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ASSESSMENT OF THE EFFECT OF EXTRACTS FROM *DISTEMONENTHUS BENTHAMIANUS* BAILL (FABACEAE) SHEETS ON BIOCHEMICAL PARAMETERS OF DIABETIC RATES.

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ABSTRACT

This work deals with the effect of aqueous and hydroethanolic extracts of stem bark of *Distemonenthus benthamianus*, family Fabaceae, on the evolution of some biochemical parameters in Wistar rats made diabetic with alloxane. Natural substances and compounds have shown great potential in the treatment of human diseases such as cancer, diabetes and infectious diseases. The stem bark of *Distemonenthus benthamianus* was harvested, dried, crushed and subjected to aqueous and hydroethanolic (70/30) extraction. After chemical screening the various extracts of *Distemonenthus benthamianus* at different doses (100 and 200 mg/kg) and amarel were administered by daily gavage for twenty-eight (28) days to forty (40) rats of albino wistar strains made diabetic with alloxane at a dose of 120 mg/kg; these rats were divided into eight batches of five rats each. At the end of treatment the animals were sacrificed and blood glucose, insulin, renal, lipid and cardiac parameters were determined. The phytochemical test of the different extracts (aqueous and hydroethanolic) of *Distemonenthus benthamianus* revealed the presence of tannins, alkaloids, glycosides (sterols and triterpenes), polyphenols, flavonoids, quinones. The results of the pharmacological study obtained show an improvement of the various biochemical parameters of rats treated with the hydroethanolic extract of *Distemonenthus benthamianus* at the dose of 200 mg/kg. *Distemonenthus benthamianus* could delay the onset of degenerative complications of diabetes.

KEYWORDS: *Distemonenthus benthamianus*, biochemical parameters, diabetes.

INTRODUCTION

Diabetes is a metabolic disorder due to insufficient or improper use of insulin characterized by a fasting blood glucose level of more than 1.26g/L tested twice.[1] This condition is affecting more and more people around the world and is now considered a real public health problem. This chronic hyperglycaemia leads to long-term damage, dysfunction and eventual disability of organs, particularly the eyes, kidneys, nerves and cardiovascular system.[2] Indeed, the global prevalence of diabetes in the world population is estimated to be between 7.8% and 11.3% and could reach between 8.2 % and 12.7 % in 2045 [3]. In Africa, prevalence is estimated by the International Diabetes Federation (IDF) to be between 2.1% and 6.0%. Particularly in Côte d'Ivoire, the prevalence of diabetes is between 1.4% and 4.6%.[3] The high costs of conventional treatment are driving people with diabetes to traditional remedies.[4] Moreover, medical care for diabetes is limited by the inaccessibility of some populations to health centres. In these conditions, people often resort to medicinal plants for treatment.[5]

The recent development of phytotherapy offers an opportunity to find natural molecules that can have beneficial effects on the regulation of carbohydrate metabolism while avoiding the side effects of synthetic substances.[6] Thus, extracts of certain plants have been tested for their antidiabetic activity.[7, 8] Our choice was Distemonanthus benthamianus, which belongs to the fabaceae family, which is found throughout the forests of tropical Africa.[9] It is used in traditional African medicine to treat bacterial and viral infections. In addition, *Distemonanthus benthamianus* is used to treat skin diseases (abscesses, boils), palpitations and hepatitis.[10] This plant contains many biologically active compounds, such as flavonoids.[11]

In this study we prepared aqueous and hydroethanolic extracts from the stem bark of *Distemonanthus benthamianus* and evaluated the effect of these extracts on the biochemical parameters of rats made diabetic with alloxane.

1. MATERIALS AND METHODS

1.1. Materials

1.1.1. Plant material

The plant material consists of stem bark of *Distemonantus benthamianus* harvested in the Region of Upper Sassandra Department of Issia Republic of Côte d'Ivoire. The plant has been identified by the National Floristic Centre of Côte d'Ivoire where a sample of this plant is kept.

