

Full Length Research Paper

Toxicological and hypoglycemic studies on the oil extracted from seeds of *Khaya senegalensis* on blood glucose levels of alloxan-induced diabetic albino rats

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Diabetes mellitus is a metabolic disorder found in all nations of the world. It is one of the most prevalent epidemics of the 21st century. Despite the numerous research on this area, its effects are still on top gear. Nature has provided abundant plants which possess medicinal values and several claims on the uses of plants by traditional healers were also on the increase, yet no known solution. There is an obvious need to evaluate all these abundant plants for better use in medical practice. Hence, the present study aims at evaluating the diabetes claim of *Khaya senegalensis*, and also to assess its safety. Aqueous oil extract of *K. senegalensis* was subjected for hypoglycemic activity in 25 hyperglycemic induced Wistar rats. 3 different concentrations (6, 3 and 1.5 mg/kg) of the extract were tested against a standard drug (500 mg/kg of metformin). Blood glucose lowering effect was determined using Accu-check glucometer. The oral administration of the extract shows hypoglycemic effect and its concentration dependent. However, the extract does not significantly lower blood glucose levels as compared to the standard drug used as a positive control. Hence we concluded, that the extracted oil can serve as an alternative in the treatment of mild diabetes, we have equally shown that at concentration tested, and no sign of toxicity was recorded.

Key words: Toxicological, diabetes, effect, hypoglycemic.

INTRODUCTION

Diabetes mellitus is a metabolic disorder found in all nations of the world. It is one of the most prevalent epidemics of the 21st century (Mann et al., 2004). Recent global estimates indicate that the total number of patients affected by diabetes in 2004 was close to 190 million, a figure likely to have reached 325 million by 2005, that is, an increase of more than 70% (Lefebvre, 2005). Despite the numerous research on the issue there are still more to do due to the resistance to the existing medical treatment, the implication is that there, the disease will be listed among the most killer diseases that threaten the existence of humanity in this planet (Hostettmann et al., 2000). The practical approach to this problem is to explore the most popular traditional approach where many herbal products are used locally by traditional herbal

practitioners. Plants and plant products present some hope to scientists, serving as an alternative avenue to discovery from the current mainstream approach of attempting to find solutions to diseases that have proved very resistant to western drugs for specific health problems (Jassim and Naji, 2003). Numerous medicinal plants have formed the basis of health care throughout the world since the earliest days of humanity and are still widely used and have considerable importance in international trade. In certain African countries for instance, up to 90% of the population still relies exclusively on plants as a source of medicines (Momoh and Adikwu, 2008). As a consequence, the World Health Organization (WHO) had in one of its charters in Geneva recommended further investigation into this area, particularly as it concerns chronic and debilitating diseases such as diabetes mellitus (WHO, 1980). *Khaya senegalensis* is a popular plant from the mahogany family called *Meliaceae* has a history of medicinal value, all the parts of the plant were considered to have commercial value (Rates, 2001).

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The nut contains several oil-rich kernels or seeds of average about 63% oil, which is pale yellow in colour. The oil is used traditionally as wound healing, insect repellent and in the treatment of bacterial infection (Oberley, 1988). The present study aims at studying the antidiabetic activity of oil extracted from the seed of *K. senegalensis* in an alloxan-induced diabetes in rats.

MATERIALS AND METHODS

Chemical used

All chemical and drugs were obtained commercially and were of analytical grade.

Plant materials

Dried seeds of *K. senegalensis* called (Mahogany) were collected from IKeme in Enugu state. The seed was identified by Mr. Ozioko of bioresources development and conservation program (BDGP), Nsukka where voucher of the leaf samples were kept in the University herbarium for reference.

Extract preparation

The dry seed was grinded using pestle and mortar, whole plant was collected and dried under the shade and ground into powder. The powder (100 g) was steamed; essential oil obtained by steam distillation of the macerated seeds was used for the study (Trease and Evans, 2003).

Animals

Wistar strain albino rats of both sexes weighed between 120 to 150 g, which were bred in the Department of Pharmacology University of Nigeria Nsukka. The animals were housed in standard environmental conditions with 12 h light-dark cycle. The animals were divided into extract treated groups and the control groups. All the animals were fasted for 12 h, but were allowed free access to water, before commencement of the experiments.

Phytochemical screening

The oil seed extract of *K. senegalensis* were subjected to preliminary phytochemical screening, to identify the chemical constituents, a standard method was used (Trease and Evans, 2003).

