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Journal of Advances in Plant Biology

ISSN: 2638-4469

DOI: 10.14302/issn.2638-4469.japb-22-4102

Research Article

Freely Available Online

# Dose Response of Total Saponins Isolated from the Stem Bark of *Dialium guineense*

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**Keywords:**

Fasting blood glucose, Hypoglycemic effect, Medicinal plant, Quantal dose-response, Wistar rat.

**Received:** Feb 11, 2022

**Accepted:** Mar 18, 2022

**Published:** Mar 21, 2022

**Editor:**

Zhongzhou Chen, China agricultural university

## Abstract

The safety of plant-derived bioactive compounds has become a global concern. The present study investigated the dose response of total saponins isolated from the stem bark of *Dialium guineense.* Adult male Wistar rats (n = 15) weighing 170 – 190 g (mean weight = 180 ± 10 g) were randomly assigned to three groups (5 rats per group). The rats received varied doses of total saponins isolated from the stem bark of the medicinal plant (50 - 150 mg/kg body weight, bwt) orally for a period of 9 days. The concentration of fasting blood glucose (FBG) was used as the therapeutic index. The results of the analysis revealed that total saponins isolated from the stem bark of *D. guineense* significantly reduced the Fasting Blood Glucose (FBG) levels of normal Wistar rats ($p < 0.05$). The graded and quantal dose-response curves showed that 150 mg/kg bwt was effective in reducing the blood glucose of rats (produced the best hypoglycemic effect). The study concluded that total saponins isolated from the stem bark of *D. guineense* possesses hypoglycemic effect at a relatively good dose.

## Introduction

In recent times, plant-derived substances have become of huge importance to man due to their many applications. Extraction methods involve the separation of medicinally active portions of plant tissues from the inactive/inert components using selective solvents. These plant components exist as complex mixtures of many medicinal metabolites, such as alkaloids, glycosides, terpenoids, phenols, flavonoids, and lignans [1]. Medicinal plants have long been recognized as important sources of therapeutically active compounds. Evidence-based research supports the medical and pharmacological benefits of plant-derived compounds with interest in

the identification and characterization of bioactive compounds from natural sources [2]. There have been growing interests in the toxicity of substances purified from plants basically to determine their safety [3 - 5].

Saponins are low molecular weight secondary plant metabolites containing either a tetracyclic steroidal or a pentacyclic triterpenoid aglycone with one or more sugar chains [6]. They are a class of chemical compounds found in abundance in various plants species. Saponins are amphipathic glycosides grouped phenomenologically by the soap-like foam. They are produced in aqueous solutions when shaken, and structurally by having one or more hydrophilic glycoside moieties combined with a lipophilic triterpene or steroid derivative [7]. Saponins are categorized according to the number of sugar chains in their structures as mono, di-, or tridesmosidic saponins. The most common monosaccharides in saponins include D -glucose, D-galactose, D-glucuronic acid, D-galacturonic acid, L-rhamnose, L-arabinose, D-xylose, and D-fructose [8]. This study aimed to carry out a dose response study of total saponins isolated from *D. guineense* stem bark.

## Materials and Methods

Adult male Wistar rats (n = 15) weighing 170 – 190 g (mean weight = 180 ± 10 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. Before the 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.

The stem barks of *D. guineense* were obtained from the 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.

The stem bark was brushed and shade-dried at 30 °C for two weeks and crushed into small pieces using clean mortar and pestle. Total saponins were isolated from the stem bark using the standard method [9].

The rats were randomly assigned to three groups (5 rats per group). They received varying doses of isolated total saponins (50 - 150 mg/kg bwt) orally for 9 days. The concentration of FBG was used as the therapeutic index.

Data are expressed as mean ± SEM (n = 5). Statistical analysis was performed using SPSS (20.0). Groups were compared with Duncan multiple range test. Values of $p < 0.05$ were considered statistically significant.

## Results

Total saponins isolated from the stem bark of *D. guineense* significantly reduced the FBG levels of normal Wistar rats ($p < 0.05$). The graded and quantal dose-response curves showed that 150 mg/kg bwt was effective in reducing the blood glucose of rats (produced the best hypoglycemic effect) (Tables 1-3). Figure 1 and 2)

## Discussion

The graded dose-response relationship is a fundamental aspect of Pharmacology. It is employed to study the effects of increasing drug dose and its response in a system. For instance, individual fibres of the skeletal muscle are capable of eliciting progressively increasing responses with increasing doses of a particular drug. The corresponding increase in response can be measured. With the increase in the response of dose, at first, there is a considerable increase in response and then, there are smaller increments as the dose approaches the maximum limit. After the maximum response has been reached, no further increase in response can be obtained with a further increase in dose. Generally, the dose-response curve assumes a shape or sigmoid pattern, and as a rule, the relationship between the dose and response is linear and well pronounced in the main body of the curve. This part of the curve (between 25 and 75 % of the curve) is

