

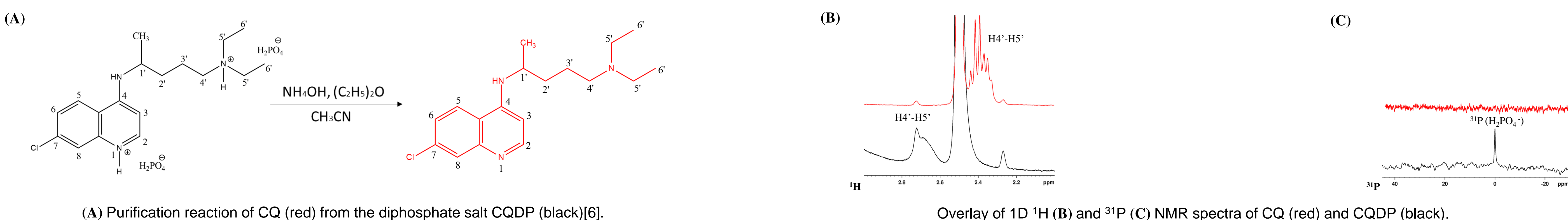
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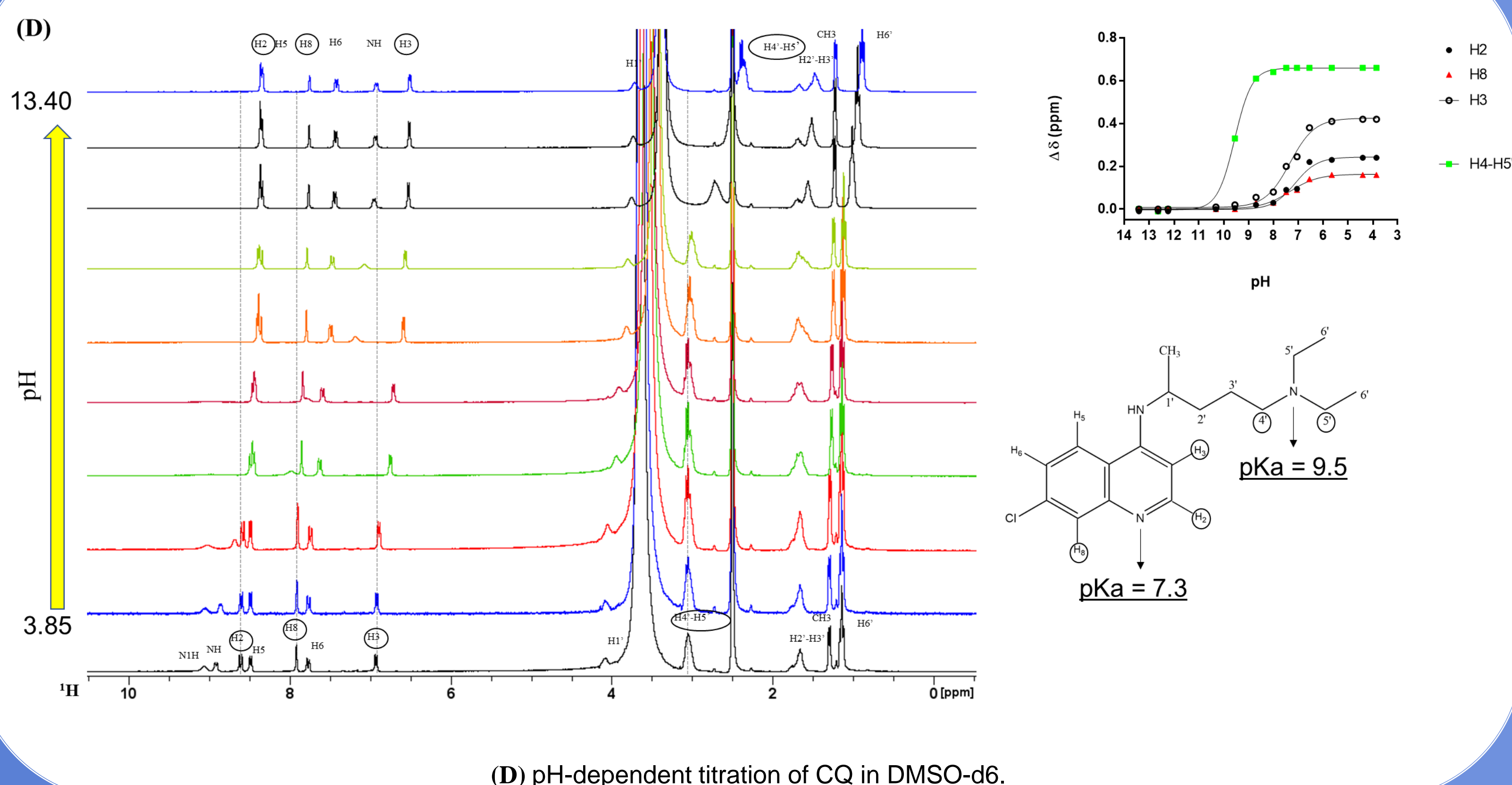
## Introduction

