

ANTIDIABETIC AND BIOLOGICAL ACTIVITIES OF *NICOTIANA TABACUM*: POSSIBLE MECHANISMS

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ABSTRACT

Diabetes mellitus is a growing global health problem. Reports predicted that diabetes mellitus could reach a pandemic level affecting people in both developing and developed countries. According to the World Health Organization, high blood glucose is seen as the third highest risk factor for premature mortality in diabetics. For several thousands of years before the advent of orthodox medications, human beings have been using medicinal plants in the treatment of various disease conditions such as cancer, cardiovascular disease, infertility, bacterial, viral infections, and diabetes mellitus. The beneficial effects of selected medicinal therapies in the treatment and management of diabetes and diabetic complications have been reported. Many medicinal plants across Africa and Asia are known for their rich phytochemicals with effective components that have been observed to effectively reduce high blood glucose either in diabetic persons or diabetes-induced animals. The motivation for the use of medicinal plants includes availability, affordability, knowledge, effectiveness, and safety and some are of the opinion that medicinal plants and their derivatives could be effective and safe alternative treatment for diabetes and diabetic complications. *Nicotiana tabacum* is one of those plants with antidiabetic and pharmacological potentials which could benefit humans and animals if appropriately utilized; however, less attention has been focused on its antidiabetic properties. In fact, there is a paucity of information on the antidiabetic activities of *N. tabacum*. Therefore, this paper examines the antidiabetic and other biological activities of *N. tabacum*.

Keywords: Medicinal plants, Antimicrobial activity, Diabetes mellitus, Human health, Animal health.© 2020 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>) DOI: <http://dx.doi.org/10.22159/ajpcr.2020.v13i3.35546>**INTRODUCTION**

In several developing countries such as in both Africa and Asia, knowledge of medicinal plants has been passed down by word of mouth from one generation to another generation. Inherent in this approach is the danger that the knowledge could be lost due to the difficulty of remembering all the information passed down from the ancestors or due to loss of cultural heritage. It is important to note that indigenous traditional knowledge of medicinal plants of different communities passed from one generation to another through oral means is disappearing as a result of modern technology and transformation in traditional culture. The key role medicinal plants play in human and animal health was recognized internationally over 40 years ago when the World Health Assembly adopted a resolution asking government of nations to pay adequate attention to the use of traditional medicine in their national health systems once relevant regulations are put in place. Honestly, the use of medicinal plants is gaining interest not just across Africa and Asia but even in developed countries such as America and Europe [1,2]. The increase in the use of medicinal plants in developing countries is prompted by poverty, high cost of orthodox drugs, availability of medicinal plants coupled with adequate knowledge of the local community, effectiveness of medicinal plants in the treatment of certain conditions, and availability of scientific findings that support the use of medicinal plants and the perception of the low side effects as well as the improved quality in the preparation of medicinal products in developing countries [3-5]. Medicinal plants continue to play an important role in the treatment of various diseases and one of such plants is *Nicotiana tabacum* that has gained global attention and application as therapeutic agent.

N. tabacum belongs to the family Solanaceae; it is a perennial herbaceous plant, native to tropical and subtropical America but now grown in many countries of the world. It grows 1–2 m in height with sticky parts, covered with viscid glandular hairs exuding a yellow secretion which contain nicotine [6]. Documented evidence of the use of *N. tabacum*

started in 1492 when Christopher Columbus reported that American Indians used the leaves of the plant in the treatment of various disease conditions/infections. Interestingly, in 1536, the European, based on the acquisition of indigenous knowledge from the local Indians also began to apply the plant as therapeutic agent. Consequently, West European doctors adopted the plant as medicine [7]. The leaves, flowers, and other parts of the plant are used traditionally and for other uses throughout the globe. It is a drug of choice in the treatment of urinary tract infection, asthma, and good analgesic and used in the treatment of dental pain and fungal infections, to reduce the poison of scorpion bite [8]. The leaves are known for their antispasmodic effects; their use as diuretics, expectorants, and sedative and their use in the treatment of rheumatic swelling have been reported [9]. The biological activities of *N. tabacum* are principally due to nicotine content which is known to stimulate nicotine receptors and in turn leads to the release of chemicals such as acetylcholine, norepinephrine, dopamine, serotonin, growth hormone, and vasopressin. *N. tabacum* has been reported to promote angiogenesis and wound healing in diabetic animal model and these biological activities have been attributed to the presence of nicotine [10]. This review will examine the antidiabetic and other biological activities of *N. tabacum*.

ANTIDIABETIC ACTIVITY OF *N. TABACUM*

Diabetes mellitus is a growing global health problem [11]. Reports predicted that diabetes mellitus could reach a pandemic level, affecting people in both developing and developed countries. According to the World Health Organization, high blood glucose is seen as the third highest risk factor for premature mortality in diabetics [12]. The same WHO report says that 422 million adults were diagnosed with diabetes mellitus in 2014. The International Diabetes Federation reports that 425 million people (between the ages 20 and 79) had diabetes mellitus, accounting for 8.8% of the global population [11]. Sadly, this figure is expected to increase by 2030 [13].

