Antiplasmodial-guided investigation of *Lantana camara* (Verbenaceae)

- **Good Health and Well Being (SDG 3)** through the design of Improved Traditional Medicines (*MTA*)
- **Quality education (SDG 4)** through the acquisition of new Analytical Methods and Technics

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1 Introduction

Despite great efforts to control and eliminate malaria, it is still one of the major causes of death and poverty in Africa. It disproportionately affects vulnerable groups, including women and children, particularly from the poorest households (**WHO, 2021a, and b**). Therefore, there is a need to develop new and more efficient antimalarials with novel mode of actions to combat resistant pathogens and reduce the burden of this infectious disease (**Ariey *et al.*, 2014**). An inventory of traditionally plants used in Cameroonian folk medicine in the treatment of parasitic diseases caused by protozoa, was carried out by means of in-depth bibliographic studies and ethnopharmacological field surveys in the South region of Cameroon. This survey revealed that, *Lantana camara* (Verbenaceae) are locally used to cure malaria, leishmaniasis, and many other diseases.

✓ General objective

The aim of this work is to obtain bioactive material (extracts and fractions) that can serve as raw material for the development of phytomedicines or actives compounds that can be use as lead for a development of a new drug against malaria.

✓ Specifics objectives

-Perform a bioguided isolation from *Lantana camara;*

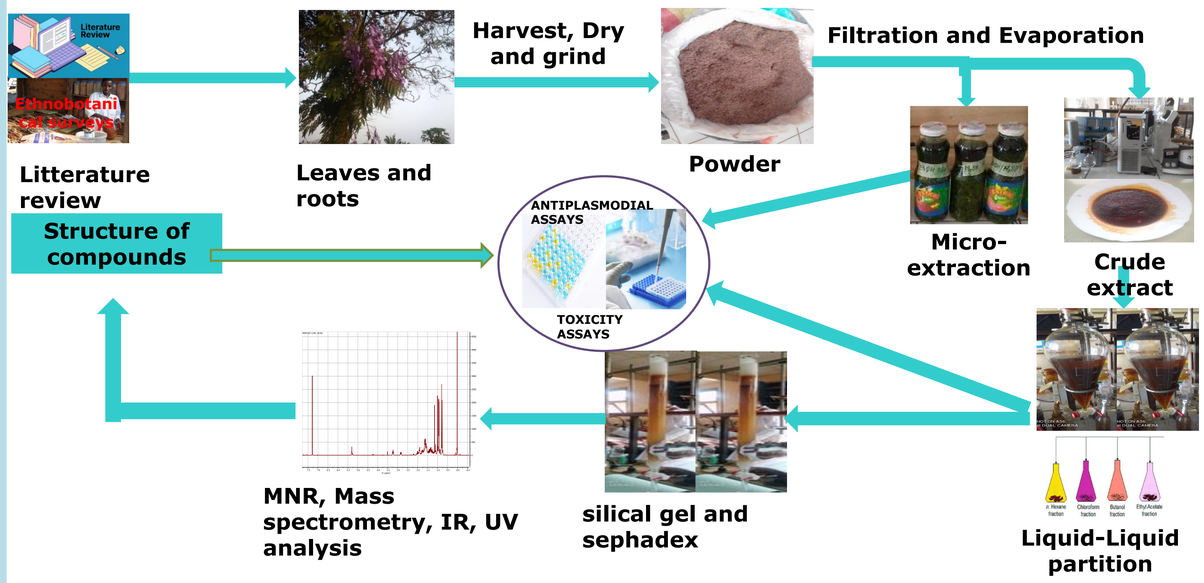
- Purify and characterize secondary metabolites ;

-Perform *in vitro* antiplasmodial, cytotoxic and toxicity assays in view of formulating a phytodrug.