Table 1. Concentrations of Fasting Blood Glucose of Rats Treated with Isolated Total Saponins of D. guineense Stem Bark

| **Dose (mg/kg bwt)** | Blood Glucose Concentration (mg/dL) | | | | |
|---|---|---|---|---|---|
| | **Basal** | **Day 3** | **Day 5** | **Day 7** | **Day 9** |
| 50 | 72.50 ± 0.50 | 59.50 ± 1.50 | 66.50 ± 3.50 | 50.00 ± 3.00 | 51.50 ± 5.50 |
| 100 | 102.50 ± 2.50 | 83.00 ± 4.00 | 87.50 ± 5.50 | 74.50 ± 4.50 | 76.00 ± 4.00 |
| 150 | 96.00 ± 5.00 | 89.00 ± 4.00 | 76.00 ± 5.00 | 45.50 ± 4.50 | 61.00 ± 4.00 |

Table 2. Glycemic Change of Rats Treated with Total Saponins of D. guineense Stem Bark

| **Dose (mg/kg bwt)** | Blood glucose reduction (mg/dL) | | | |
|---|---|---|---|---|
| | **Day 3** | **Day 5** | **Day 7** | **Day 9** |
| 50 | 13.00 ± 2.00 | 6.00 ± 1.00 | 22.50 ± 3.50 | 21.00 ± 4.00 |
| 100 | 19.50 ± 1.50 | 15.00 ± 3.00 | 28.00 ± 4.00 | 26.50 ± 2.50 |
| 150 | 7.00 ± 1.00 | 20.00 ± 3.00 | 28.00 ± 4.00 | 35.00 ± 3.00 |

Table 3. Percentage Glycemic Change of Rats Treated with Total Saponins of D. guineense Stem Bark

| **Dose(mg/kg bwt)** | Blood glucose reduction (mg/dL) | | | |
|---|---|---|---|---|
| | **Day 3** | **Day 5** | **Day 7** | **Day 9** |
| 50 | 17.93 ± 3.19 | 8.28 ± 0.55 | 31.03 ± 1.94 | 28.97 ± 2.06 |
| 100 | 19.02 ± 3.94 | 8.28 ± 0.55 | 27.32 ± 2.95 | 25.85 ± 2.49 |
| 150 | 7.29 ± 0.52 | 20.83 ± 2.90 | 52.60 ± 5.11 | 36.46 ± 3.62 |

