

**TECHNICAL REPORT**

**ON**

**STUDENTS INDUSTRIAL WORK EXPERIENCE SCHEME (SIWES)**

**UNDERTAKEN AT**

**NATIONAL INSTITUTE FOR PHARMACEUTICAL RESEARCH AND DEVELOPMENT (NIPRD), 1 IDU INDUSTRIAL LAYOUT, IDOGWARI, ABUJA.**

BY

ADEOYE RACHAEL FAVOUR

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DEPARTMENT OF PHARMACOLOGY AND THERAPEUTICS

COLLEGE OF MEDICINE AND HEALTH SCIENCES (MHS)

AFE BABALOLA UNIVERSITY, ADO-EKITI, EKITI STATE, NIGERIA.

SUPERVISOR: Pastor Oni James Olukayode

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**REPORT OVERVIEW**

I, ADEOYE RACHAEL FAVOUR, hereby submit this report in fulfilments of the requirements of my course of study, B. Sc Pharmacology and Therapeutics. The aim and purpose of this report is to convey the knowledge acquired during the course of the Students Industrial Work Experience Scheme for the period of 3 months.

It gives a comprehensive account of the knowledge attained at the National Institute for Pharmaceutical Research and Development located at Idu Industrial Area, Abuja.

**DEDICATION**

I would like to dedicate this report first and foremost to God Almighty, our Heavenly Father for making all this possible, for His Everlasting Grace and Mercy, for His protection and provision of health to be able to be present for the training program.

Secondly, I would like to dedicate this to my wonderful parents, Mr. Michael Adelaja Adeoye and Dr. Mrs. Oluwatoyin Joan Adeoye for all the love and support, for being able to provide for my academic needs to be able to get to this point in my education. I also dedicate this report to my one and only sibling Michael Adeoye for being there for me and also to my friends for always encouraging and supporting me.

**ACKNOWLEDGEMENT**

I would like to acknowledge the Industrial Training Fund (ITF) for funding and making this program possible for undergraduate students to be able to attain work experience that will enable us to work more effectively and efficiently after the conclusion of our undergraduate studies. My appreciation goes out to the Department of Pharmacology and Therapeutics, Afe Babalola University, Ado-Ekiti (ABUAD) for the knowledge that has been instilled in me which further aided me during the course of my training.

I am grateful to the National Institute for Pharmaceutical Research and Development (NIPRD) for granting me the opportunity to learn from the Institute for the period of the 3 months.

I want to appreciate my Supervisor at NIPRD, Mr. Solomon Fidelis and the other staffs at NIPRD for the knowledge provided.

I would like to appreciate my parents for the support they have given me both morally and financially.

To my Supervisor at school, I am grateful for the visit at NIPRD during industrial training.

Thank you all. I am eternally grateful.

**CHAPTER ONE**

1. HISTORY OF NIPRD

The need for the advancement of indigenous pharmaceutical research and development (R&D) in order to enhance development and commercialization of pharmaceutical raw materials, drugs and biological products have been long recognized in Nigeria.

Therefore in 1987, The Federal Government approved the establishment of the National Institute for Pharmaceutical Research and Development (NIPRD) as a parastatal under the Federal Ministry of Science and Technology. This approval was based on the recommendation of the Pharmaceutical Society of Nigeria (PSN).

Under the Science and Technology Act of 1980, the Institute was established with the primary objective of developing drugs, biological products and pharmaceutical raw materials from indigenous resources.

Financial contributions towards the take-off of the Institute were made from the Pharmaceutical Society of Nigeria (PSN) and the Pharmaceutical Manufacturers Group of the Manufacturers Association of Nigeria (PMG-MAN). A Board of Governors governs the Institute with representations from the PSN, PMG-MAN, Traditional Medicine Practitioners, Federal Ministry of Health (FMH) and Federal Ministry of Science and Technology (FMST) while the Chief Executive serves as member and Secretary to the Board.

