Conference abstract PO-24

Large-Scale Synthesis of Dihydroartemisinin and Artesunate

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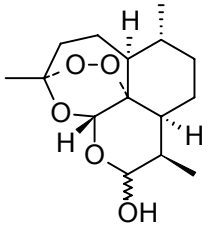
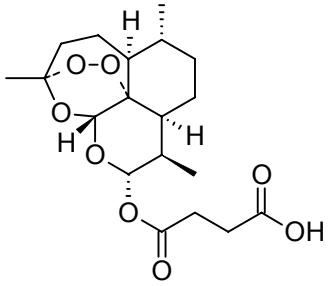
Sci Pharm. 2009; 77: 223 doi:10.3797/scipharm.oephg.21.PO-24

In many malaria stricken areas affordable medicines, such as chloroquine or mefloquine, which have been used for many years, are no longer effective, because the parasites have become resistant [1].
Since 2001, WHO has therefore recommended the switch to artemisinin-based combination therapies (ACTs), which provide a rapid and reliable cure with very few side effects [2].
Because of its poor oral availability artemisinin is less used directly anymore. In contrast, its partialsynthetically generated derivatives like dihydroartemisinin (**1**) or artesunate (**2**) are widely employed in combination therapies [3, 4].



1



2

We report here an efficient large-scale procedure for the chemical modification of artemisinin to the key-compound **1** by reduction with sodium borohydride in methanolic suspension. The hemisuccinate **2** was achieved by esterification of **1** with succinic anhydride under basic conditions.
The accomplished reactions were monitored by TLC and HPLC, the obtained derivatives **1** and **2** were completely characterized by NMR.

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[2] Antimalarial drug combination therapy. WHO 2001; WHO/CDS/RBM/2001.35.
[3] Li Q, Weina PJ, Milhous WK. Pharmacokinetic and pharmacodynamic profiles of rapid-acting Artemisinins in the antimalarial therapy. Curr Drug Ther 2007; 2: 210–223. doi:10.2174/157488507781695649
[4] Warsame M, Atta H, Klena JD, Waqar BA, Elmi HH, Jibril AM, Hassan HM, Hassan AM. Efficacy of monotherapies and artesunate-based combination therapies in children with uncomplicated malaria in Somalia. Acta Trop. 2009; 109: 146–151. doi:10.1016/j.actatropica.2008.10.009