Chloroquine is a 4-amino-quinoline and a first-choice drug for the treatment of malaria and autoimmune diseases with an important lysosomotropic character [1]. Endosome alkalization is believed to be an antiviral mechanism [2]. Chloroquine is also considered a ionophore of zinc [3], able to inhibit the RNA-polymerase enzyme in vitro [4]. Based on the literature data [5], we decided to investigate the coordination chemistry of chloroquine mainly through Nuclear Magnetic Resonance (NMR) with the aim of inferring its mechanism of action in cell.

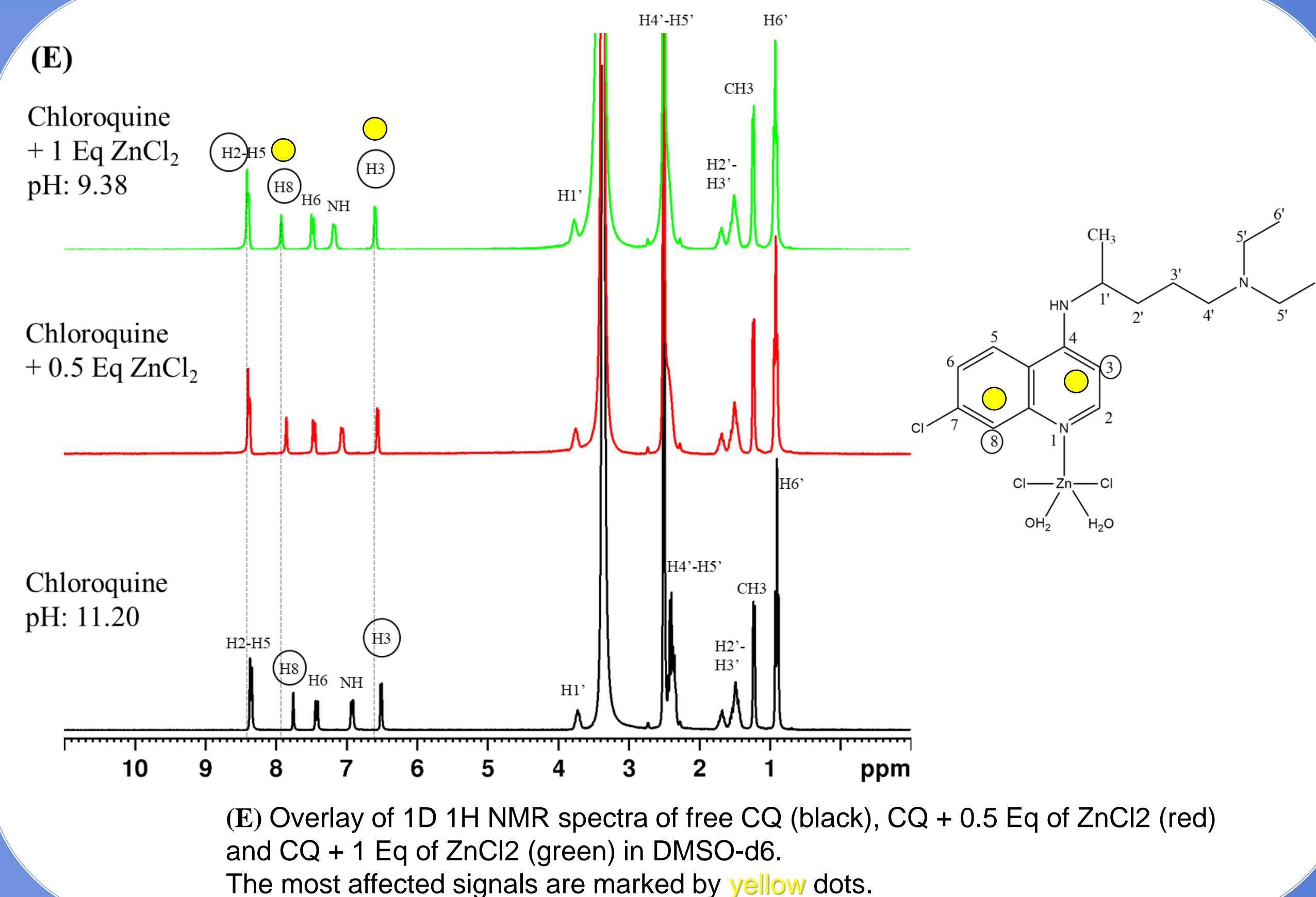
## Purification of chloroquine from diphosphate salt confirmed by Nuclear Magnetic Resonance



