

New Chemical Entities (NCE) for treatment of malaria and CNS disorders

EXECUTIVE SUMMARY

New Chemical Entities (NCE) that may be employed as potential leads to prepare antimalarial drugs or treatment of Central Nervous System (CNS) disorders.

BACKGROUND

Plasmodium falciparum strains are growing increasingly resistant to current line of drugs owing to their highly adaptive nature. Alternative drugs with novel structures and varying mechanisms of action are constantly needed to treat the disease. Alkaloid compounds are an important class of drugs with proven anti-malarial activity. Novel alkaloid based substituted molecules are being explored as potential anti-malarial drugs. Some of these compounds have also shown effective inhibition of a known target for CNS disorders.

TECHNOLOGY DESCRIPTION

NCL scientists have discovered NCEs (substituted pyridine based alkaloids) and an efficient, fully synthetic route for their synthesis. The NCEs have antimalarial activity and some analogues could be used to treat CNS disorders. The process has an overall yield of >65%. The reaction temperature is mild (~50 °C).

MARKET POTENTIAL

- In 2008, there were 247 million cases of malaria and nearly one million deaths*
- Over \$1.8 billion was spent in 2010 to control malaria**
- The CNS drugs market is set to face an increase from \$78 billion in 2010 to nearly \$81.8 billion by 2015#

* <http://www.who.int/mediacentre/factsheets/fs094/en/>, ** World Malaria Report, 2010, World Health Organization, #<http://www.bccresearch.com/market-research/pharmaceuticals/drugs-central-nervous-system-disorders-phm068a.html>

VALUE/ADVANTAGES

- Potential drug candidates (with high anti-malarial activity) for the treatment of *plasmodium* and potentially, CNS disorders
- Efficient synthetic approach, with milder reaction conditions
- Higher yields in the order of >65% for all the compounds

APPLICATIONS

- Treatment of malaria
- Potential treatment of various CNS disorders

TECHNOLOGY STATUS/LINKS

- Demonstrated at the lab scale
- On the lookout for potential partners for licensing
- Patent application filed: IN# 0356/DEL/2012; [WO2013117986 A1](#)
- Lead molecules NCLite-M1 and its analogues; CAS# 1404195-28-3
- IUPAC Name: 4(3H)-Quinazolinone, 3-(3H-pyrrolo[2,3-c]quinolin-4-ylmethyl)
- Mhaske, S.B. et al. (2012) Pd-catalysed Imine Cyclization: Synthesis of Antimalarial Natural Products Aplidiopsamine A, Marinoquinoline A, and their potential hybrid NCLite-M1, Organic Letters, 14 (22) 5804-5807.
- Panarese, J. D. and Lindsley, C. W. (2012) Biomimetic Synthesis and Biological Evaluation of Aplidiopsamine A, Organic Letters, 14 (22), 5808-5810.