

Proposed Research Title (Ph. D Mauritania)

Phytochemical Characterization and Integrated Pharmacological Evaluation of Selected North African Saharan Plants as Antidiabetic Agents: A Combined *InSilico*, *In Vitro*, and *In Vivo* Approach

1. Introduction & Background

The North African Sahara represents one of the most extreme arid environments in the world. To survive intense drought, thermal fluctuations, and high salinity, endemic Saharan flora have evolved complex secondary metabolic pathways. These pathways generate structurally diverse bioactive compounds such as phenolics, flavonoids, terpenoids, and alkaloids—possessing exceptional therapeutic potential.

In North African traditional medicine, specific Saharan plants have been used for generations to manage chronic metabolic disorders, most notably Type 2 Diabetes Mellitus (T2DM). While synthetic antidiabetic drugs are widely available, their long-term side effects and high costs call for the discovery of safer, cost-effective natural alternatives. This doctoral project aims to scientifically validate the traditional anti-diabetic claims of selected North African Saharan plants, mapping their chemical profiles and deciphering their exact molecular mechanisms of action through an integrated computational, biochemical, and animal-model framework.

2. Research Objectives

Main Objective: To valorize the botanical heritage of the North African Sahara by identifying, characterizing, and validating potent antidiabetic bioactive compounds from selected resilient plant species.

Specific Objectives:

1. **Selection & Extraction:** To select promising Saharan species based on ethnobotanical data across the region and optimize green extraction protocols.
2. **Chemical Profiling:** To identify and quantify the major phytochemical constituents using advanced chromatographic and spectroscopic techniques.
3. **Computational Screening (*In Silico*):** To predict the binding affinities and molecular mechanisms of the identified compounds against key diabetic target proteins.
4. **Enzymatic Evaluation (*In Vitro*):** To assess the inhibitory potential of the extracts against carbohydrate-hydrolyzing enzymes.
5. **Biological Validation (*In Vivo*):** To evaluate the hypoglycemic efficacy, lipid-lowering capabilities, and histopathological safety profile of the extracts in diabetic animal models.

3. Methodology & Work Plan

The research design is structured into four highly integrated work packages (WPs):

WP 1: Phytochemical Extraction and High-Resolution Analysis

- **Sample Collection & Verification:** Selected Saharan plants will be gathered from targeted arid zones in North Africa, authenticated, and cataloged with herbarium voucher numbers.
- **Advanced Green Extraction:** Eco-friendly techniques, such as Ultrasound-Assisted Extraction (UAE) or Microwave-Assisted Extraction (MAE), will be deployed using solvents of varying polarities to maximize bioactive yields.
- **Quantitative and Qualitative Profiling:**

- Total Phenolic Content (TPC) and Total Flavonoid Content (TFC) will be determined using standard colorimetric assays.
- Comprehensive phytochemical fingerprinting and identification of major metabolites will be performed using High-Performance Liquid Chromatography coupled with Diode Array Detection (HPLC–DAD) and Gas Chromatography–Mass Spectrometry (GC–MS).

WP 2: Virtual Screening and Molecular Modeling (*In Silico*)

- **Molecular Docking Simulations:** A chemical library of the compounds identified in WP 1 will be docked into the active sites of key human enzymes and receptors regulating diabetes, including:
 - Digestibility enzymes: α -amylase and α -glucosidase.
 - Metabolic receptors & transporters: Peroxisome Proliferator-Activated Receptor gamma (PPAR γ) and Glucose Transporter 4 (GLUT–4).
- **Pharmacokinetic (ADMET) Prediction:** Computational algorithms will predict the Absorption, Distribution, Metabolism, Excretion, and Toxicity profiles of the compounds, filtering out toxic structures and highlighting drug-like lead candidates.

WP 3: Biochemical and Enzymatic Assays (*In Vitro*)

- **Enzyme Inhibition Assays:** The inhibitory kinetics of the plant extracts against α -amylase and α -glucosidase will be measured spectrophotometrically, calculating the IC₅₀ values and comparing them to the standard drug Acarbose.
- **Antioxidant Profiling:** Because oxidative stress drives pancreatic β -cell exhaustion, the radical scavenging capacities of the extracts will be thoroughly evaluated using DPPH and ABTS assays.

WP 4: Biological and Histopathological Studies (*In Vivo*)

- **Animal Model Design:** Healthy adult Wistar rats will be acclimatized and divided into experimental cohorts: Normal Control, Diabetic Control (untreated), Diabetic + Plant Extract (varying doses), and Diabetic + Metformin (standard reference drug).
- **Induction of Diabetes:** Hyperglycemia will be chemically induced via a single intraperitoneal injection of Streptozotocin (STZ) or Alloxan, causing partial destruction of pancreatic β -cells.
- **Biochemical Parameters:** Over the treatment period, key biomarkers will be monitored, including Fasting Blood Glucose (FBG), Oral Glucose Tolerance Test (OGTT), serum insulin levels, and a full lipid profile (Cholesterol, Triglycerides, HDL, and LDL).
- **Histopathology:** At the end of the study, structural changes in the pancreas (Islets of Langerhans), liver, and kidneys will be microscopically evaluated to confirm cellular protection and assess overall systemic safety.

4. Expected Outcomes & Scientific Impact

1. **Regional Botanical Mapping:** The generation of a comprehensive chemical and pharmacological map for highly resilient North African Saharan plants, bridging traditional knowledge with modern science.
2. **Mechanism Elucidation:** A clear understanding of the molecular-level mechanisms through which these desert plants modulate glucose metabolism, validation backed by correlated *in silico* and *in vitro* data.
3. **Novel Therapeutic Candidates:** Identification of safe, natural "lead compounds" that can serve as structural blueprints for future phytomedicines or nutraceuticals targeting Type 2 Diabetes.
4. **High-Impact Publications:** Publication of 2 to 3 peer-reviewed research papers in top-tier international journals indexed in Scopus/Web of Science

(e.g., *Journal of Ethnopharmacology*, *Phytomedicine*, or Springer Nature titles).

5. Project Timeline (Gantt Chart)

Phase / Research Activity	Months 1–4	Months5– 10	Months 11–20	Months 21–30
Fieldwork, Plant Collection, and Extraction Processing	X			
Chromatographic Profiling (HPLC/GC–MS) & <i>In Silico</i> Simulations		X		
<i>In Vitro</i> Enzymatic Assays & Intensive <i>In Vivo</i> Animal Trials			X	
Statistical Analysis, Thesis Compiling, and Manuscript Submissions				X