leaves (5, 22). It is unlikely that Nyctanthes arbortristis' ability to lower blood glucose levels is due to the Z-Sitosterol. Currently, the observed effect of lowering blood glucose may be attributed to the possible chemical components of Nyctanthes arbortristis. Nonetheless, various examiners have shown that a large group of optional plant metabolites with different compound designs have the last properties in different trial creatures model (5, 22). It is not unreasonable to speculate that the chemical compounds Z-Sitosterol, 6-ZHydroxyloganin, and Nyctanthes arbortristis may have contributed, at least in part, to the observed decrease in blood serum glucose effect of extract in this study (5, 22). Thus, this study may confirm people's use of this plant; However, in order to verify its effectiveness and general safety, a controlled clinical trial will be required.

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