Acute toxicity study

The acute toxicity of the extract was tested using 25 Wistar rats divided into 5 groups of 5 rats each, group A received normal saline, other groups receiving graded dose of *K. senegalensis* (1.5, 3.0 and 6.8 mg/kg body weight), for B, C, D and E respectively oral of the aqueous oil extract of *K. senegalensis* plant as described by Ghosh (1984). After administration of the oil extract of *K. senegalensis* the rats were observed for toxic effects after 48 h treatment. The toxicological effects were observed in terms of mortality expressed as LD₅₀. The number of animals dying during a period was noted (Litch and Wilcoxon, 1959).

House or cage observation

The animals were also observed for effect like: food intake, water intake, reckless action, biting cage effect and general mobility status.

Induction of experimental diabetes

Diabetes was induced by intraperitoneal injection of alloxan monohydrate dissolved in normal saline as a vehicle at a dose of 200 mg/kg body weight. 48 h later, the blood (2 drops) was collected from the tail vein and immediately used for the determination of glucose. Only animals with raised glucose levels greater or equal to 200 mg/dL were enlisted into the study, which consisted of a single oral administration of extracts of *K. senegalensis* using gastric intubation. The rats (25) were divided into 5 groups of 5 rats and were used for the experiments. The oil extract of *K. senegalensis* were sub-divided into 3 different concentrations of (6, 3, and 1.5 mg/kg) and were assessed for their hypoglycemic effect in Wistar rats. Group E, served as control, which received normal saline, rats in Group D received the standard drug metformin 500 mg/kg served as a positive control and Group C, B and A received various concentrations of the extract orally by gastric intubation (6, 3, and 1.5 mg/kg) respectively. All the rats were fasted overnight (12 h). The rats were completely starved throughout the period, but have access to water.

Blood collection and glucose analysis

Blood samples (2 drops) were collected from the tail vein under mild ether anesthesia and the glucose level was measured at 0, 1, 2, 4, 6 and 8 h after the administration of the extracted oil orally. The blood sugar level was determined using Accu-chek[®], (Roche, Switzerland). The percentage glycemic change in the experimental animals was calculated as a time function using the following formula:

$$\text{Glycemic change (\%)} = \frac{\text{InitialConc} - \text{FinalConc}}{\text{InitialConc}} \times 100$$

Statistical analysis

Results were expressed as mean blood glucose levels S.E.M. Data were analyzed using one-way ANOVA. The level of significance was set at 0.05.

RESULTS

The Groups A to D show a decreased in the level of glucose reduction from 100 to 83%, 52, 51 within 6 and 38 within 8 h respectively, the negative control show a decrease from 100 to 99% and further raised to 122% within 6 h of the study as shown in Figure 1. There was a general reduction in the glucose level in all the tested doses of the oil extract.

DISCUSSION

The results (Figure 1) of this study clearly indicate that

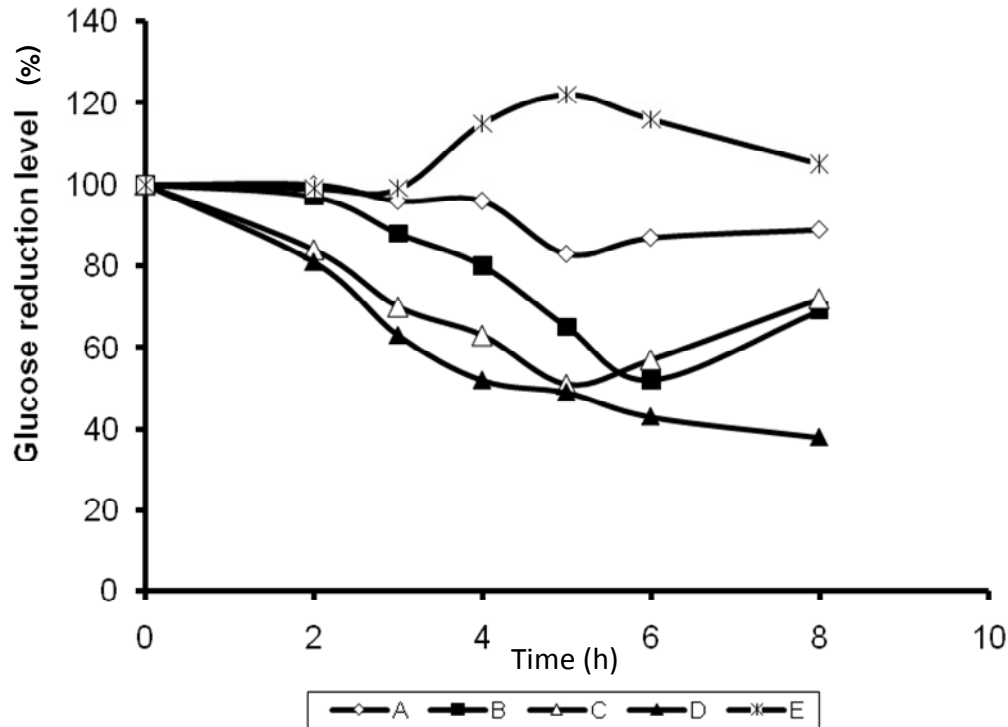


Figure 1. Effect of the formulation on glucose level.

