Scientific report writing

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Course content

- Day 1 and 2
  - Lectures (60 min)
  - Students to start with writing proposals based on Hons projects

- Day 3 and 4 (Dr du Toit)
  - External lecture on the use of language in proposal writing
  - One page introduction/background to your project needed

- Day 5
  - Continue with writing

Proposals to be handed in for assessment

What is a research proposal

- Importance of a proposal
  - Guides research
  - Plan
  - formats

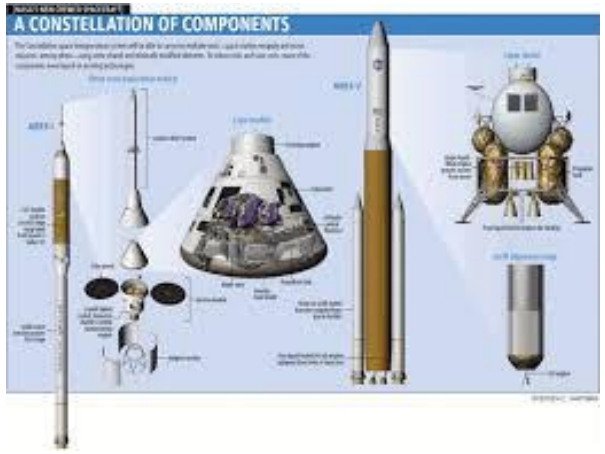
- Who is the reader?
  - Convince the reader – salesman
  - Selling a promise

Important questions

- Why?
  - Background
  - Problem statement
- What am I going to about it?
  - Aim or goal
- How am I going to do it?
  - Objectives
- When, where, monitoring etc
  - Tasks, activities, timelines, measurements of success, budgets

Story of NASA
“Send a man safely to the moon”

We must be the first to send a man to the moon safely



Designing, engineering, communication

I wonder when they coming to collect me

What goes into a proposal?

- Background Context
  - Set the scene
  - Contextualise the project
  - How would you contextualise the “man on the moon” story

- Literature
  - Concise literature review
  - Evidence of the problem – not a rumour
  - Current status
  - Literature on “man on the moon” project?

- Problem statement
  - What is the problem and briefly how you going to solve it
  - Problem statement for “man on moon” project?

What goes into a proposal?

- Aims or Goal
  - What is the overall goal/s you want to achieve
  - “send a man to the moon AND bring him back to earth safely”

- Objectives
  - Meet the overall goal
  - measurable
  - achievable
  - Objectives “man on the moon” project?

- Research significance
  - What will the impact be in the field
  - Research significance for “man on moon”?

What goes into a proposal?

- Limitations
  - What will be covered and what will not be covered
- Assumptions
  - Form of a protection or “disclaimer”
- Research design and methodology
  - Linked to the objectives
  - What methods you will use to reach the objectives

What goes into a proposal?

- Deliverables and budget
  - What tasks/activities will be performed
  - What are you going to deliver per task/activity
  - Deliverables must be measurable
  - Budget gives and idea of financial resources needed

Activity	Deliverable	Milestone
Evaluation San traditional knowledge on plant preparation and use	Report on the recommendations of suitable extracts and formulations Hoodia further development	A road map for Hoodia extraction and formulations
Preparation of extracts of the plant ensuring active ingredients and other compounds contributing to synergetic effects are retained.	Suitable extracts prepared with the spray dried extract of higher priority	Extracts fully chemically profiled, quantified with active ingredients, specifications completed and ready for formulation
Determine the safety profile of formulations containing the extract following the administration to healthy volunteers	Clinical trial completed with report on the findings on the formulations and traditional preparations	Clinical trial data showing safety, tolerability, bilirubin metabolism, hepatotoxicity detailed ECG (QTc) for cardiac effects cardiac effects. Efficacy study results.
Assess the efficacy of the selected formulation and containing Hoodia extract as a complimentary medicine for weight management	Clinical trial completed with report on the findings	Clinical trial data showing safety, tolerability and efficacy of the formulations as a complimentary medicine for weight management
Resuming of cultivation with community sites and by the various growers who are part of the stakeholders	Hoodia cultivated on various sites in South Africa	High quality plants with appropriate active ingredient/s concentration suitable for processing