1.1.2. Animal material

This study was followed the guiding principle of the Ethics Committee and followed the guide for the care and employ of laboratory animals. Forty (40) male Wistars strain rats weighing between 200 and 220 g were used in this experiment. These animals are from the Laboratory of Animal Physiology of the Félix Houphouët-Boigny University of Abidjan. They were randomly divided into groups of 5 in standard cages for an acclimatization period of two (2) weeks before use. During this period, the animals had free access to food and water. They were kept in the animal house of the Ecole Normale Supérieure (ENS) at a constant temperature of 22 ± 2 °C and subjected to a light/dark cycle.[12]

1.2. Method

The stem bark of *Distemonanthus benthamianus* was washed, dried and then crushed using an IKAMAG mill and subjected to extractions in appropriate solvents.

1.2.1. Extraction and phytochemical study

Extraction

The aqueous extract was prepared as described in [13]. Thus, 1000 ml of distilled water was added to the bark powder (100g). The mixture thus prepared was heated on a hot plate equipped with a magnetic stirrer for 30 min. The aqueous extract was obtained by filtering the water-powder mixture through a filter paper. For the preparation of the hydroalcoholic extracts, the extraction method of [14] was used.

Thus, the pulverized raw material (100g) was macerated in 1000 ml of a hydro-ethanol solution (v/v, 95° alcohol) for 24 hours under magnetic stirring. The resulting filtrates were then placed in single-use aluminium containers, frozen at -20 °C and freeze-dried. The extracts thus obtained were weighed to evaluate their yield and stored in a refrigerator at 4 °C.

Phytochemical screening

The phytochemical tests were carried out on the basis of differential reactions of the main groups of chemical compounds contained in the plant according to the method adapted to the laboratory conditions.[15]

1.2.2. Induction of alloxane diabetes and determination of blood glucose levels

In this experimental model, animals were made diabetic by intraperitoneal injection of a single dose of alloxane at 120 mg/kg bw according to the method used by [16]. Blood glucose was determined 72 hours after injection using a glucometer (Acua Check).

1.2.3. Treatment of animals and determination of biochemical parameters

Rats with a blood glucose level 2g/l higher than 2g/l are considered diabetic and homogeneously distributed in 08 groups of 05 rats each.

Group I (normal control) receives gavage with physiological water. Group II (diabetic control) received a single intraperitoneal injection of 120 mg/kg alloxane and daily gavage with physiological water. Groups III, IV, V and VI receive daily gavage with 100 mg/kg/day and 200 mg/kg/day respectively of aqueous and hydroethanolic extract of Distemonantus benthamianus, groups VII and VIII receive 10 and 20 mg/kg daily gavage of Amarel (a hypoglycemic drug, belonging to the class of sulphonamides). The animals were treated for 21 days. Blood glucose, insulin and body weight were measured weekly. At the end of the treatment, the animals were sacrificed for the determination of biochemical parameters.

2. Statistical analysis

Blood glucose values are expressed as mean ± standard error to the mean. Analysis of variance (ANOVA) followed by the t-student test for multiple comparisons of the data were used for the statistical analyses using GraphPad software version 5.1. The variation of the different parameters was considered significant at the threshold of $P< 0.05$.

3. RESULTS AND DISCUSSION

3.1. Results

3.1.1. Phytochemical characterization of extracts

Phytochemical screening shows that the two types of extracts from *Distemonanthus benthamianus* have polyphenols, flavonoids, alkaloids, quinones and sterols in common. One also notes the presence of saponosides in the aqueous extract contrary to the hydroethanolic extract. (**Table I**).

Table I: Phytochemical screening of aqueous and hydroethanol extracts of *Distemonanthus benthamianus.*

Distemonanthus benthamianus	Extracts	Ta.	Fla.	Alc.		Sap.	Quin.	Ster.	Pol.
	Aqueous	+	+	+	+	+	+	+	+
	Hydroethanolic	+	+	+	+	-	+	+	+

Ta : Tanin ; Fla : Flavonoïdes ; Alc : Alcaloïdes ; Sap : Saponosides ; Quin : Quinones ; Ster : Stérols ; Pol : polyphénols. + : Presence ; - : Absence

3.1.2. Effects of extracts on biochemical parameters

Table II and Figure 1 present the results of the effect of the different extracts on biochemical parameters. Significant differences ($p<0.01$) in blood glucose and insulin levels were observed after 28 days of treatment of alloxanized animals with the different extracts with an advantage for the hydroethanol extract. Indeed, these two parameters remained around their initial values in the two groups treated with the hydroethanolic extract at a dose of 200 mg/kg (0.64 ± 0.05 and 13.46 ± 1.67 µU/ml).

