



Research Article

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Dose Response Study of Aqueous Extract of Dialium Guineense Stem Bark

OD Abu^{1*}, IO Onoagbe¹ and I Ojo²

¹Department of Biochemistry, University of Benin, Benin City, Nigeria

²Department of Chemistry, University of Kentucky, Lexington, USA

*Corresponding author: OD Abu, Department of Biochemistry, Faculty of Life Sciences, University of Benin, Benin City, Nigeria.

To Cite This Article: OD Abu, IO Onoagbe, I Ojo, Dose Response Study of Aqueous Extract of Dialium Guineense Stem Bark. Am J Biomed Sci & Res. 2022 - 15(2). AJBSR.MS.ID.002099. DOI: [10.34297/AJBSR.2022.15.002099](https://doi.org/10.34297/AJBSR.2022.15.002099)

Received: 📅 October 01, 2021; Published: 📅 January 13, 2022

Abstract

Background and Objective: What distinguishes a poison from a remedy is dose. The safety of plant-derived bioactive compounds has become a global concern. The present study investigated the dose response of aqueous extract of Dialium guineense stem bark using Wistar rats. Methods: Adult male Wistar rats (n=30) weighing 160-180 g (mean weight =170 ± 20 g) were randomly assigned to six groups of five rats each. The aqueous extract of the medicinal plant stem bark was obtained using cold maceration method. The rats received varied doses of extract (200-2000 mg/kg body weight, bwt) orally with the aid of gavage for a period of 28 days (4 weeks). Concentration of Fasting Blood Glucose (FBG) was used as the therapeutic index. Results: Aqueous extract of D. guineense stem bark significantly reduced the FBG levels of normal Wistar rats (p<0.05). The graded and quantal dose response curves showed that 1000 mg/kg bwt was effective in reducing the blood glucose of rats (produced the best hypoglycemic effect).

Keywords: Dialium Guineense, Dose Response, Rats, Extract, Effective Dose

Introduction

According to Paracelsus “the right dose differentiates a poison from a remedy”. The science of toxicology is based on the principle that a relationship exists between a toxic reaction (the response) and the amount of toxic substance received (the dose). An important assumption in this relationship is that there is almost always a dose below which no response occurs or can be measured [1]. Another assumption is that when the maximum dose is reached any further increase in dose will produce no increase in effect. Exposure refers to any condition which provides an opportunity for an external environmental agent to enter the body, while dose refers to the amount of agent deposited within the body. Response refers to the biological effect elicited by the agent. Dose and response are related and can be represented by a dose-response curve. Data from toxicological testing can be represented by a dose-response curve.

A dose-response curve is a curve which shows the relationship between the dose administered and the observed response [1].

A dose-response curve can be developed for most chemicals. From these curves the threshold level and relative toxicity of chemicals can be obtained to establish safe levels of chemical exposure. There are two types of dose-response curves: one that describes the graded responses of an individual to varying doses of the chemical and one that describes the distribution of responses to different doses in a population of individuals. The dose is represented on the x-axis, while the response is represented on the y-axis [2]. An important aspect of dose-response relationships is the concept of threshold. This is the dose below which no adverse effect is observed. The identification of the threshold beyond which the human body cannot remain healthy depends on the

type of response that is measured and can vary depending on the individual being tested [2-3].

Materials And Methods

Experimental Rats: Adult male Wistar rats (n=30) weighing 160-180 g (mean weight =170 ± 20 g) were obtained from the Department of Anatomy, University of Benin, Benin City, Nigeria. The rats were housed in metal cages under standard laboratory conditions: temperature of 25 °C, 55-65 % humidity and 12-h light/12-h dark cycle. They were allowed free access to rat feed (pelletized growers mash) and clean drinking water. Prior to commencement of the study, the rats were acclimatized to the laboratory environment for one week. The study protocol was approved by the Ethics Committee on Animal Use of the Faculty of Life Sciences, University of Benin, Benin City, Nigeria.

Collection of Plant Material: The stem barks of *D. guineense* were obtained from Auchi Area of Edo State, Nigeria and authenticated at the herbarium of the Department of Plant Biology and Biotechnology, University of Benin, Benin City, Nigeria.

Plant Preparation and Extraction: The stem bark was brushed and shade-dried at 30 °C for a period of two weeks and

crushed into small pieces using clean mortar and pestle. Aqueous extract of the stem bark was obtained using cold maceration method as described previously [4-6].

Dose Response Study: The rats were randomly assigned to six groups of five rats each. They received varied doses of extract (200-2000 mg/kg bwt) orally with the aid of gavage for a period of 28 days (4 weeks). Concentration of FBG was used as the therapeutic index.

Statistical Analysis: Data are expressed as mean ± SEM (n=5), and statistical analysis was performed using GraphPad Prism Demo (6.07). Groups were compared with Duncan multiple range test. Statistical significance was assumed at p<0.05.

Results

Concentrations of Fasting Blood Glucose: Aqueous extract of *D. guineense* stem bark significantly reduced the FBG levels of normal Wistar rats (p< 0.05). The graded and quantal dose response curves showed that 1000 mg/kg bwt was effective in reducing the blood glucose of rats (produced the best hypoglycemic effect) (Tables 1 and 2).