Hyperglycemia, a characteristic feature of diabetes, promotes the production of reactive oxygen species (ROS), linking oxidative stress as a significant factor in the development of secondary diabetic complications [14]. Oxidative stress is highly implicated in the development of male infertility and other complications due to its harmful effects [15]. A potential relationship between diabetes-induced oxidative stress and cellular damage has been established. Overproduction of ROS in diabetic male patients is a significant cause of male infertility and other complications. Depending on the concentration and nature of ROS, excessive amount of ROS can produce harmful effects on cellular functions and integrity [16].

Diabetes-induced ROS has the ability to cause significant damage to biomolecules such as lipids, proteins, and nucleic acids [17]. Cell membranes are made up of lipids which are responsible for membrane fluidity including spermatic changes that occur in the female reproductive tract such as capacitation. Excessive amount of ROS as seen in diabetic situations promotes lipid peroxidation of the polyunsaturated lipid membrane leading to cellular damage [18,19]. Diabetic male patients have been reported to have more pronounced DNA fragmentation and high levels of glycation end products attached to their receptors [20]. Available data suggest that diabetes affects fertility at multiple levels such as the endocrine control of spermatogenesis, the process of spermatogenesis itself or by impairing penile erection and ejaculation [21]. An estimated 90% of diabetic patients have disturbances in fertility and abnormal morphology [22]. Oxidative stress as a product of hyperglycemia is capable of inducing apoptosis [23]. It is characterized by cellular biochemical and morphological alterations that lead to cell death. Onyeyili *et al.* [19] established a positive relationship between hyperglycemia-induced oxidative stress and apoptosis. Report has implicated pancreatic alpha-amylase and intestinal alpha-glucosidase in hyperglycemic condition. Pancreatic alpha-amylase breaks down complex polysaccharides to yield oligosaccharide while intestinal alpha-glucosidase breaks down disaccharides to monosaccharide such as glucose which are absorbed by the small intestine into hepatic vein [24]. An important principle in the treatment and management of diabetes mellitus is aimed at reducing postprandial hyperglycemia through reduction in the absorption of glucose by inhibiting alpha-amylase and alpha-glucosidase. Orthodox medications that operate on this principle are available in the treatment of diabetes mellitus, but they are also associated with side effects coupled with the fact many diabetic individuals in rural settings cannot afford these drugs. Interestingly, many medicinal plants are known to exhibit inhibitory actions on alpha-amylase and alpha-glucosidase. Furthermore, plant-derived inhibitors of alpha-amylase and alpha-glucosidase have been isolated and are known to display less side effects compared to synthetic drugs. This clearly reveals that extracts from medicinal plants and plant-derived compounds could be useful therapeutic agents in the treatment and management of diabetes mellitus. There is a scarcity of information on the antidiabetic activity of *N. tabacum*. To test the antidiabetic activity of *N. tabacum*, Kazeem [25] assessed the inhibitory effect of *N. tabacum* leaf extract on alpha-amylase and alpha-glucosidase as possible approach to treating and managing diabetes mellitus. For this study, fresh leaves of the plant were collected from specific locality in Badagry, Lagos State, Nigeria. The plant was correctly identified by a botanist and was extracted using known methods in acetone, ethanol, and water [26]. For alpha-amylase inhibitory assay, the authors used a modified method of McCue and Shetty while a previous method described by Ali *et al.* was adopted [27,28]. The outcome of the study revealed that the aqueous extract of *N. tabacum* demonstrated the most effective inhibition of alpha-amylase, showing the aqueous extract of the plant as a mild inhibitor of alpha-amylase. This seems to support the view that mild inhibition of alpha-amylase is a better antidiabetic agent since excessive pancreatic alpha-amylase inhibition has been linked to abnormal bacterial fermentation of undigested carbohydrates in the colon which could culminate in gastrointestinal problems [24,25,29]. On the other hand, acetone extract of *N. tabacum* displayed the

most effective inhibition toward alpha-glucosidase. The flavonoids content of *N. tabacum* could be responsible for the activities of the plant extract. This is because flavonoids possess antioxidant and antidiabetic potentials consequent to the existence of hydroxyl groups, thus acting as powerful scavengers of ROS, thereby playing a significant role in preventing lipid peroxidation and preserving beta-cell function and cellular integrity [5,25,30-32].