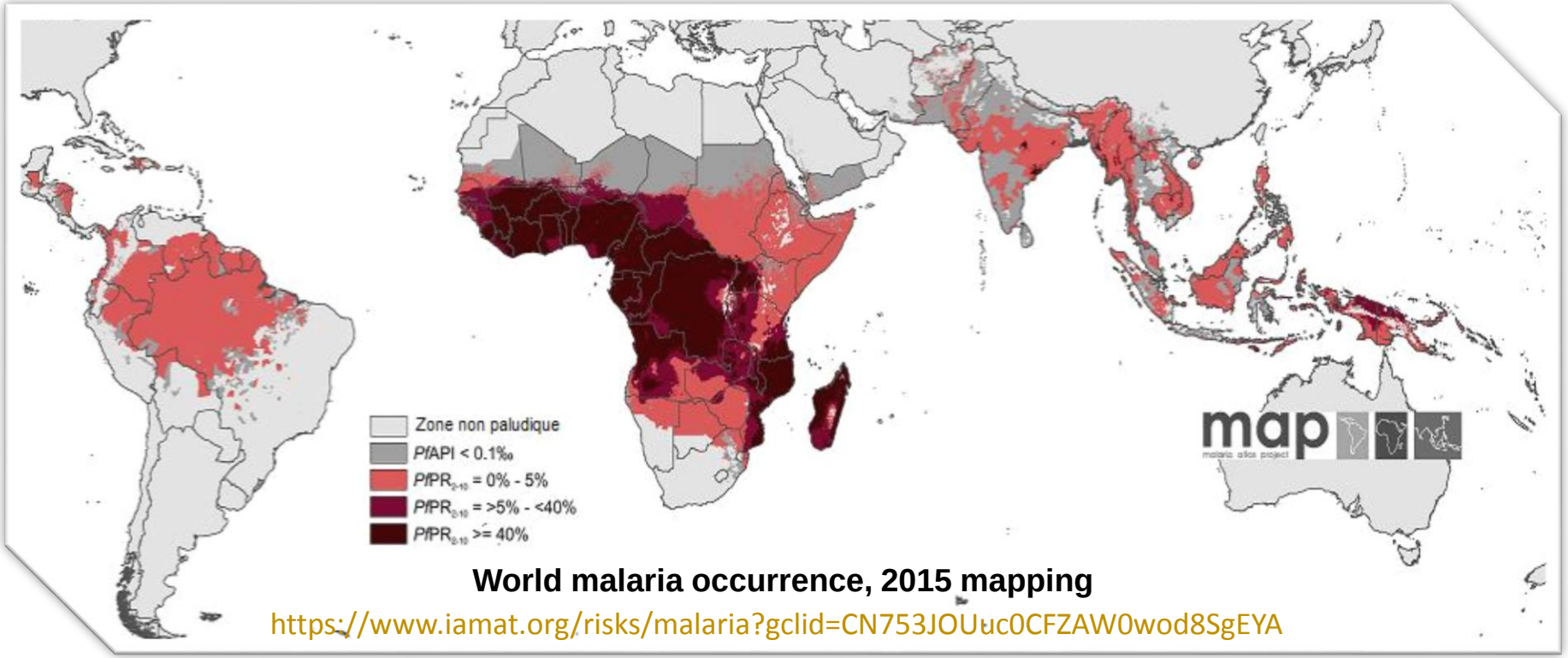
What goes into a proposal?

