**Methods & Materials**: LC-ESI-MS/MS methods were validated for simultaneous bioanalysis of lumefantrine and 99-411 and of piperaquine and 99-411 combinations. The interaction studies were performed in rats using these validated methods.

**Results**: The total systemic exposure of 99-411 increased when administered with either lumefantrine or piperaquine. However, co-administration of 99-411 significantly decreased the systemic exposure of piperaquine by half-fold while it had no effect on the kinetics of lumefantrine. 99-411, thus, seemed to be a good alternative to artemisinin derivatives for combination treatment with lumefantrine. To explore the reason for increased plasma levels of 99-411, an *in situ* permeability study was performed by co-perfusing lumefantrine and 99-411. In presence of lumefantrine, the absorption of 99-411 was significantly increased by 1.37 times than when given alone.

**Conclusion**: Short-acting CDRI candidate antimalarial trioxane derivative, 99-411, was found to be pharmacokinetically compatible with long-acting prescription antimalarials, lumefantrine.

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## Designing new antimalarial hits from African medicinal plants at the University of Buea (Cameroon); Part I: Isolation, in vitro activity, in silico "drug-likeness" and Pharmacokinetic profiles

D. Zofou

*University of Buea, Buea, Cameroon*

**Background**: Drug resistance has drastically exacerbated the burden of malaria in Africa. It is therefore an urgent need to design novel therapies both efficacious, safe and affordable especially to poor people of endemic remote areas. The Malaria Drug discovery programme of the University of Buea (Cameroon) aims to identify the compounds responsible for the anti-malarial activity of medicinal plants commonly used in handling malaria symptoms by traditional healers of Cameroon. The present paper report on the potential of selected compounds idenfied from *Dacryoedes edulis* (Burseraceae), *Kigelia africana* (Bignoniaceae) and *Hypericum lanceolatum* (Hypericaceae), and their suitability as leads for the treatment of drug resistant malaria.

**Methods & Materials**: 17 compounds were isolated from the various extracts of the three plants and tested against both chloroquine-susceptible (3D&, and D6) and multidrug-resistant Dd2, W2, K1 and W2mef) strains of *Plasmodium falciparum*, using the parasite lactate dehydrogenase method. Cytotoxicity studies were carried out on LLC-MK2 monkey kidney epithelial cell-line. *In silico* analysis was conducted by calculating molecular descriptors using the MOE software running on a Linux workstation. The "drug-likeness" of the isolated compounds was assessed using Lipinski criteria, from computed molecular properties of the geometry optimized structures. Computed descriptors often used to predict absorption, distribution, metabolism, elimination and toxicity

**Results**: Antiplasmodial activity was demonstrated for the first time in 7 major natural products previously identified in *D. edulis*, *H. lanceolatum* and *Kigelia africana*, but not tested against malaria parasites. The most active compound identified was termed DES4 from D. edulis. with $IC_{50}$ of 0.37 and 0.55 μg/mL, against 3D7 and Dd2 respectively. In addition, this compound was shown to act in synergy with quinine, satisfied all criteria of "Drug-likeness" and showed considerable probability of providing an antimalarial lead. The remaining four compounds also showed antiplasmodial activity, but were less effective than DES4. None of the tested compounds was cytotoxicity against LLC-MK2 cells, suggesting their selective activities on malaria parasites.

**Conclusion**: Based on the high *in vitro* activity, low toxicity and predicted "Drug-likeness" DES4 merits further investigation as a possible drug lead for the treatment of malaria.

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## Distribution of emm types of beta hemolytic streptococci associated with necrotizing fascitis: Clinical profile and outcome

T. Abraham*, S. Sistla, S. Chandra Sistla

*JIPMER, Pondicherry, India*

**Background**: Necrotizing fasciitis (NF) is a rapidly progressive, potentially life threatening infection with a median mortality rate of 32% which may reach 100% without prompt treatment. Based on etiology necrotizing fascitis is classified into, type I (polymicrobial infections), type II (monomicrobial infections, classically caused by *Streptococcus pyogenes*), and type III (Clostridial infections). The present study was undertaken to find the prevalence and emm types of beta hemolytic streptococci (BHS) causing necrotizing fascitis and to investigate the clinical characteristics and outcomes associated with it.

**Methods & Materials**: All BHS isolated from necrotizing fascitis cases over a period of two years (1st October 2013 to 30th September 2015) in the Department of Microbiology, JIPMER were included in the study. These isolates were further characterized by bacitracin sensitivity, PYR test, Lancefield antigen detection and spy1258 PCR. PCR amplification and sequencing of emm genes and assignment of emm types was performed as described by the Center for Disease Control and Prevention, Atlanta.

**Results**: Out of a total of 651 cases of NF, 23(3.5%) were associated with BHS. Eight (34.7%) were monomicrobial, and 15(65.2%) were polymicrobial. In monomicrobial NF, the major pathogen was GAS. Among BHS isolates 19 were group A streptococci (GAS), 2 each belonged to group F and group C and 1 was group G. All the 19 M typed isolates (GAS-17, GCS-2, GGS-1) belonged to different emm types (*emm*44 (n=3), *emm*222.2, *emm*4.5, *emm*8, *emm*193, *emm*63, *emm*86.2, *emm* 80, *emm*74, *emm*15.2, *emm*82.1, *emm*113, *emm*110, *emm*209, StC28k, StC1741, StG11).