Keywords: Malaria; *Lantana camara* ; *Plasmodium falciparum* ; Furanonaphthoquinones

2 Method

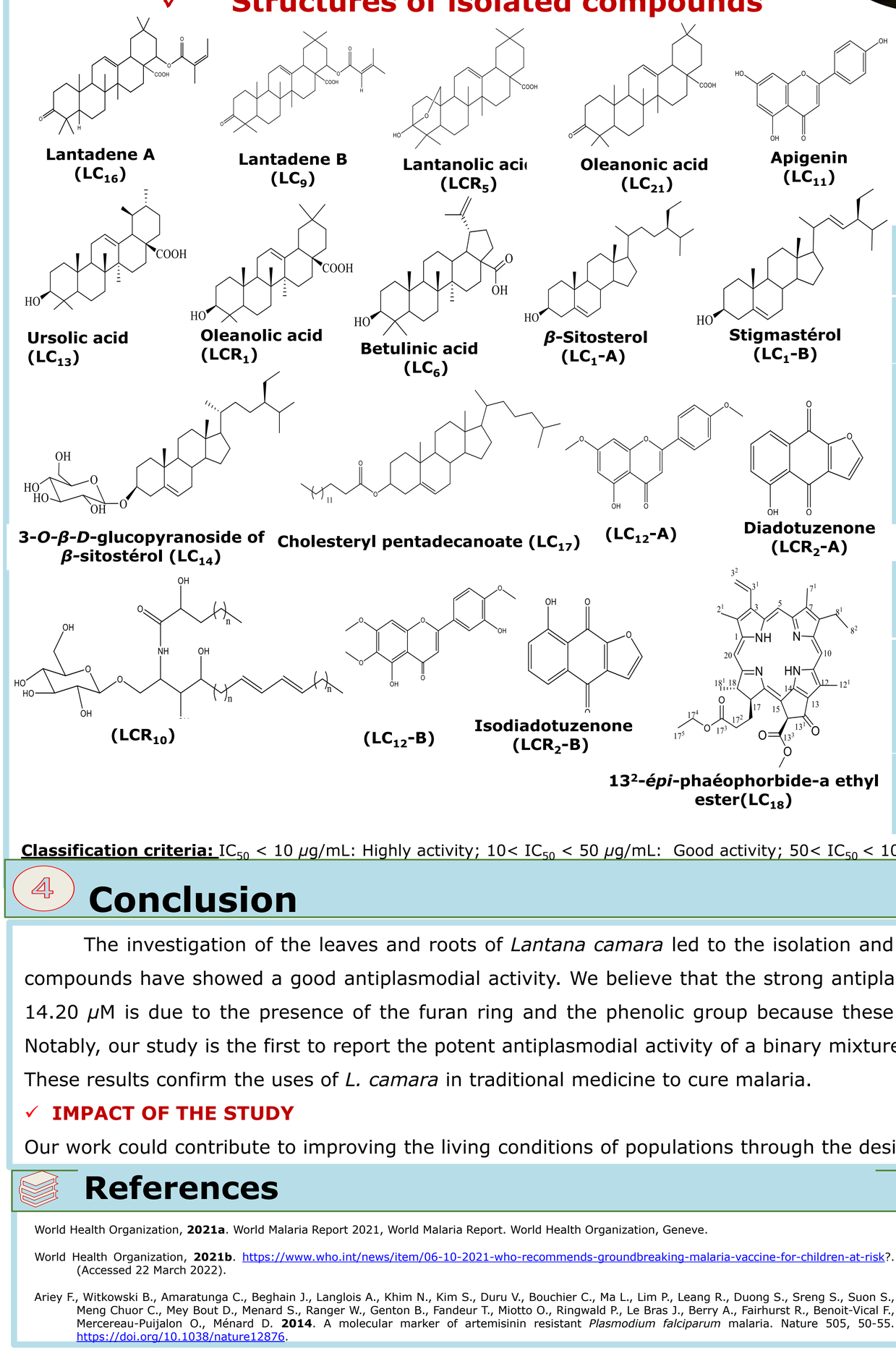
GENERAL PROTOCOL OF ISOLATION



The structures of isolated compounds were established based on their spectroscopic (1D and 2D NMR) data analysis. The *in vitro* antiplasmodial assay was performed following the method using SYBR Green-I based with chloroquine as reference drug described by Smilkstein and collaborator in 2004.