The first major activity of the Institute was the organization of an International Workshop on “Strategies and Priorities for Indigenous Pharmaceutical Research and Development” in October 1989. In 1991, the proceedings of the workshop were published and in 1990, the Institute embarked on the documentation of medicinal and aromatic plants within the Federal Capital Territory (FCT) of the Federal Republic of Nigeria. The data accumulated during the ethnobotanical survey are being compiled into a National compendium of medicinal and aromatic plants in Nigeria.

1.1 VISION OF NIPRD

To build a centre of excellence in research and development of phytomedicines, pharmaceutical and biological products and diagnostics towards improving the health and well-being of man-kind.

1.2 MISSION OF NIPRD

* To apply appropriate modern science and technological resources to stimulate local production of drugs through effective collaboration with the industry and experts within and outside Nigeria.
* Drugs and diagnostics for the purpose of regulation and control.
* Develop quality standards for phytomedicine.
* Develop herbal and phytomedicines to pilot state of commercialization.
* Provide quality assurance services on all drugs used in healthcare delivery.
* Provide safety date and essential information on herbal and other towards achieving self-sufficiency in the production and control of essential drugs in such a way that would guarantee the overall health of Nigerians and mankind in general.

1.3 FUNCTIONS OF NIPRD

NIPRD which formally took off in January 1989, has the following functions:

* Undertake research and development work on drugs, biological products including vaccines and pharmaceutical raw materials from indigenous natural resources and by synthesis using appropriate science and technology methodologies.
* Develop methodologies for quality assessment of biological products, orthodox and herbal medicines including their raw materials.
* Establish and operate a quality assurance laboratory for pharmaceutical raw materials and products.
* Conduct appropriate investigations and consequents applications in the areas of evaluation, preservation, purification, standardization, safety and rational utilization of traditional medicine.
* Conduct research and development work into pharmaceutical biotechnology, nutrition, cosmetics and environmental science for improved quality of life and the conservation of medicinal and aromatic plants.
* Promote and sponsor staff development through training courses, workshops, and fellowship within and outside Nigeria.
* Serves as reference centre for research work on the biopharmaceutics, pharmacokinetics, storage and stability of imported and locally manufactured drugs and biological products.
* Promote and sponsor the local development and production of drugs, vaccines, pharmaceutical machinery, devices and accessories.
* Promote the pilot production unit of the Institute into a limited business venture.
* Establish and maintain relevant laboratories, clinics, medicinal plant gardens in strategic ecological zones of Nigeria as may be necessary for the performance of the functions.
* Compile and publish relevant data resulting from the performance of the functions of the Institute.
* Transfer pharmaceutical products and machinery technologies to private sector industries, and render consultancy and extension services to such and other organizations.
* Sponsor such national and international conferences, workshops, and symposia, as may be considered appropriate.
* Patent and register new products and processes with appropriate national bodies, international organizations, and selected countries.
* Establish and develop drug information system, collate and synthesize relevant research information for drug manufacturing industries and research centres.
* Enter into commercial and other appropriate agreements with relevant national and multinational corporations regarding the marketing and utilization of the Institute’s products and services.

1.4 VARIOUS DEPARTMENTS OF NIPRD AND THEIR FUNCTIONS

(A) Office of the Director General

The Office of the Director General oversees the entire Institute, but however has some Units directly under its supervision. These Units include;

1. NIPRD Research Clinic

2. Legal Unit;

3. Protocol/Public Relations Unit

4. Consultancy Unit (NIPRD CONSULT)

5. ICT Unit

6. Library, Information and Documentation Services Unit

7. Procurement Unit

8. Audit Unit;

9. SERVICOM Unit; and

10. Planning, Monitoring & Evaluation.

(B)Microbiology & Biotechnology

The functions of the department are;

1. Microbiological quality assessment of foods, water, raw materials, drugs preparations and phytomedicines.

2. Determination of anti-bacterial and anti-fungal potency of extracts, bioactive compounds and drugs.

3. Supports the development of new antimicrobial and antifungal agents to address drug resistance in the management of Malaria, TB and HIV/AIDS

4. Bio-screening for anti-parasitic agents for the treatment of locally endemic diseases, e.g. malaria, e.t.c.

5. Determination of viral load and CD4 count to support HIV/AIDS research and clinical services.

6. Conducts clinical chemistry and hematological analysis to support drug research and development and clinical services.