With regard to the lipid profile, the results show that in diabetic rats treated for four weeks with the different extracts at the dose of 200 mg/kg, these parameters decreased. Nevertheless, this reduction is much more observed with the hydroethanolic extract compared to the aqueous extract. Thus, the injection of alloxane caused an increase in serum levels of TG, Chol. T and LDL-c at values of 200.1 ± 12.08, 157.14 ± 0.36 and 2.48 ± 0.02 mg/dl respectively and a reduction in serum HDL levels to 0.14±0.02 mg/dl. After treatment with hydroethanolic extract, these parameters show a significant reduction ($p<0.01$) with respective values of 118.01 ± 2.06 mg/dl for TG, 67.78 ± 0.36 Chol T, 0.41 ± 0.02 mg/dl for HDL and 1.32 ± 0.02 mg/dl for LDL-c compared to the diabetic group.

In addition, induction of diabetes causes a significant increase in renal (urea, creatinine) and hepatic (AST, ALT and albumin) parameters in rats. The different treatments with hydroethanolic extract of *Distemonanthus benthamianus* to the animals reduce the different parameters around the initial values. Moreover, these parameters remain high in untreated diabetic rats.

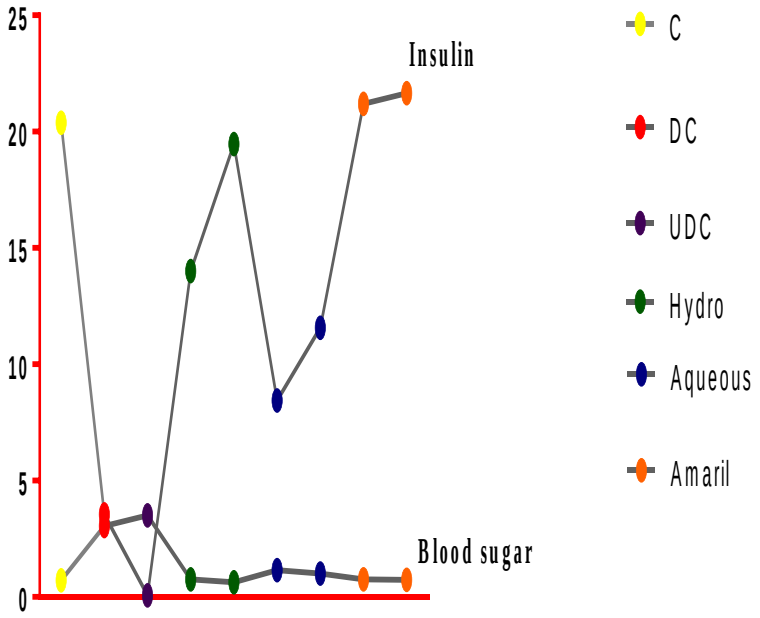

Figure 1: Evolution of blood sugar and insulinemia after treatment of diabetic rats

C : control ; DC : diabetic control ; UDC : untreated diabetic ; hydro : hydroethanolic extract ; Aqueous : aqueous extract.

Table II: Effect of aqueous and hydroethanolic extracts of *Distemonanthus benthamianus* and Amarel on the parameters Biochemicals in diabetic rats.