the administration of aqueous oil seed extract of *K. senegalensis* produced a significant hypoglycaemic effect at $P > 0.005$. This study showed that extract produced a marked decrease in blood glucose of diabetic rats. These findings had been reported by the traditional medicine practice in the northern Nigeria. The reduction rate follows concentration dependent. The highest was observed in the animal administered with $6.0 > 3.0 > 1.5$ mg/kg. When the results is compared with the oral administration of the marketed metformin hydrochloride, it was observed that the metformin hydrochloride have a high effect on the rats than the oil at the dose tested. As the effects on the glucose reduction were compared in line with difference concentration of the oil, the reduction in the glucose level was found to be significant at $P > 0.005$ when analysed using one way ANOVA. The possible mechanism for this observable effect is not clear, it may be possible that as the oil is administer it enhances or restored the destroyed insulin cells and enhanced the release of more insulin, other opinion was that there is possibility of regenerating the cells as observed in many plants that exhibit the same features (Litch and Wilcoxon, 1959). Several researchers have demonstrated the uses of plant for the management of diabetes and their findings were in agreement with this current study (Akah and Ekekwe, 1995). Previously we have reported other uses of plants and plant product in the management of health related condition where the offending agents are mainly bacterial infections (Akeem

et al., 2011).

Acute toxicity studies

Table 1 shows the result of the toxicity study at various concentrations of the oil extract used in the study. The important of this test was necessitated as a result of much dependent in the plant product for health cases and the possibility of overdose, side effect and some harmful effect that need clarifications. The determination of the safety of drugs and plant products for human use was part of the research cletaria, hence, the toxicological evaluation form the bases for correct dosage formulation and critical evaluation for better uses of drug in clinical settings (Jones, 1996). Although medicinal plants may produce several biological activities in humans, generally very little is known about their toxicity and the same applies for *K. senegalensis*. There was no mortality or morbidity observed in animals through the 5-day period following single oral administration at all selected dose levels of *K. senegalensis* (Table 1). The LD_{50} value for oral administration of *K. senegalensis* is larger than 10 mg/kg body weight. The animals did not show any changes in the general appearance during the observation period. All the morphological characteristics appeared normal. No tremor or any obvious physiological changes, diarrhoea, lethargy or unusual behaviours such as self mutilation, walking backward and so forth were

Table 1. Toxicity study on oil extract.

Batch	No. of animal	Food intake level			No. of death
		1st day	3rd day	5th day	
A	5	Fair	Poor	Poor	0/5
B	5	Fair	Fair	Fair	0/5
C	5	Fair	Fair	Good	0/5
D	5	Fair	Fair	Good	0/5
E	5	Fair	Good	Good	0/5

Key: > half of the meal = good, half of the meal = fair, < half of the meal = poor. A = control received only normal saline, B, C, D and E received 1.5, 3.0, 6.0 and 8.0 mg/kg of extracted oil, respectively.

observed; no loss of hair and posture or ability to stand, reactivity to handling or sensory stimuli, grip strength were all normal. There was no obvious toxicological effect in all the doses of the extracted seed oil used in this study. There is a relationship in daily food intake along the diabetics treated groups, animal with saline response poorly to the food in take, this could be due to progression in the diabetics state, several have linked diabetes cases to poor intake of food (Vivek et al., 2007) while a better intake of food were observed in the treated groups and the responses was better in the group that received highest dose of the oil extract.

This development is associated with the improvement in the insulin secretion or the muscle re-uptake of glucose or the regeneration of the beta cells (Szkudelski, 2001), which was not so in negative control groups because the diabetes condition progresses therefore, deterred the animal from there normal activities including food intake (Mahesh and Menon, 2004).

Conclusion

In this study, the oil extract produced important hypoglycemic effects in diabetes rats at the concentration tested. Further study and pharmacological investigations need to be done to ascertain the active constituent and its mechanism of action.

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