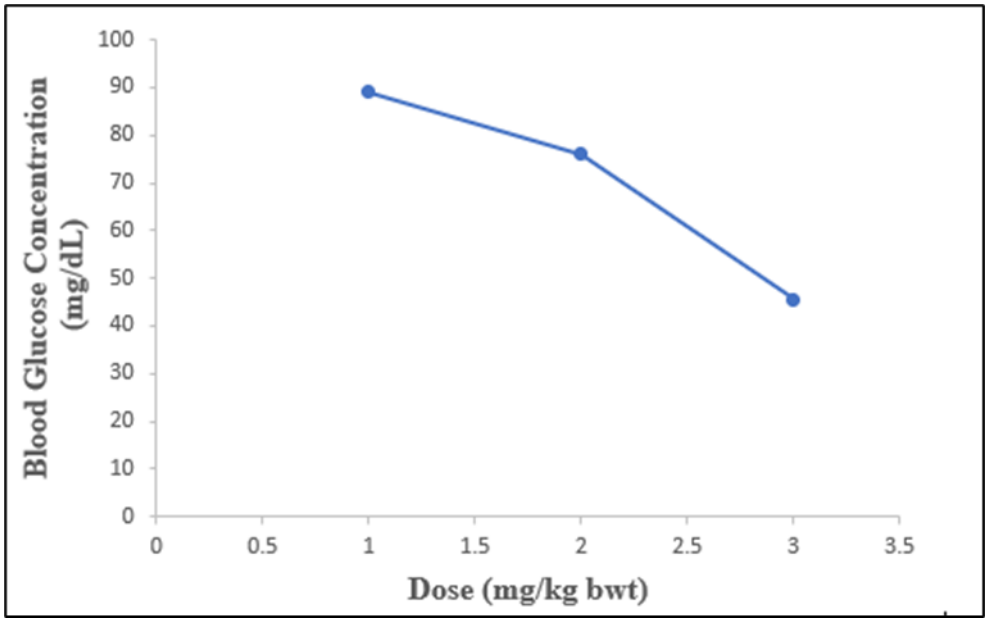


Figure 1. Graded Doses Response Curve for Isolated Total Saponins

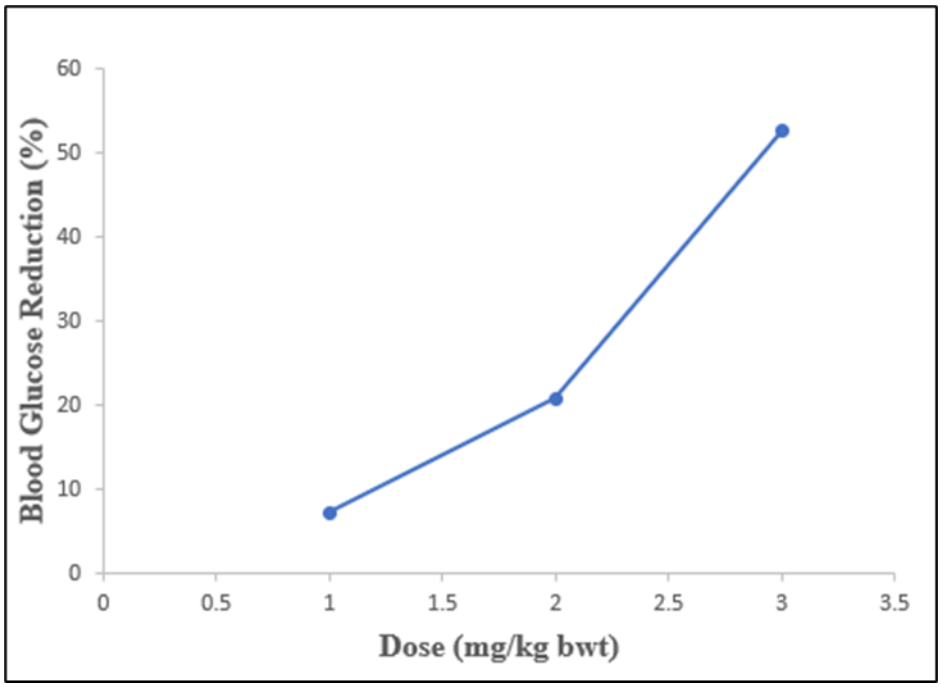


Figure 2. Quantal Dose Response Curve for Isolated Total Saponins

important in analytical and practical Pharmacology. Boundaries of the linearity can be extended utilizing certain mathematical transformations of other doses or responses [10].

It is critical when performing dose-response analyses to have a clear concept of what type of "dose" to use. Three basic types of "dose" arise from scientific investigations: (1) the administered or external dose; (2) the internal (absorbed) dose; and (3) the target or tissue dose. These doses are interrelated, and each of them can be used to express dose-response relationships [10].

External dose refers to the amount of an agent or chemical administered to an experimental animal or human in a controlled experimental setting by some specific route at some specific frequency. The external dose is often referred to as exposure or intake. It is frequently the dose metric that is used in observational epidemiological studies. Internal dose is the amount that is systemically available and can be regarded as the fraction of the external dose that is absorbed and enters the general circulation [11].

It is a consequence of absorption, distribution, metabolism and excretion of the chemical and can be derived from suitable toxicokinetic mass balance studies. The analytical method used in the toxicokinetic studies determines whether the "dose" refers to the parent compound alone or the parent compound plus first-pass metabolites. Biomarkers of internal doses, such as plasma concentrations or urinary excretion, are sometimes available in epidemiological studies. The tissue dose is the amount that is distributed to and present in a specific tissue of interest. Two parameters are important determinants of dose: the dose frequency and duration of dosing. Dosing can be acute, sub-chronic or chronic.

The description of dose reflects the magnitude, frequency and duration over which it applies [12, 13]. Response, in this context, generally relates to an observation or effect seen following exposure *in vivo* or *in vitro*. Possible end-points cover a broad range of observations, from early responses such as biochemical alterations to more complicated responses such as cancer and developmental defects. Responses can be either adaptive or adverse. Adverse effects are defined as a change in the morphology, physiology, growth, development, reproduction or life span of an organism or subsystem (subpopulation of cells) that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress or an increase in susceptibility to other influences [14, 15].

Most responses of interest in the context of dose-response assessment fall into one of four basic categories: quantal responses, counts, continuous measures and ordinal categorical measures. Quantal responses relate to an effect that is either observed or not observed in each subject (laboratory animal or human). For each dose, the number of subjects responding out of the number of subjects available is reported (for example, the proportion of animals with a tumour in a cancer bioassay) [11, 12]. The results of this study showed that total saponins isolated from the stem bark of *D. guineense* significantly reduced the FBG levels of normal Wistar rats. The graded and quantal dose-response curves showed that 150 mg/kg bwt was effective in reducing the blood glucose of rats.

## Conclusion

The results of this study suggest that total saponins isolated from the stem bark of *D. guineense* possess a hypoglycemic effect at a relatively good dose.

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