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Daabs-2^{r}: A Novel Ethnomedicinal Polyherbal Formulation For The Management Of Diabetes Mellitus.

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Abstract: *Being aware of the Panorama the Continuous use of ineffective pharmaceuticals whose side effects outweigh the beneficial effects poses on diabetics, it becomes pertinent that halting these side effects associated with these conceivably orthodox medicaments needs to be a global priority, one of such ways is to return to the natural products.*

This research was aimed at evaluating the efficacy of DAABS-2, a novel ethnomedicinal polyherbal formulation on Insulin Depended Diabetes mellitus and non Insulin Dependent Diabetes mellitus by using streptozotocin-induced diabetic laboratory animals and the result showed that the administration of 180mg/kg and 100mg/kg with the corresponding DAABS-2 extracts decreased blood glucose by 90% compared to the placebo treated diabetic animals respectively.

Keywords: *Natural products, DAABS-2, Streptozotocin, Diabetics, Ethnomedicinal.*

I. Introduction

According to the International Diabetes Federation (IDF), around 194 million People suffer from diabetes all over the world. Therefore, it has been classified as a serious problem to public health for it is the fourth or fifth cause of death in developed countries and an epidemic for developing ones.

Being aware of this Panorama, some researches have been carried out to obtain useful drugs to treat Diabetes, including plants.

Some curative plants are used empirically as hypoglycemics, such as Dioscorea alata L, Vernonia amygdalina and zingibir officinale. These are the constituents of DAABS 2

The medicinal uses of the constituents of DAABS 2^{R} are well documented in literature (Dalziel 1937).

Continued use of ineffective pharmaceuticals whose side effects outweigh the beneficial effects not only contributes to the debilitating state of diabetes but also causes a deafening increase in diabetes-related morbidity and mortality.

Complementary and alternative (herbal) preparations could prevent a substantial percentage of the deaths each year from diabetes.

Halting these side effects associated with these conceivably orthodox medicaments needs to be a global priority, and resources must be focused on those areas of the world where the burden from the disease is greatest. One of such ways is to return to naturaceuticals, variously tagged; herbal medicines, natural products, complementary and alternative medicine (CAM) or even traditional medicines

The use of herbal medicine dates back to thousands of years. Although it originated in India and China, it is widely practiced in Africa. Herbal therapy which started as folk medicine in most developed countries is becoming increasingly more popular with patients seeking alternative treatment options

Eisenberg et al., (1998) reported that, in developed countries the number of visits to the alternative medicine practioners is growing rapidly with the number of visits in US was estimated to be 629 million in 1997; it was believed to have exceeded the number of visits to all primary care physicians.

It is a known fact that, a large proportion of African population uses some form of alternative medicine and many do not inform their physician about it.

Most patients seek alternative medicine because of lack of basic health facilities, when conventional therapy has failed or they feel the products have no side effects because they are of natural origin

Herbal therapy has also been used extensively in Nigeria. Although more than 80 percent of the people in both the underdeveloped and the developed countries depend on herbal medicines for their medical needs

The major problems with herbal medicines in such countries still remains their poor and sometimes unhealthy presentation.

The most common animal model of human diabetes is streptozotocin(STZ)-induced diabetes in the rat.

This study therefore was carried out to evaluate and provide information on the efficacy of DAAB-2^{R}. Data generated will form part of the preclinical dossier required by the World Health Organization (WHO) and the Nigeria's food and drug regulatory body, the National Agency for Food and Drug Administration and Control

(NAFDAC) in phytomedicines development. The information may also be useful in the development of Nigeria's herbal pharmacopoeia.

II. Materials And Methods

Experimental Animals

Laboratory bred Swiss albino mice of either sex, 6-8 weeks of age, weighing 25-30 g were Obtained from the National Veterinary Research Institute Vom, plateau state.

The mice were kept in the animal house of the Ben Amodu farm and research centre, Abuja. The animals were allowed to acclimatize to the environment for 2 weeks before the experiment. They were fed with commercial feeds pellet and clean water ad-libitum. The cages were cleaned daily. The animals were housed in a polypropylene cages inside a well ventilated room. Each cage contained not more than 3 rats. They were maintained under standard laboratory conditions of temperature 24-28^{0}C, relative humidity 60-70% and 12 hours light/dark cycle.

Induction Of Diabetes Mellitus

Streptozotocin was obtained from Sigma Chemicals Co., St. Louis, MO, USA.STZ was dissolved in cold 0.01 M citrate buffer, pH 4.5 and always prepared freshly for immediate use within 5 min. STZ injections were given intraperitoneally and the doses were determined according to the body weight of animals. The blood glucose concentration was measured every week from the day of STZ injection. The blood samples were collected from the tail vein once a week and the blood was deproteinized. The obtained supernatant was used immediately for the determination of blood glucose by glucose Oxidase/peroxidase method spectrophotometrically

Experimental Groups And Protocol

The animals were distributed in to five experimental groups. Each group consisted of 8 rats in the beginning of the study. Animals in group I were intraperitoneally administered single injection of 180 mg/kg of STZ with 50mg/kg of the DAABS 2 extracts. Animals of group II were intraperitoneally administered a single injection of 100 mg/kg of STZ with 50mg/kg of the DAABS 2 extracts. Animals of group III were intraperitoneally administered 180mg/kg of STZ with 50mg/kg of placebo. Animals of group IV were intraperitoneally administered a single injection of 100mg/kg of STZ with 50mg/kg of placebo. Animals of group V served as control group were injected with equivalent amount of cold citrate buffer (pH 4.5). All the doses of STZ were administered at a volume not exceeding 1ml/100 g body weight of mice.

