

Appendix 2.

SRDC Thematic Research Programme, 2020 - 2022

Title: 'Engkabang, the Wonders of Sarawak'

Aim: To develop comprehensive research programme into phenotypic characterisation and establishing the medicinal properties of *Shorea macrophylla* (Engkabang)

Objectives

- 1.** To elucidate the medicinal properties of aqueous and organic extracts of *Shorea macrophylla*
- 2.** To isolate, purify and chemically characterise compounds derived from *Shorea macrophylla* extracts that showed medicinal properties
- 3.** To establish in depth understanding on the molecular mechanism of action of, and accelerate therapeutic discovery from, compounds derived from *Shorea macrophylla*
- 4.** To characterise the phenotype and understand the growth biology, disease resistance and ancestry of *Shorea macrophylla*

Targeted medicinal properties:

- a. Anti-microbial properties
- b. Anti-oxidant properties
- c. Anti-inflammatory properties
- d. Anti-proliferative properties

Target diseases:

- a. Microbial infection (from clinically relevant microbes such as *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Enterobacter* spp.)
- b. Cardiovascular diseases
- c. Cancer

Objectives:

1. To elucidate the medicinal properties of aqueous and organic extracts of *Shorea macrophylla*

Description: A strong fundamental biology and in-depth understanding of the medicinal potential of *Shorea macrophylla* extracts in terms of anti-inflammatory, anti-microbial, anti-fungal, anti-oxidant and anti-proliferative properties. *In vitro* high throughput screening will be carried out utilising the extracts against clinically relevant microbes and appropriate cell lines to establish the medicinal properties of *S. macrophylla*. Chemical and lipid compositional profiling will be conducted using high resolution high throughput analytical equipment such as nuclear magnetic resonance spectroscopy and mass spectrometry to characterise the

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chemical and lipid components of the extracts. This objective is expected to provide the fundamental knowledge to underpin many of the other activities in subsequent objectives.

Expected outcomes:

- a. provide better understanding of the medicinal properties of *Shorea macrophylla*; and
- b. identify potential extracts of *S. macrophylla* for further purification, isolation and characterisation.

2. To isolate, purify and chemically characterise compounds derived from *Shorea macrophylla* extracts that showed medicinal properties

Description: Working across disciplines, the identification of potential new chemical entity through the application of molecular, systems and synthetic biology will be accelerated. Chemical compound isolation, purification and characterisation coupled with bioinformatics, structural activity relationship study and mathematical modelling will facilitate drug design, establishing fundamental pharmacology of the isolates and identifying potential new disease-specific receptors that can be targeted by the isolates *via* virtual screening. Preliminary toxicity testing *in vitro* will be carried out to establish the safety profile of the isolates.

Expected outcomes:

- a. identify new chemical entity with pharmaceutical, nutraceutical and cosmeceutical potentials.
- b. reveal new potential binding sites for diseases and structural modification (*in silico*) to enhance binding affinity and drug effectiveness

3. To establish in depth understanding on the molecular mechanism of action of, and accelerate therapeutic discovery from, compounds derived from *Shorea macrophylla*

Description:

In vitro high throughput screening i.e. single dose and/or combination screening, and validation of purified isolates for anti-inflammatory, anti-microbial, anti-fungal, anti-oxidant and anti-proliferative properties and disease targets. Further, *in silico* virtual screening, target drugability and validation will be carried out in tandem with continuous screening to ensure retention of isolate properties against desired disease(s). *In vitro* cytotoxicity study will be carried on the isolates identified and validated to have effects on disease(s) of interest.

Expected outcomes:

- a. Greater understanding on the molecular mechanism of action of *S. macrophylla* isolates;
- b. Establishing of virtual compound structure and isolate databases;
- c. Identification and optimisation of potential lead

4. To characterise the phenotype and understand the growth biology, disease resistance and ancestry of *Shorea macrophylla*

Description: This objective covers detailed phenotypic analyses of *S. macrophylla*. Genomic analyses allow detailed insight into evolutionary processes such as speciation or past hybridization events and allow further examination of tree evolution. Introgressive hybridization, speciation with gene flow, and incomplete lineage sorting may cause different local genealogies across the genome that can be detected by analyzing whole-genome sequences. Current genomic data on *S. macrophylla* are very limited. Establishment of *S. macrophylla* genome sequences would enable comparative analyses of genome architecture and the evolution of key traits for seed plants, including flower or fruit development and life history. Further, accurate understanding of the genetic structure *S. macrophylla* is necessary for conservation purposes, because wild populations often contain a spatial genetic structure linked to specific local ecosystems. Establishing the whole genome of *S. macrophylla* utilising next generation sequencing approach will also help in addressing issues relating to forest tree breeding, biodiversity and conservation.

Expected outcomes:

Establish the complete genome and transcriptome of *S. macrophylla* using next generation sequencing approach to enable comprehensive functional annotation.

To establish the chloroplast genome of *S. macrophylla* using next generation sequencing approach to establish lineages of Sarawak Engkabang.