The use of plants and their derivatives for the treatment and management of diverse disease conditions including diabetes mellitus is gaining prominence in various regions of the world as alternative therapy. The hypoglycemic effect of the leaf of *N. tabacum* was assessed by Emordi *et al.* [33]. The authors collected fresh leaves of the plant, identified it and performed extraction techniques to obtain 14 g dry extract. To assess the hypoglycemic potentials of *N. tabacum*, 15 rats were randomly divided into three groups. Group A received 0.5 ml of 2% acacia and Groups B and C received oral dose of 40 mg and 80 mg/kg body weight. Blood samples were then collected to estimate the blood glucose level. After 30 min, rats in each group received 40% glucose (1 ml/100 g body weight) through oral route. Blood glucose levels were estimated at 30 min, 60, 90, and 120 min and average level was recorded. Animals that received 40 mg/kg dose demonstrated a significant reduction in blood glucose level at 120 min compared to control while animals that received 80 mg/kg showed a significant reduction in blood glucose at 2 h and 6 h compared to control. The extract demonstrated hypoglycemic activity by reducing blood glucose level. This may be related to increase insulin release from the pancreatic beta cells. It is, therefore, possible to deduce that the presence of phytochemicals in the extract of *N. tabacum* may be responsible for the hypoglycemic effect observed in the study [34].

ANTIBACTERIAL ACTIVITY OF *N. TABACUM*

To investigate the antibacterial activity of the extract of this plant, Malik *et al.* used three species of bacteria which are *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* [35]. Appropriate media were prepared according to previous methods and commercial discs were used by incorporating the two plant extracts, then incubated for 24 h. The results showed that *S. aureus* had the highest diameter of inhibition (26 mm) at the highest plant concentration while the minimum plant extract concentration showed a zone of inhibition of 15 mm in diameter. On the other hand, *P. aeruginosa* demonstrated the highest diameter of inhibition (21 mm) at the highest plant concentration while the minimum plant extract concentration showed minimum inhibition of 11 mm in diameter, while *E. coli* showed highest and minimum inhibition at 20 mm and 13 mm, respectively. Plants contain various biologically active compounds with antibacterial effects and extract from this plant demonstrated antibacterial potential against pathogenic bacterial species. Adeleye *et al.* also reported on the antibacterial activity of *N. tabacum* [36].

ANTHELMINTIC ACTIVITY OF *N. TABACUM*

N. tabacum continues to gain widespread use in traditional medicine in developing countries as anthelmintic agent. To this end, Iqbal *et al.* assessed the anthelmintic activity of *N. tabacum* leaves using live *Haemonchus contortus* (*in vitro* study) and *in vivo* testing by applying sheep naturally infected with mixed infection of gastrointestinal nematodes [37]. Fresh leaf of *N. tabacum* was obtained from the local market, identified by a botanist and crude extract of the leaves prepared according to previously described method using methanol and water [38]. *In vitro* study, the effectiveness of water and methanol extract of the plant is observed in the mortality of the worms when compared to a levamisole – a standard anthelmintic drug. On the other hand, in the control group (saline), none of the worms died. In the *in vivo* aspect of this study, both extracts were effective against the worms in a dose-dependent manner. Both *in vitro* and *in vivo* tests showed that *N. tabacum* leaves have anthelmintic potential, explaining its continual application in traditional medicine.

OTHER BIOLOGICAL ACTIVITIES OF *N. TABACUM*

Due to the eco-friendly, cost-effective, and relatively safe plants and plant-derived products, the utilization of plant products has moved beyond its local use to global applications, primarily promoted by research in both developing and developed countries. The WHO noted that about 21,000 plants are used for medicinal purposes and significant portion of the plants is used commercially and *N. tabacum* is one of such plants with extensive commercial value due to its multiple biological activities [39-42].

Antifungal activity of *N. tabacum* has been reported [43]. Extract of the plant has been observed to demonstrate improved memory in neurodegenerative disorder associated with loss of neurons in specific brain sections [44] and known to stimulate series of sensory receptors [45] and known to demonstrate various action on nervous system [46], believed to contribute to the activation of chemoreceptors of the aortic and carotid bodies [6], and observed to increase tone and motor activity of the gastrointestinal tract [47].

CONCLUSION

Several scientific reports have linked metabolic disturbances with hyperglycemia in diabetic condition and the potential of insulin to modulate glucose uptake is a vital function in glucose homeostasis. The application of orthodox medications in the treatment of diabetes mellitus is associated with side effects such as severe hypoglycemia and digestive disorder. Interestingly, medicinal plants and their derivatives as alternative approach in the treatment of diabetes mellitus and other chronic diseases have been recognized because people believe that they are safe, cheap, and efficient in the treatment and management of diabetes mellitus. Several studies both in developed and developing countries have been conducted to investigate the antidiabetic properties of medicinal plants and many of these studies support the use of medicinal plants not only in the treatment and management of diabetes mellitus but also in other diseases. It is evident from previous studies as revealed in this paper that *N. tabacum* displayed antidiabetic properties and further studies are suggested with a large sample size to determine its safety, toxicity especially when on long-term use both in humans and animals.

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AUTHOR'S CONTRIBUTIONS

Oluwafemi Omoniyi Oguntibeju conceptualized the research idea, performed literature search, wrote and edited the manuscript, revised the manuscript, and acted as the corresponding author.

CONFLICTS OF INTEREST

The author declares that there are no conflicts of interest.

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