3 Results

✓ Structures of isolated compounds



✓ Antiplasmodial activity

• Crude extracts

Plants parts	Crude extracts code	Solvent of extraction	Antiplasmodial activity IC_{50} ± SD (µg/mL)		Resistance Index: $IC_{50}PfDd2/IC_{50}Pf3D7$
			Pf3D7	*PfDd2*	
Leaves	FEBLC	Ethanol	14.31 ± 1.68	35.95 ± 2.21	2.51
Roots	REBLC	EtOAc-MeOH (12:13)	11.36 ± 0.59	18.07 ± 3.11	1.59

• Fractions

Plants parts	Fractions code	Solvent	Antiplasmodial activity IC_{50} ± SD (µg/mL)		Resistance Index: $IC_{50}PfDd2/IC_{50}Pf3D7$
			Pf3D7	*PfDd2*	
Leaves	FFHLC	Hexane	14.30 ± 1.54	22.69 ± 5.99	1.58
	FFALC	Ethyl acetate	13.89 ± 0.98	25.41 ± 4.2284	1.82
	Ffnbu	n-butanol	84.49 ± 4.50	>100	-
Roots	R_1LC	Hex Hex: AE (3:1)	12.90 ± 0.97	18.86 ± 3.35	1.46
	R_2LC	Hex: AE (3:1)	21.90 ± 0.54	7.73 ± 1.10	0.35
	R_3LC	Hex: AE (3:1) Hex: AE (1:1)	14.34 ± 1.32	13.22 ± 0.75	0.92
	R_4LC	Hex: AE (1:1) Hex: AE (1:3)	19.91 ± 0.18	14.37 ± 0.36	0.72
	R_5LC	Hex: AE (1:3) AE: MeOH (3:1)	11.94 ± 0.19	13.80 ± 4.90	1.15
	R_6LC	AE: MeOH (3:1) MeOH	21.71 ± 1.07	30.63 ± 0.98	1.10

• Compounds

Plants parts	Compounds code	Solubility solvent	Antiplasmodial activity IC_{50} ± SD (µg/mL)		Resistance Index: $IC_{50}PfDd2/IC_{50}Pf3D7$
			$Pf3D_7$	*$PfDd_2$*	
Leaves	LC_{12}	Acetone	90.41 ± 2.80	45.84 ± 2.59	0.50
	LC_{17}	Dichloromethane	48.52 ± 4.98	34.02 ± 0.10	0.70
	LC_{16}		30.68 ± 1.01	19.04 ± 0.04	0.62
	LC_{21}		11.17 ± 0.61	9.44 ± 1.19	0.84
	LC_{14}	Pyridine	59.98 ± 6.73	31.82 ± 0.63	0.53
Roots	LCR_1	Dichloromethane	34.18 ± 3.37	29.49 ± 4.69	0.86
	LCR_2		6.05 ± 0.73	2.59 ± 0.35	0.42
	LCR_4	DCM-MeOH	61.25 ± 2.28	33.61 ± 1.55	0.54
	LCR_6	Dichloromethane	11.17 ± 0.61	9.44 ± 1.19	0.84

Classification criteria: IC_{50} < 10 µg/mL: Highly activity; 10< IC_{50} < 50 µg/mL: Good activity; 50< IC_{50} < 100 µg/mL: Moderately activity; IC_{50} > 100 µg/mL: inactive **(Singh *et al.*, 2015)**

4 Conclusion

The investigation of the leaves and roots of *Lantana camara* led to the isolation and characterization of eighteen (18) compounds. The crude extract, fractions and some isolated compounds have showed a good antiplasmodial activity. We believe that the strong antiplasmodial potency of compound LCR_2 on *P.fDd*$_2$ and *P.f3D*$_7$ with respective IC_{50} of 6.07 µM and 14.20 µM is due to the presence of the furan ring and the phenolic group because these skeletons generate the production of free radicals which leads to the death of the parasite. Notably, our study is the first to report the potent antiplasmodial activity of a binary mixture (LCR_2) of diodantunezone and isodiodantunezone derived from *L. camara.*

These results confirm the uses of *L. camara* in traditional medicine to cure malaria.

✓ IMPACT OF THE STUDY

Our work could contribute to improving the living conditions of populations through the design of Improved Traditional Medicines (*MTA*).

References

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