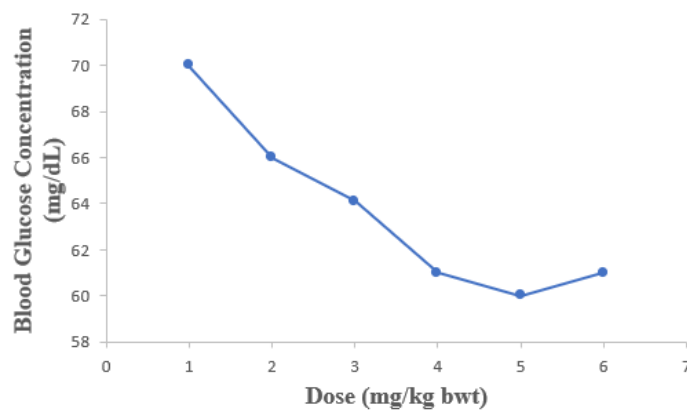


Figure 1: Graded Doses Response Curve for Aqueous Extract of *D. guineense* Stem Bark.

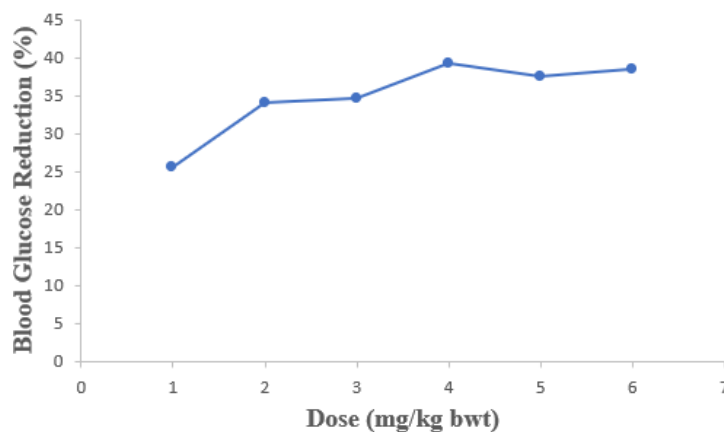


Figure 2: Quantal Dose Response Curve for Aqueous Extract of *D. guineense* Stem Bark.

Table 1: Concentrations of Fasting Blood Glucose in Rats Treated with Aqueous Extract of *D. guineense* Stem Bark.

Days	200 mg/ kg bwt (mg/dL)	600 mg/kg bwt (mg/dL)	800 mg/kg bwt (mg/dL)	1000 mg/kg bwt (mg/dL)	1500 mg/kg bwt (mg/dL)	2000 mg/kg bwt (mg/dL)
0	94.00±2.80	100.00±2.50	98.00±3.00	100.20±4.00	96.00±3.10	99.50±4.00
7	88.00 ± 4.20	80.50±4.50	83.10±3.70	80.00 ± 4.00	90.00±3.00	80.00±3.00
14	81.50±3.50	80.00±4.00	79.00±3.00	74.40±4.10	81.50±3.10	72.50±4.50
21	73.00±3.00	75.50±4.50	70.50±4.10	67.00±3.00	69.50±3.50	72.50±2.05
28	70.00±3.50	66.00±3.00	64.10±3.05	61.00±3.06	60.00±4.00	61.00±3.10

Data are concentrations of FBG and are expressed as mean ± SEM (n=5).

Table 2: Glycemic Change in Rats Treated with Aqueous Extract of *D. guineense* Stem Bark.

Days	200 mg/kg bwt (mg/dL)	600 mg/kg bwt (mg/dL)	800 mg/kg bwt (mg/dL)	1000 mg/kg bwt (mg/dL)	1500 mg/kg bwt (mg/dL)	2000 mg/kg bwt (mg/dL)
7	6.38 ± 0.92	19.50 ± 2.55	15.20 ± 2.15	20.00 ± 2.50*	6.25 ± 0.55	23.81 ± 4.11*
14	13.30 ± 1.57	20.00 ± 2.00	19.39 ± 2.71	25.60 ± 2.20	15.10 ± 2.75	30.95 ± 2.55*
21	22.34 ± 1.94	24.50 ± 2.50	28.06 ± 2.01	33.00 ± 2.00	27.60 ± 2.13	30.95 ± 1.95
28	25.53 ± 1.95	34.00 ± 2.50	34.59 ± 2.71	39.20 ± 1.82	37.50 ± 2.90	38.50 ± 1.06

Data are concentrations of FBG and are expressed as mean ± SEM (n=5). *p < 0.05, when compared with group 1 (200 mg/kg bwt group).

Discussion

What distinguishes a poison from a remedy is the dose. The safety of plant-derived bioactive compounds has become a global concern. The present study investigated the dose response of aqueous extract of *Dialium guineense* stem bark using Wistar rats. Toxicologists develop extrapolations and hypotheses to explain the adverse effects of chemical agents in situations where there is little or no information [6]. Any agent (chemical, drug, food or plant) capable of producing deleterious response in a biological system and seriously injuring functions or causing death is regarded as poison. Similarly, the continuous administration of uncontrolled doses of medicinal plant may possibly lead to any of the following four categories of exposure to poison: acute, sub-acute, sub-chronic and chronic [5-7].

The characteristics of exposure and the spectrum of effects come together in a correlative relationship customarily referred to as the dose-response relationship. This is a relationship between exposure and health effect, which can be established by measuring the response relative to an increasing dose. This relationship is important in determining the toxicity of a particular substance. It relies on the concept that a dose, or a time of exposure (to a chemical, drug, or toxic substance), will cause an effect (response) on the exposed organism [8]. The results obtained in this study showed that aqueous extract of *D. guineense* stem bark significantly reduced the blood glucose levels of normal Wistar rats. The graded and quantal dose response curves showed that 1000 mg/kg bwt was effective in reducing the blood glucose of rats (produced the best hypoglycemic effect).

Conclusion

The results of this study suggest that aqueous extract of *D. guineense* stem bark possesses hypoglycemic effect at a relatively good dose.

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