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Supramolecular derivatization of an anti-malarial imidazopyridazine drug lead

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Pharmacologically active drug leads are often preemptively rejected at an early stage of development if they display undesirable physicochemical properties. The aim of synthesizing new solid-state forms of drugs through supramolecular derivatization is to alter their properties while maintaining their pharmacological activity. This is achieved by the formation of non-covalent bonds with biocompatible partner molecules (in co-crystals, salts, inclusion complexes, solvates or hydrates) or by altering the way in which these molecules are arranged and interact within their various polymorphic crystals. These new forms can have significantly different values for their dissolution rates, processability or physical and/or chemical stability, which can translate into positive effects such as reduced doses, required for the same effect, longer shelf-life and reduced side-effects, among many others. An anti-malarial drug lead which displayed good in vitro potency (IC50: K1=6.3 nM, NF54=7.3 nM) against multidrug resistant (K1) and sensitive (NF54) plasmodial strains and exhibited 98% activity in the in vivo Plasmodium berghei mouse model in a 4-day test at 4×50 mg/ kg po, showed poor aqueous solubility (<5 μM at pH 6.5). New crystal forms of the drug lead were created in an attempt to overcome this inadequacy. We report novel co-crystals, polymorphic forms and a hydrated form of this new drug candidate. Their characterization was performed using X-ray diffraction, hot stage microscopy and differential scanning calorimetry. Future work is aimed at assessing these forms in terms of solubility, dissolution rate and bioavailability through studies in animal models.

Biography

Terence James Noonan has completed his BPharm degree at the North-West University's Potchefstroom campus in 2010 and MSc in Pharmaceutics in 2012. He is currently enrolled as a PhD candidate at the University of Cape Town, South Africa.

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