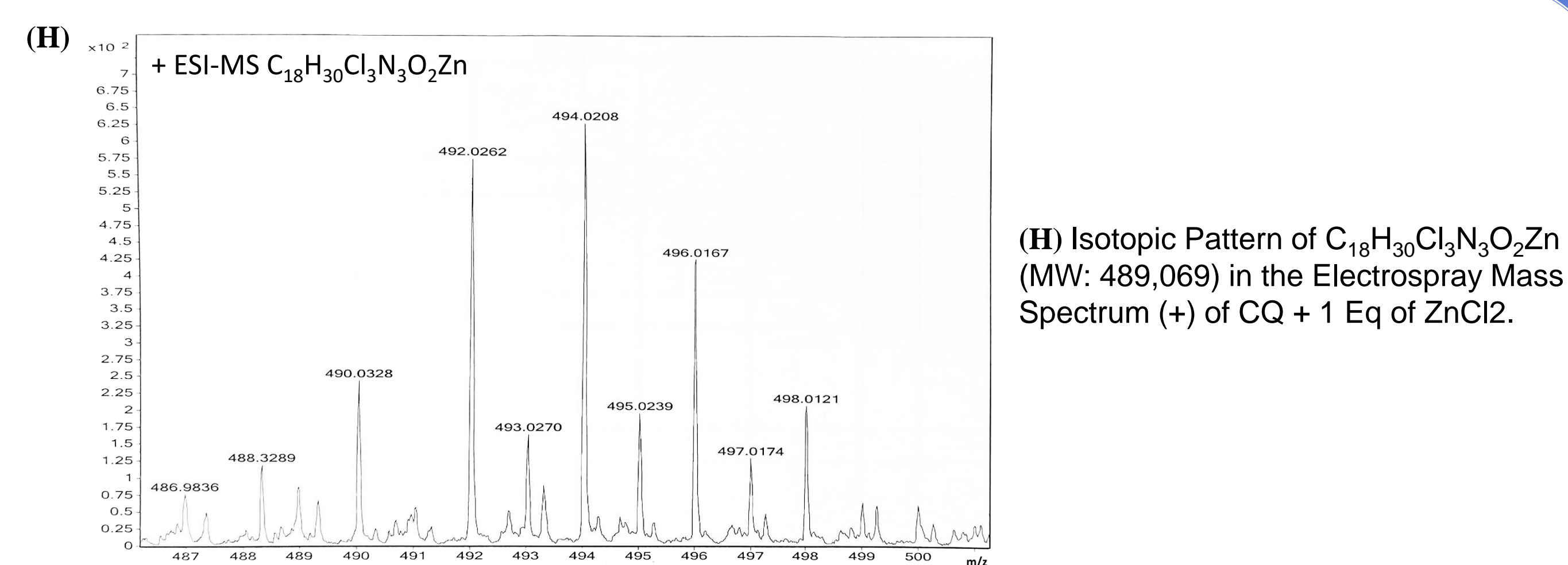
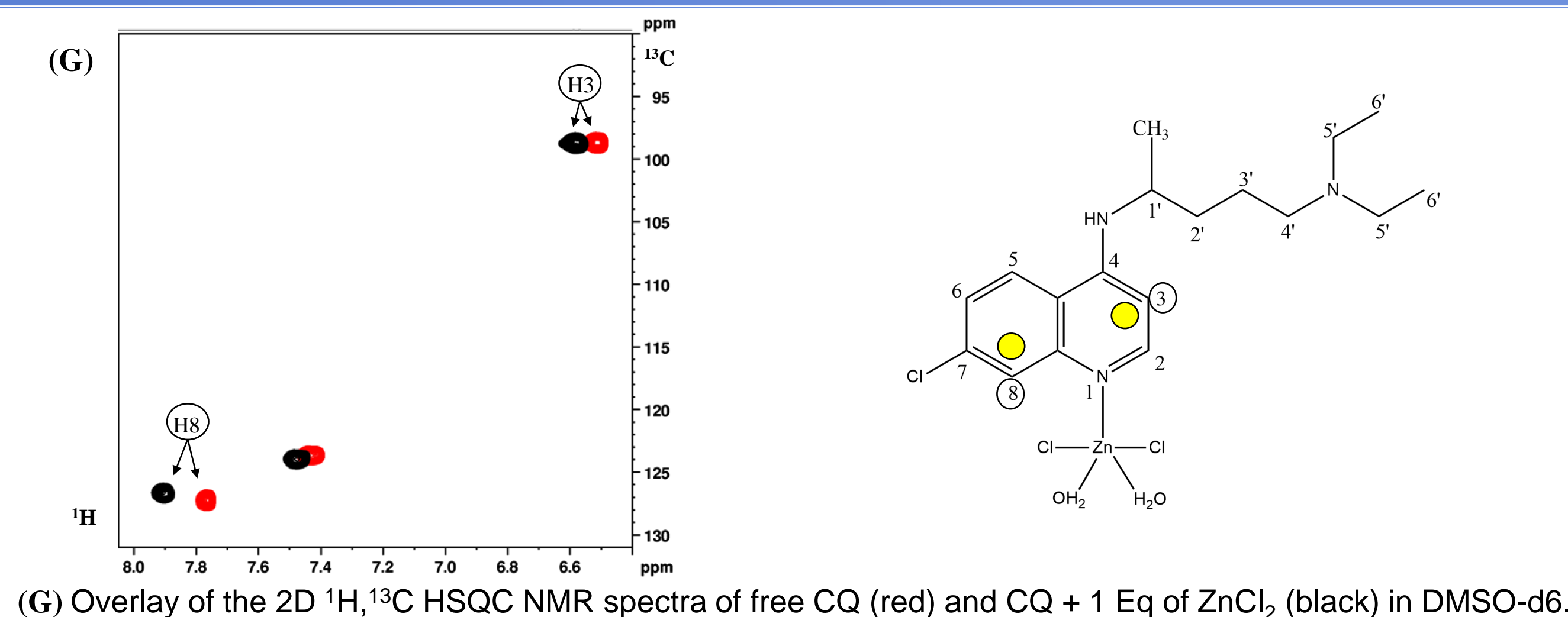
## pKa determination of purified chloroquine