Parameters					Treatments					
					Hydroéthanolic		Aqueous		AMA	
		Control	DC	UTD	100	200	100	200	10	20
	Blood Glucose (g/l)	0,72 ± 0,03	3,05 ± 0,07	3,51 ± 0,34	0,75 ± 0,02***	0,71± 0,05***	1,16 ± 0,52**	1,003 ± 0,08***	0,77± 0,01***	0,74 ± 0,02***
	Insulin (uUI/ml)	20,39 ± 2,14	3,56 ± 0,08	0,07 ± 0,02	8,02 ± 1,22**	13,46 ± 1,67***	5,45 ± 0,21	6,58 ± 0,28	21,66 ± 2,86***	21,19 ± 5,30***
lipid Profile	TG (mg/dl)	117,56 ± 2,06	200,01 ± 12,08	258,14 ± 22,03	137,12 ± 5,04***	118,01 ± 2,06***	175,23 ± 9,09*	137,63 ± 3,16***	198,12± 11,12*	165,23 ± 4,79**
	Chol T (mg/dl)	73,45 ± 3,36	157,14± 5,48	201,12± 2,45	87,14 ± 3,27**	67,78 ± 1,12***	132,36 ± 2,06*	117,33 ± 1,09**	100,02 ± 1,04**	98,12 ± 0,36**
	HDL (mg/dl)	0,42 ± 0,03	0,14 ± 0,02	0,08 ± 0,01	0,24 ± 0,02*	0,41 ± 0,02***	0,16 ± 0,01^{ns}	0,31 ± 0,01**	0,11 ± 0,02^{ns}	0,16 ± 0,01^{ns}
	LDL (mg/dl)	1,26 ± 0,02	2,48 ± 0,04	4,87 ± 1,02	2,15 ± 0,05^{ns}	1,32 ± 0,03***	2,35 ± 0,04^{ns}	1,89 ± 0,02*	2,17 ± 0,13^{ns}	2,12 ± 0,05^{ns}
Renal	Urea	0,31 ± 0,01	2,47 ± 0,08	3,78 ± 0,12	1,45 ± 0,03*	0,65 ± 0,02***	2,18 ± 0,08^{ns}	0,93 ± 0,02**	2,41 ± 1,02^{ns}	2,38 ± 0,11^{ns}
	Creatinine	22,46 ± 1,03	46,05 ± 3,02	52,12± 4,07	35,97 ± 2,05*	28,42 ± 1,22**	45,08 ± 3,09^{ns}	28,65 ± 1,08**	32,84 ± 0,04**	23,45 ± 1,02***
Hepatic	ASAT (UI/L)	125,23 ± 5,04	178,78 ± 7,05	208,49 ± 21,04	152,14 ± 7,06*	119,48 ± 8,02***	164,78±12,32^{ns}	132,26 ± 6,02**	170,12 ± 15,01^{ns}	168,25± 11,05^{ns}
	ALAT (UI/L)	97,52 ± 3,12	134,12 ± 7,04	165,81 ± 12,02	112,48 ± 6,04*	99,48 ± 3,21***	135,16±6,04^{ns}	118,63±5,11*	124,15 ± 5,38^{ns}	139,32 ± 6,01^{ns}
	Albumin	53,12 ± 2,32	22,14 ± 1,05	11,48 ± 0,22	32,98 ± 0,42^{ns}	58,16 ± 2,15***	31,45 ± 1,06^{ns}	47,97 ± 1,18**	35,69±0,02*	37,14±0,02*

*C : control ; DC : diabetic control ; UTD : untreated diabetic ; hydro : hydroethanolic extract ; Aqueous : aqueous extract Each bar represents the mean ± SEM. *** : significant difference compared to the control batch at p <0.01; ** : significant difference compared to the control at p<0.05 ; ns : insignificant*

3.2. DISCUSSION

The purpose of this study is to investigate the effect of aqueous and hydroethanolic extracts of *Distemonanthus benthamianus* on the biochemical parameters of rats rendered diabetic. Induction of experimental diabetes in animal models is essential for promoting knowledge and understanding of various aspects of pathogenesis, with the ultimate goal of developing new therapies[17]. Alloxane, a monohydrate, is an indicator of diabetes that causes selective necrosis on the beta cells of the pancreas resulting in chronic insulin deficiency.[18]

The triphytochemical revealed that the aqueous and hydroethanolic extract of *Distemonanthus benthamianus* contains tannins, flavonoids, alkaloids, sterols, polyphenols, quinones and only the aqueous extract contains saponosides. The effect of the extracts on the reduction of the glycaemia of rats subjected to permanent hyperglycaemia could be related to the presence of flavonoids as it was underlined by certain authors.[19] Indeed the flavonoids act by improving the sensitivity of the cells of the body to insulin which makes it possible to reduce the incidence of the diabetes of the type 2.[20]