- Ethics clearance
  - Mainly if working with blood and animals
- Collaborators
  - What are the collaborators contribution
- Quality control
- Risk assessment
  - Factors that could undermine the research and how this will be mitigated
  - Think of the “man on the moon project”

Example

Search for new drugs to treat malaria

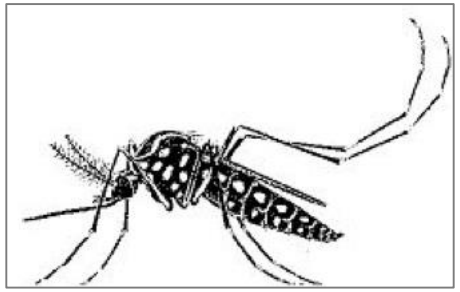
Malaria: a devastating disease



World malaria occurrence, 2015 mapping

https://www.iamat.org/risks/malaria?gclid=CN753JOUuc0CFZAW0wod8SgEYA

- **250 million clinical cases per annum**
- **A million death**
- **90 % contamination in Africa: *Plasmodium falciparum*!**

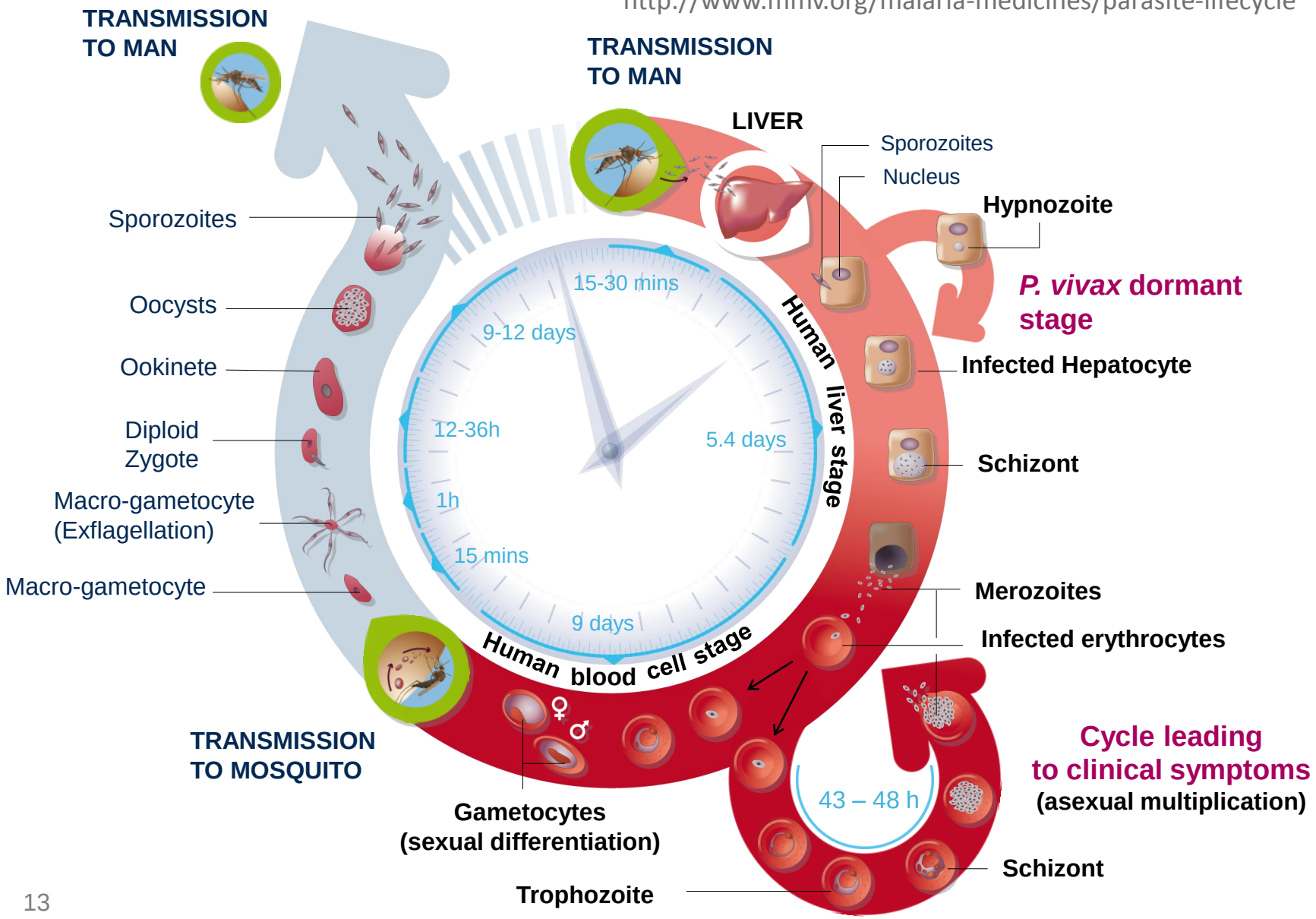


Anopheles gambiae

Clin. Microbiol. Rev. **2011**, *24*, 377-410.

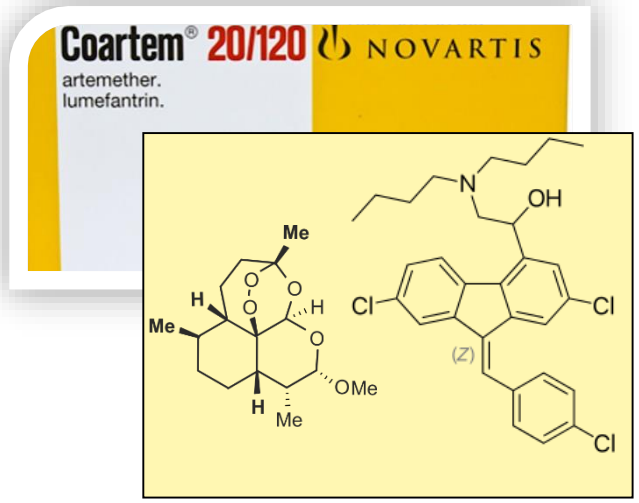
Malaria: a devastating disease – parasites' life cycle

http://www.mmv.org/malaria-medicines/parasite-lifecycle

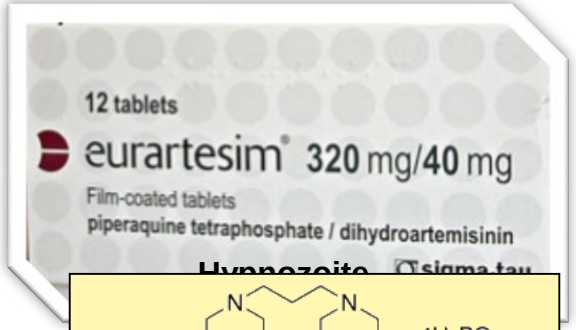


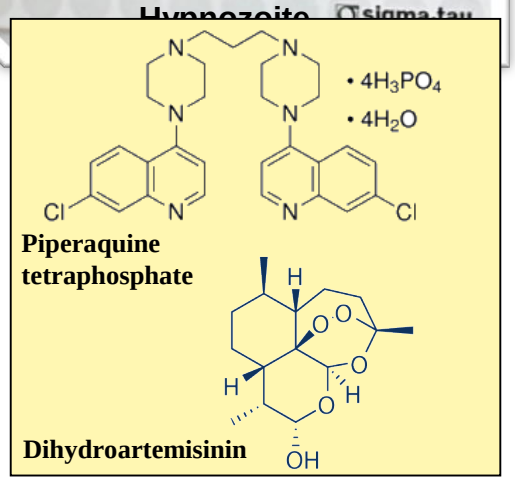
Science **2005**, *307*, 82-86.