7. In vitro screening of natural and synthetic products for the management of HIV/AIDS.

8. Development and evaluation of HIV diagnostic kits.

Areas of specialization/collaboration include;

– Bacteriology;

– Biotechnology;

– Virology (collaboration with Institute of Human Virology, Nigeria)

– Parasitology

**(C) Medicinal Chemistry & Quality Control**

Activities of the Department include;

1. Operational research for health policy formulation.

2. Database on quality of drugs in use in Nigeria.

3. Pharmacokinetics of drugs of interest to Nigeria.

4. Development of analytical techniques for food and drug.

5. Drug and Food analyses.

6. Bioavailability and bioequivalence of orthodox drug products.

7. Development of quality specifications for the raw materials/extract/finished products.

8. Isolation/chemistry of natural products

9. In vitro drug/enzyme inhibition studies

Areas of specialization/Collaboration include;

– Collaboration with the National Sports Commission in setting up the National Doping Control Laboratory.

– Establishing the chemistry – manufacturing control for candidate drug.

– Determination of bioavailability/bioequivalence (BA/BE) of ACTs/ARVs in Nigeria.

– Provision of research and development facilities for undergraduates, post-graduate studies and researchers from universities and other organizations.

– Consultancy services and technical support to local entrepreneurs in food and herbal drugs.

**(D) Medicinal Plant Research & Traditional Medicine**

Activities in the Department include

1. Qualitative and quantitative pharmacognosy and phytochemistry of medicinal/aromatic plants.

2. Herbarium services

3. Medicinal/Aromatic plants propagation and cultivation. Development of medicinal plant nursery and greenhouses.

4. Isolation, structure elucidation, synthesis and SAR studies of organic molecules.

5. cGMP compliant pilot scale extraction of medicinal plants and their essential oils.

6. Freeze-drying of medicinal plant parts/materials and extract.

Areas of Specialization/Collaboration include but not limited to;

– Plant microscopy, chemomicroscopy/macroscopy;

– Phytochemical screening for secondary metabolites;

– Chromatographic isolation and analysis (open column, HPLC, GC-MS);

– Freeze-drying of plant materials;

– Domestication of wild medicinal plant/foreign plant species; and

– Cultivation of medicinal plant plantation.

**(E) Pharmacology & Toxicology**

Areas of Research include Neuropharmacology, Gastrointestinal tract studies, Immunological studies, Endocrinology, Respiratory studies, reproduction and fertility studies, parasitology and toxicological studies.

The department has contributed to the following Institute’s R&D projects such as:

1. Anti-malaria (AM1),

2. Anti-ulcer (AUL2),

3. Anti-sickling (NIPRISAN), and

4. HIV/AIDS (Immuno-stimulatory), (CONAVIR).

**(F) PT & RMD**

Functions of the Department

– Preformulation studies

– Formulation studies/design

– Stability studies

– Pharmaceutical raw materials development

Areas of Specialization

1. Nanotechnology and its applications in medicine

2. Dosage form design, preparation and assessment

3. Development and stability profiling of raw materials and dosage forms

**CHAPTER TWO**

2.1 ORAL ACUTE TOXICITY STUDY

AIM: To determine the toxicity of proposed test drugs or extracts within 24 hours after administration.