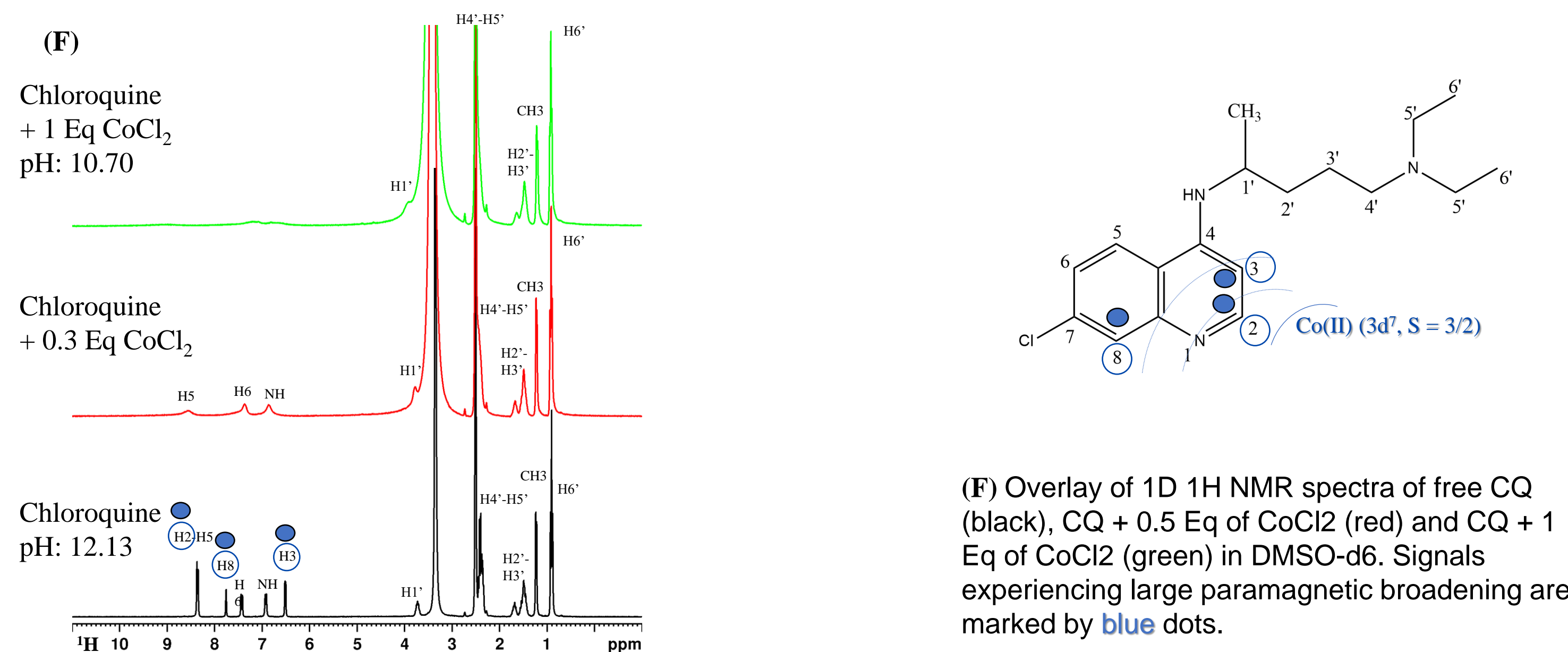
## NMR titration of Chloroquine with Zinc(II) Chloride



## Characterization of Zinc-Chloroquine complex: 2D HSQC NMR and ESI-MS spectra



## NMR titration of Chloroquine with Cobalt(II) Chloride



## Conclusions

The stoichiometry of the pentacoordinate complex [Zn(CQ)(Cl)<sub>2</sub>(OH)<sub>2</sub>] was obtained by ESI-MS. Heteronuclear NMR experiments were used to identify quinoline nitrogen as the coordination site of the Zn(II) ion and the paramagnetic Co(II) ion. Future studies will address the coordination of Zn(II) to CQ in lysosomes and the effect of pH modulation.

### References

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- [2] Mercer J et al., Annu. Rev. Biochem. (2010), doi: 10.1146/annurev-biochem-060208-104626
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- [5] Navarro M. et al., J Inorg Biochem. (2005), doi: 10.1016/j.jinorgbio.2005.05.002
- [6] Sánchez-Delgado R. A. et al., J. Med. Chem. (1996), doi: 10.1021/jm950729w