Malaria: a devastating disease – available therapy



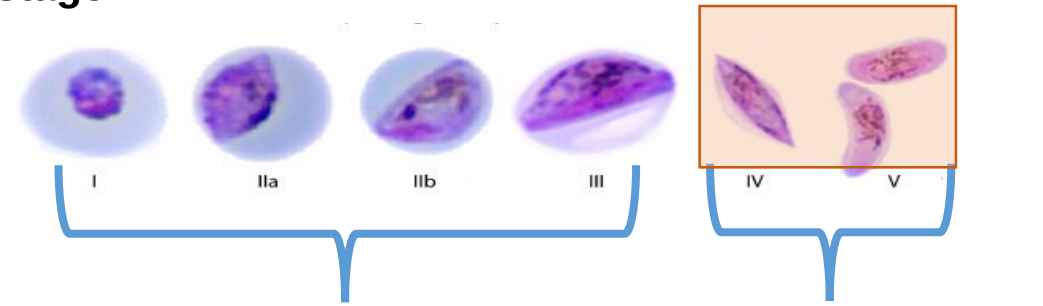
Artemisinin combination Therapy (ACT)





- **ACTs are first-line treatment for uncomplicated malaria cases**
- **ACTs act with rapid reduction in parasitemia, destroying asexual stage and early stage gametocytes**
- **Survival of mature gametocytes (late stage): post treatment contamination!!!**

Involved in the host to mosquito transmission



Early stage (phases I to III)

Late stage (IV and V)

Details of Research: Problem Identification

Malaria is amongst the major leading causes of death around the world and Africa in particular. It is estimated that annually there are between 350 and 500 million clinical cases of malaria with a mortality rate of over a million. Drugs such as chloroquine and artemisinin have played a crucial part in the control of this parasitic disease. However, their value in this endeavor is fast diminishing largely owing to the evolution and spread of drug resistant strains of Plasmodium falciparum. The current state of affairs is made even more desperate by the lack of development of new therapeutic agents to combat this disease. There is therefore an urgent need f research and development in search of novel and effective chemotherapeutic agents for the treatment of malaria. Historically, plants have contributed immensely in the management of malaria as some of the mainstay treatment drugs have been isolated from herbs. These include artemisinin and quinine along with derivatives such as chloroquine. The proposed work is based on the development of naphthylisoquinoline alkaloid type compounds, specifically jozimine A2 which was shown to have goo activity against the P. falciparum NF54 Luc and 3D7A-CBG99 Luc cell lines late stage gametocytes.

Details of Research: Rationale and Motivation

Malaria control in the past and current centuries has solely been based on the employment of what has been a two point strategy. These have been vector control and the use of chemotherapeutic drugs. The former has been directed towards the eradication of the mosquito as well as reducing the number of their bites on humans while the latter has been used as a preventative means (prophylaxis) and for the cure of diseased patients.

Along with vector control, malaria treatment drugs have been a major factor behind the success in the control and eradication of the disease in some parts of the world. It is probably the oldest and first attempt made by humans in the control of the disease having been in use since the 17th century. The use of chemotherapy is currently being undermined by the development of drug resistant Plasmodium species, a phenomenon that was likely caused by the misuse and abuse of these drugs.

Primaquine, a prophylax, is a

Chloroquine, a 4-aminoquinoline c

Artemisinin was isolated from the herb Artemisia annua (qinghao in Chinese),

Details of Research: Rationale and Motivation

Justification

The resurgence of malaria is a matter of great concern which requires urgent attention. While progress has been made in the control of the disease in the past few decades, malaria still affects close to half a billion people annually killing over a million in the process. Pregnant women and children under the age of 5 years are the most vulnerable to it. Resistance of Plasmodium to the current first line treatment regime makes the current and future scenarios even more worrisome. This is further exacerbated by the lack of new chemotherapeutic agents for the treatment of the disease. Moreover, the current existing portfolio of malaria drugs is mainly targeted towards the blood asexual stages with a few drugs effective against the liver stage and gametocytes. If P. falciparum gametocytes are not eliminated, patients continue to spread malaria for weeks after asexual parasite clearance. Asymptomatic individuals can also harbour gametocyte burdens sufficient for transmission, and a safe, effective gametocytocidal agent could also be used in community-wide malaria control programs. There is need to develop and introduce new drugs targeting liver stage and gametocytes of the parasite.