In addition, the strong presence of polyphenolic compounds reinforces the observations of[21] who found a correlation between the hypoglycemic activity of plant drugs and the presence of polyphenolic compounds which have a protective activity of the capillaries and an antioxidant property. In our extracts, in addition to flavonoids, we noted the presence of cardiac glycosides and saponosides. The antihyperglycemic effect of saponosides has been demonstrated.[22] In addition, cardiac glycosides inhibit the sodium Na+/K+ATPase pump which is involved in insulin secretion.[23] In addition, there is a reduction in blood glucose and an increase in insulin levels after treatment with Amarel (the reference molecule). Amarel is an oral antidiabetic drug of the class of hypoglycemic sulfonamides that correct insulin secretion deficiency by potentiating the insulin-secretory response to glucose.[24] Thus, the hydroethanolic extract could act in a similar way by improving hepatic and muscular insulin sensitivity. This effect could be achieved either by a direct post-receptor impact, or by an indirect effect by lifting the glucotoxicity phenomenon.

In our study, a strong increase in the serum concentration of the lipid profile was observed in rats made diabetic by

alloxane compared to the group of healthy control rats. Lipids play an important role in the pathogenesis of diabetes mellitus.

Hyperlipidemia, hypercholesterolemia, and hypertriglyceridemia are observed in the pathology of diabetes and are risk factors for atherosclerosis and coronary heart disease.[25] Our results are in agreement with several other studies such as those published by.[25,26]

It should be noted that several authors such as.[27] have suggested that the abnormally high serum lipid concentration observed in diabetic subjects could be essentially due to the increased mobilization of fatty acids from adipose tissue.[28] Indeed, diabetes is linked to hyperlipidemia and causes profound disturbances in plasma lipid content and composition.[29] Treatment of diabetic rats with various plant extracts at a dose of 200 mg/kg caused a decrease in serum concentrations of the lipid profile compared to the diabetic control group. Indeed, a large number of research studies on the biological activity of plant drugs have mentioned the antihypercholesterolemic effect of several bioactive molecules such as flavonoids, triterpenes and saponosides.[30] The marked lipid-lowering effect of the hydroethanolic extract of the plant could therefore be linked to the strong presence of some of these molecules in this extract.

In terms of renal parameters, there was a significant increase in serum creatinine and urea levels in diabetic rats. Disturbances in these parameters are related to chronic renal dysfunction and failure which may result in nephrotoxicity,[31] resulting from alloxane toxicity to the kidneys (nephropathy). Indeed, diabetes can damage the blood vessels of the kidneys, leading to renal dysfunction, according to,[32] the increase in creatininemia indicates a decrease in glomerular filtration rate, and thus renal failure. Thus, diabetic nephropathy is one of the primary causes of chronic renal failure.[33] The results obtained after treatment of diabetic rats show a beneficial effect of the various extracts. However, the dose of 200 mg/kg bw of the hydroethanolic extract seems to be the most effective. This is because it causes a highly significant decrease in the two parameters whose value is close to normal.

In addition, in the present study, the increase in serum transaminase activity (AST and ALT) in diabetic rats compared to control rats was noted. This increase in transaminases could be considered a biomarker of liver dysfunction and alloxane-induced liver damage. Indeed, AST and ALT are two liver enzymes.[34] Increases in these enzymes are indicative of liver injury and are explained by the leakage of enzymes from tissue to plasma due to the altered membrane permeability caused by alloxane.[35]

In our work, the treatment of diabetic rats with the different extracts showed a decrease in serum transaminase activity. And this reduction is much perceived with the hydroethanolic extract at a dose of 200 mg/kg. This beneficial effect could be explained by the presence of flavonoids and alkaloids in our extract, which are known for their hepatoprotective activity.[36]

CONCLUSION

The main objective of this study was to evaluate the biochemical parameters of the stem bark of *Distemonanthus benthamianus*, a plant of the Ivorian pharmacopoeia. Phytotherapy can be an alternative medicine or at least as a complement to traditional pharmacy. The need to find new molecules remains a public health priority. The hydroethanolic extract at a dose of 200mg/kg has the most therapeutic effect, reducing the appearance of degenerative complications of diabetes. This extract could therefore offer therapeutic prospects for better diabetes management. *Distemonanthus benthamianus* could play a role as a dietary adjuvant as a preventive measure, or to increase the efficacy of oral antidiabetic agents in order to delay the appearance of the degenerative complications of diabetes.

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