Statistical Analysis

The data were expressed as mean. To obtain comparable results, data of six rats from each group was used for statistical analysis.

III. Results

The values of blood glucose concentrations are presented in Table 1&2. All the animals were weighed weekly and their general conditions were also monitored throughout the experimental duration

Effect Of Single Stz Injection (180 Mg/Kg, I.P.) On Blood Glucose

All the animals develop diabetes mellitus within a week after administration of 180 mg/kg STZ. A significant rise in blood glucose concentration was observed till 3rd week in comparison with control. By the completion of 5th week >20% mortality was observed (2 out of 8 animals died) because of which we have included only the data of six rats survived till the end of the study.

Effect Of Single Stz Injection (100 Mg/Kg, I.P.) On Blood Glucose

None of the animal develops diabetes with STZ 100 mg/kg. Though a insignificant increase in blood glucose concentration was observed at the 2nd and 3rd week after STZ injection. But the blood glucose concentrations were far below the threshold value for the animals to be considered as diabetic. No mortality was observed in this group.

Table 1: Blood glucose levels with streptozotocin-induced type 1&2 Diabetes and the extracts in mice

Time period	STZ 180(n=6)	STZ 100(n=6)	Control (distilled water)
Blood Glucose Mmol/L			
0 day	7.7	6.2	5.0
Week 1	7.9	6.9	5.2
Week 2	8.0	7.0	5.2
Week 3	7.9	6.2	4.8
Week 4	6.9	5.2	4.9
Week 5	6.2	5.0	5.0
P≤ **0.05**			

Table 2: Blood Glucose levels with streptozotocin-induced type 1&2 Diabetes with the placebo in mice.

Time period	STZ 180 (n=6)	STZ 100(n=6)	Control (distilled water)
Blood Glucose Mmol/L			
0 day	28.00	8.00	5.00
Week1	29.95	8.90	5.20
Week 2	34.32	9.98	4.80
Week 3	34.01	9.11	4.90
Week 4	33.46	8.00	5.00
Week 5	34.00	7.72	5.10
P≤ **0.05**			

IV. Discussion

Streptozotocin induced diabetes is a well documented model of experimental diabetes. Previous reported literature indicates that the type of diabetes and characteristics differ with the employed dose of STZ and animal and species used [4-7]. Streptozotocin induced diabetes provides a relevant example of endogenous chronic oxidative stress due to the resulting hyperglycemia [16]. STZ is a pancreatic cell toxin that induces rapid and irreversible necrosis of cells [6]. Whereas a single diabetogenic dose of STZ (70-250mg/kg, body weight) has been demonstrated to induce complete destruction of cells in most species within24 hour, multiple sub-diabetogenic doses of STZ partially damage islets, thereby triggering an inflammatory process leading to macrophage and subsequent lymphocyte infiltration, which is followed by the onset of insulin deficiency[17,11].

In the present study, we studied the effects of DAABS extracts on streptozotocin-induced diabetes in mice using two models, one specific for type 1 by administering a single I.P injection of STZ 180mg/kg with 50mg/kg of the extracts, another specific for type II by administering a single I.P injection of STZ 100mg/kg with 50mg/kg of the extracts.

The table two that was served with placebo showed marked and steady rise in the blood sugar level of the mice.

Present study results demonstrate that a single i.p injection of STZ 180mg/kg produced diabetes mellitus in the very first week and the animals remained in that state till 3rd week similar to the previous study report in which mice administered 200mg/kg STZ induced a sharp rise with an accompanying marked fall in serum insulin levels from the first day after STZ administration in mice and produced type 1 or insulin dependent diabetes mellitus (12). In another development, a single i.p. injection of STZ 180mg/kg with the DAABS-2 extracts produced no sign of diabetes mellitus at any moment, and it continued throughout the course of the experiments. This lends credence to the fact that the extracts did indeed halted diabetes mellitus with no side effects.

Furthermore, this study also reported that mice administered 100mg/kg STZ, non fasting serum glucose level continued to increase gradually after STZ administration without affecting the non-fasting serum insulin-dependent diabetes. However, STZ 100mg/kg administered mice failed to produce diabetes mellitus in our study; this is probably due to the incorporation of the extracts in the mice feeds.

In another development, where the placebo was used, STZ 100mg/kg only produced hyperglycemia in the 2nd and 3rd week and the blood glucose begin to decline after the 4th and 5th week and the values were far below the threshold value (13.89Mmol/L) for the animals to be considered as diabetic. Although this findings

are not in agreement with previous other reports (13,14) where STZ 100mg/kg has been reported to produce type II or non-insulin dependent diabetes mellitus and blood glucose concentrations remained high till 9th week. Our study however assessed the blood glucose level till 5th week only because it was observed that blood glucose concentration was abating in 5th week.

In summary, the present study results indicate that single i.p. injection of STZ 180mg/kg and 100mg/kg with the correspondent extracts produced no diabetes of any form, while the same i.p injection of 180mg/kg and 100mg/kg with the corresponding placebo produced type 1 or insulin dependent diabetes, however, the latter failed to produce diabetes mellitus. The severity and mortality of diabetes with STZ 180mg/kg is more in comparison to 100mg/kg. The long-term complications of diabetes mellitus and the characteristics of progressive diabetes mellitus in the group with the placebo could be studied.

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