This project will……

chemotherapeutic agents for the treatment of malaria. Historically, plants have contributed immensely in the management of malaria as some of the mainstay treatment drugs have been isolated from herbs. These include artemisinin and quinine along with derivatives such as chloroquine. A collaborative project between the University of Pretoria (Department of Chemistry and Biochemistry) and the University of Würzburg (Germany) under the leadership of Prof Dr G Bringmann have screened selected naphthylisoquinoline alkaloids isolated from west African plants against the P. falciparum NF54 luc reporter cells lines and the 3D7A-CBG99 Luc reporter cell lines cell lines late stage gametocytes. The results have shown that jozimine A2 a naphthylisoquinoline dimer at 5μM to have good activity against the NF54 Luc and the 3D7A-CBG99 Luc cell late stage gametocytes with 100% and 70% inhibition, respectively. The new dimeric naphthylisoquinoline alkaloid, jozimine A2, was isolated from the root bark of an Ancistrocladus species by Prof Bringmann's research group. Based on this collaboration with the leaders in this field, the promising results has led us to propose the further investigation of this compound and related structural types together with synthetic analogues agai

Details of Research: Research Objectives

• To produce sufficient quantities of jozimine A2 through extraction and purification from plant material, but also by total or semisynthesis, for further in vitro bioassays against erythrocyte asexual stages and gametocytes and in vitro toxicity assessment

• To conduct in vitro bioassays against erythrocyte asexual stages and gametocytes and in vitro toxicity assessment a series of structurally related compounds from our collaborator at the University of Würzburg (Germany) in the gametocyte assays

• Preparation of synthetic analogues of jozimine A2 and related active naphthylisoquinoline alkaloids and in vitro bioassays against erythrocyte asexual stages and gametocytes

• To conduct in vitro bioassays against erythrocyte asexual stages and gametocytes and in vitro toxicity assessment of extracts of other of other Ancistrocladus species. These are accessible to Prof Dr G Bringmann at the University of Würzburg (Germany). Isolate and elucidate the structures of those compounds from those extracts of other Ancistrocladus species that show promising activity.

• Elucidate the biochemical pathways in gametocytes through which jozimine A2 and related naphthylisoquinolines alkaloids may be acting

Details of Research: Workplan: Research Activities

Objective:
To produce sufficient quantities of jozimine A2 through extraction and purification from plant material, but also by total or semisynthesis, for further in vitro bioassays against erythrocyte asexual stages and gametocytes and in vitro toxicity assessment

Activities:
1. Collection of plant material containing jozimine A2 by Prof G Bringmann (University of Würzburg, Germany), from the Democratic Republic of the Congo. Prof G Bringmann has established a successful collaboration of scientists in DRC from the University of Kinshasa more than 20 years ago.
2. Semi-synthesis of jozimine A2 using selected related compounds isolated form the plant
3. Purification of the compound including isolation of other related compounds through ion exchange chromatography and HPLC followed by the structural investigation by NMR, mass spectrometry (HPLC-MS) and HPLC MS/MS NMR-CD.
4. In vitro screening of jozimine A2 against erythrocyte asexual stages and gametocytes to generate inhibitory concentrations and IC50 values
5. In vitro cytotoxicity testing of jozimine A2

Start date: January 2016
End date: March 2017

Writing a funding proposal

- National research foundation (NRF)
- Research proposal – can be used to write funding proposal
- NRF Template
  - May not be exactly the same format as we have discussed

- Cover letter
- Title
- Executive summary or abstract
- Project information
  - Selecting your research field

Writing a funding proposal

- Details of research
  - Problem statement
  - Rationale and motivation
  - Aims and objectives
- Work plan and research activities
- Risk analysis and contingency plan
- Potential impact and equity redress
- Potential outcomes
- Research outputs

Writing a funding proposal

- Progress to date
- Funding track
- Ethical clearance
- Participating members
- Possible reviewers
- Excluded reviewers
- Financials: Operating costs
- Financials: Other sources of income