9th Joint Natural Products Conference 2016
July 24-27, Copenhagen, Denmark
www.jnpc2016.dk

# Abstract book

- Plenary lectures
- Keynote lectures
- Short lectures
- Young Researchers Workshop
- Pre-conference symposium
- Poster session Monday
- Poster session Tuesday
- Poster session Wednesday

## PL6

# Triterpenic and steroid derivatives as antimalarial compounds

Joelle Quetin-Leclercq

*LDRI-GNOS- université catholique de Louvain*

With several hundred millions of people sick each year and between one and two million deaths per year according to estimations, malaria remains the most important parasitic disease worldwide**.** Two billion people are exposed and around 500 million clinical cases occur each year. Despite efforts to develop vaccines, the antigenic variability of these parasites allows only a protection of 36%, in the best cases, and only in children and infants [1]. The treatment of malaria, especially resistant strains, remains a major problem of public health, given the development of resistance to the current best molecule in the market: artemisinin [2]. Our laboratory worked on different plants used to treat malaria symptoms in traditional medicine [3] and identified several triterpenic acids, but also esters which showed *in vitro* antiplasmodial activity in the micromolar range on chloroquine-sensitive and –resistant strains, and a selectivity index > 50 compared to mammalian cells [4]. These molecules were also analysed for their *in vivo* activity and acute toxicity on mice as well as their heme-binding potential by LC-MS. The activity of semi-synthetic derivatives or natural analogues was also determined. Collaboration with medicinal chemists from Buenos Aires (Prof. J. Palermo), allowed us to obtain hybrids from steroids (bile acids) and Cinchona alkaloids. Some of these compounds possessed increased *in vitro* antimalarial activities compared to their parent alkaloids with $IC_{50}$ in the same range or even lower than artemisinin ($IC_{50}$ = 36 nM). Some structure-activity relationships will be discussed [5]. The increased antiparasitic activity may be explained by an improvement in bioavailability, since the more lipophilic derivatives showed the lowest $IC_{50}$s. Their interaction with heme (LC-MS) compared to the parent alkaloids was also analysed (unpublished results).

**References**

[1] http://www.who.int/malaria/areas/drug_resistance/overview/en/.
[2] *RTS,S Clinical Trials Partnership*. Efficacy and safety of RTS,S/AS01 malaria vaccine with or without a booster dose in infants and children in Africa: final results of a phase 3, individually randomised, controlled trial. Lancet 2015; 386: 31-45.
[3] *Bero J, Ganfon H, Jonville MC, Frédérich M, Gbaguidi F, DeMol P, Moudachirou M, Quetin-Leclercq J*. In vitro antiplasmodial activity of plants used in benin in traditional medicine to treat malaria J Ethnopharmacol 2009; 122: 439-444.
[4] *Bero J, Hérent MF, Schmeda-Hirschmann G, Frédérich M, Quetin-Leclercq J.* In vivo antimalarial activity of Keetia leucantha twigs extracts and in vitro antiplasmodial effect of their constituents J Ethnopharmacol 2013; 149: 176-183.
[5] *Leverrier A, Bero J, Cabrera J, Frédéric M, Quetin-Leclercq, Palermo JA*. Structure-activity relationship of hybrids of Cinchona alkaloids and bile acids with in vitro antiplasmodial and antitrypanosomal activities. Eur J Med Chem 2015;100: 10-17.