Predicting Polymorphism in Chloroquine and Hydroxychloroquine crystal structures: A CSD-Materials Study

Samuel Tetteh1

1Department of Chemistry, School of Physical Sciences, College of Agriculture and Natural Sciences, University of Cape Coast, Ghana

*Corresponding author e-mail address: samuel.tetteh@ucc.edu.gh*

In crystallography, polymorphism can be defined as the existence of two or more crystal packings of the same chemical compound including solvates and hydrates. This arises as a result of free rotation around single bonds or the existence of functional groups which can be involved in various intermolecular interactions. Polymorphs have been found to have different physical properties and this of great concern in the pharmaceutical industry where the efficacy of the same chemical species could vary as a result of polymorphism

The polymorph assessment functionality in the Cambridge Structural Database (CSD) Materials package of the Mercury software is a reliable tool for predicting polymorphism in crystal structures [[1](#_ENREF_1)]. The algorithm is based on the hydrogen bond propensity and the hydrogen bond coordination score of characteristic functional groups in a molecule as determined by data mining of the >1 million entries in the database. it assigns a propensity index to each donor and acceptor pair in the molecule. The higher the index, the greater the propensity. Compounds with fewer donor-acceptor pairs of high propensity indices are ranked low and those with more donor-acceptor pairs of high propensity have high risks of polymorphism [[2](#_ENREF_2)].

This presentation investigates the risk of polymorphism in chloroquine and hydroxychloroquine. These 4-aminoquinolines have been successfully employed as antimalarial drugs and have also proven effective against SARS-CoV-2, the virus that causes covid-19. Data retrieved from the CSD version 5.42 (November 2020 +3 updates) show that hydroxyquinoline sulfate (refcode: QOBHUL01) crystalizes in a monoclinic crystalsystem with space group P21/c and unit cell dimensions: a = 10.497(1) Å, b = 8.806 Å, c = 21.860(3) Å, β = 101.074(1)o. chloroquine (refcode: CDMQUI) on the other hand crystalizes in an orthorhombic crystal system in a Pbcn space group of unit cell dimensions: a = 22.502(9) Å, b = 12.689(5) Å, c = 12.952(5) Å. These compounds have characteristic donor acceptor pairs which are involved in hydrogen bonding. A survey of the database reveal the presence of polymorphs of hydroxychloroqiune with only one crystal form for chloroquine. The polymorphism assessment functionality in the CSD will be employed to rationalize the propensity for polymorphism in these pharmaceutically important compounds.

**References**

[1] E. Nauha, J. Bernstein. (2014). *Cryst. Growth Des*. **14** (2014) 4364

[2] N. Feeder, E. Pidcock, A. M. Reilly, G. Sadiq, C. L. Doherty,K. R. Back, P. Meenan, R. Docherty. *J. Pharm. Pharmaco*. **67** (2015):857-868