CRYSTALLOGRAPHIC, SPECTROSCOPIC AND ANTIMALARIAL ACTIVITY OF 4-AMINOQUINOLINE DERIVATIVES

ABSTRACT
Submitted to the University of Delhi
for the Degree of
DOCTOR OF PHILOSOPHY

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JANUARY, 2013
Abstract

Quinoline derivatives represent the major class of heterocycles and a number of preparations have been known since the late 1800s. The quinoline ring system occurs in various natural products, especially in alkaloids. Quinoline skeleton is often used for the design of many synthetic compounds with diverse pharmacological properties like antibacterial, antifungal, antimalarial, anticancer etc. Keeping different aspects of quinoline ring system we have synthesized various analogs and screened for antimalarial activity. In chapter-1 we have synthesized four different types of small library of quinoline derivatives keeping changes mainly around amino group to overlook structure-activity relationship of quinoline derivatives. These compounds are characterised by $^1$H-NMR, $^{13}$C-NMR, FT-IR, Mass and crystallographic analysis. Further, these compounds were screened for antimalarial activity. These synthetic compounds exhibited very promising in vitro antimalarial activity. In vivo activity of the compounds is under progress.

In chapter-2 we have discussed 10 crystals of 4-aminoquinoline described in chapter-1. This chapter can be divided into two sections. In section-2a there is a complete description about the hydrogen bonding pattern in a series of quinoline analogs. The synthesis and characterization of compounds are discussed in chapter-1 in detail. In all these crystal structures, we observed the formation of N-H···Cl/N hydrogen bonds giving rise to different structural motifs, namely dimers, chains and ribbon, along with the presence of weak C-H···O, C-H···Cl and π-π van der Waals interactions which contribute towards the over-all crystal packing and stabilize the space between sheets or ribbons. Section-b describes the halogen···halogen interaction in fluoro derivative of 4-aminoquinoline scaffold. So far, the specific mode of interaction of such type of 4-aminoquinoline derivatives with albumin proteins has seldom been studied at the molecular level. In chapter-3, first we characterized the compound (7-chloroquinolin-4-yl)-(2,5-dimethoxyphenyl)-amine hydrochloride dihydrate (CQDPA) in solid state.
After that, we have studied the interaction of CQDPA with bovine and human serum albumin in detail using steady state fluorescence at three different temperatures. Thermodynamic parameters were calculated which suggested the mode of interaction between albumin proteins and small molecule. In chapter-4, we have discussed the mode of binding of quinoline derivatives to DNA. This study would be very useful to predict the interaction of small molecule to DNA in general. We have selected three compounds viz., ligand-1, 2 & 3 from three different series of synthesised derivatives of 4-aminoquinoline scaffolds. We carried out a series of spectroscopic studies including UV-visible, Tm and CD spectra. These studies are vital for the elucidation of the mechanisms of drug action and designing of more efficient and specifically targeted drugs with lesser side effects.