MATERIALS: Observation cages, Animals (Albino Rats/Mice), Test drug or extract (e.g *Cyperus articulatus*), Acute toxicity sheet, Observation cages, Laboratory coats, Gloves, Pen.

INTRODUCTION: Acute toxicity is defined as the unwanted effect(s) that occur either immediately or at a short time interval after a single or multiple administration of certain substances within 24 hours. Studies of acute toxicity tend to establish the dose-dependent adverse (or unwanted) effect(s) which may take place and this includes all the information that is important in the assessment of acute toxicity including mortality.

PROCEDURE: Administer the proposed test drug to the animals using oral route. Place the animals in observation cages and observe the presence of any action that occurs immediately after administration on the sheet provided. Also record for 10 minutes, 30 minutes, 1 hour, 2 hours, 4 hours, up until 24 hours after the time of administration on the sheet provided. The parameters to be checked for include; paw licking, tail flicking, mouth scratching, increased motility, decreased motility, lacrimation, convulsion, seizure, sedation, diarrhea, etc. The observations should be graded using + for mild, ++ for moderate, and +++ for severe depending on the severity and frequency of the action.

OBSERVATION: Reactions observed such as paw licking, tail flicking, mouth scratching and others, would depend on the severity to determine if the extract/drug is toxic.

RESULT: The test animals exhibited none or minimal adverse effects in most of the experiments.

CONCLUSION: The tested drugs/extracts are considered safe for use and free from acute toxicity if no toxic effect is exhibited and if it does not deter from its pharmacological effects.

2.2 SUB-ACUTE DERMAL TOXICITY STUDY

AIM: To determine the dermal toxicity of a proposed drug/extract.

MATERIALS: Animals (Albino Rats), Test extract, Metabolic cages, Laboratory coats, Gloves, Face mask, Scissors, Paper, Pen, Syringe, Measuring cylinder, Weighing balance.

INTRODUCTION: Dermal toxicity is the ability of a substance to cause a reaction locally and/or systemic poisoning in humans or animals when it comes in contact with the skin. The absorption of toxic substances through the skin depends on their chemical composition and solubility.

PROCEDURE: The rats were weighed, their backs were shaved and the unknown test extract was applied on their exposed skin. The rats were kept in metabolic cages and their food and water were measured and kept in tubes in the metabolic cages. The metabolic cages had a measured container were their food was kept and a measured bottle they could take water from the metabolic cages also had measured tubes were their faeces and urine went to separately. Every two days, the unknown extract was applied to their skin. Daily the rats were weighed and their food and water taken was measured and recorded. Their faeces and urine were taken from the tubes placed in the metabolic cages were weighed and measured respectively and the values were recorded. The experiment was carried on for 3 weeks and changes in their weight were recorded.

OBSERVATION AND RESULT: The rats lost weight and there were maggots found in their faeces. As days passed, the rats were known to be aggressive and isolated in a corner.

CONCLUSION: The unknown extract was found to have toxic effects on the animals.

2.3 ANTIDEPRESSANT STUDY USING FORCED SWIM TEST (FST)

AIM: To evaluate the antidepressant property of a proposed drug/extract.

MATERIALS: Animals (Albino mice), Laboratory coats, Gloves, Open cylindrical container/Bucket, Water.

INTRODUCTION: Forced swim test (FST) is a behavioural test on rodents used for the evaluation of antidepressant drugs, antidepressant efficacy of new compounds and are experimental manipulations that are aimed at rendering or preventing depressive-like states. It is a test centred on the rodent’s response to the threat of drowning, whose result has been interpreted as measuring susceptibility to negative mood.

PROCEDURE: The drug was administered 1 hour before the test was conducted. The animal was placed in an open cylindrical container filled halfway with water, and was unable to escape. The test was carried out for 6 minutes, the first minute was to eliminate the animal’s natural instinct to want to escape and the remaining 5 minutes was to test for mobility and immobility. Mobility is determined by the active/vigorous activity displayed by the animal in an attempt to escape, this includes swimming and climbing. Immobility is the passive activity displayed by animal where it only moves to maintain its head above the water, this is thought to indicate the feeling of hopelessness of the animal. Mobility and immobility time is observed and recorded.

After the experiment, the animals were dried off to prevent death by hypothermia.

OBSERVATION AND RESULT: The mobility time was greater than the immobility time which shows that the extract has antidepressant properties.

CONCLUSION: The drug/extract had antidepressant properties because the mobility time was greater than the immobility time.

2.4 WOUND HEALING STUDY

AIM: To determine if a proposed drug/extract has wound healing properties.

MATERIALS: Animals (Albino rats), Test extract, Laboratory coats, Gloves, Scalpel, Ruler, Observation cages.

INTRODUCTION: Wounds are physical injuries that come about as a result of the opening or breaking of the skin. The repair of injured tissue occurs as a sequence of events, which includes inflammation, proliferation, and migration of different cell types. The inflammation stage begins immediately after injury, vasoconstriction occurs first which favors homeostasis and releases inflammatory mediators. The proliferative phase is characterized by granulation tissue proliferation formed mainly by fibroblast and the angiogenesis process. The remodelling stage is characterized by reformulations and improvement in the components of the collagen fibre that increases tensile strength.

PROCEDURE: The backs of the animals were shaved to have a direct access to the skin. A shallow square- shaped wound of 1cm in length and breadth on the epidermis was incised using a scalpel. The test extract/drug was administered daily and the size of the wound was measured every 3 days for 21 days to check if there is a decrease in the size of the wound.

OBSERVATION AND RESULT: There was a decrease in the size of the wound and there was a replacement of the original tissue by a dysfunctional scar tissue. It was determined that the extract indeed had wound healing properties.

CONCLUSION: The extract had wound healing properties.

2.6 ANTI-CONVULSANT STUDY

AIM: To determine the anti-convulsant property of a proposed extract/drug.

MATERIALS: Animals (Albino mice), Pentylenetetrazol (PTZ), Laboratory coats, Gloves, Observation cages.

INTRODUCTION: Convulsion is a sudden, violent, irregular movement of the body caused by the involuntary contraction of muscles and it is associated especially with brain disorders such as epilepsy, the presence of certain toxins or other agents in the blood, or fever in children.

PROCEDURE: The test extract was administered 1 hour before the start of the experiment. Pentylenetetrazol (PTZ) was administered to the mice via intraperitoneal route and the animals were placed in observation cages. The animals were observed for convulsions for 5 minutes.

OBSERVATION: Some of the animals died a few seconds due to convulsion after PTZ was administered while the remaining animals died within the 5 minutes they were placed for observation.

RESULT: The extract does not have anti-convulsant properties.

CONCLUSION: PTZ is a good agent used for the induction of convulsion.

**CHAPTER THREE**

3.1 SUMMARY OF SIWES ACTIVITIES

During the course of the three (3) months training, several experiments were carried out, these include; Acute oral toxicity studies, Dermal toxicity study, Isolated tissue experiment, Methods of blood collection from Rodents (Rats/Mice), Acetic acid induced writhing, Acetic acid induced ear edema model to evaluate the anti-inflammatory properties of *Cyperus articulatus*, Forced swim test (FST), Anti-diarrhea study using castor oil induced diarrhea to evaluate the anti-diarrhea properties of *Moringa oleifera.*

Several lectures were taught by the interns and other staffs of the department of Pharmacology and Toxicology (P&T) at NIPRD. They include; The 3 R’s of animal research, Pharmacokinetics, Histamines, etc.

3.2 PROBLEMS ENCOUNTERED DURING THE PROGRAM

Transportation posed to be a problem encountered during the course of the study due to the bad roads and hold-up on the way to the Institute.

3.3 CONCLUSION

A tremendous amount of knowledge was attained during the course of the SIWES training.