Chiral HPLC of Antimalarial Drugs

Utility of Chirex™ Chiral Stationary Phases

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Introduction

Malaria is probably the most important parasitic disease affecting humans today. Unfortunately, due directly to increasing antimalarial drug resistance, suffering and death in tropical latitudes continues to grow significantly. In fact, many antimalarial drugs are becoming useless.

For many years chloroquine was the safe and inexpensive drug of choice. In fact, two chiral drugs, chloroquine and pyrimethamine were used so widely (even as a regular additive to table salt), that many people had the drugs in their blood all the time. Unfortunately, resistance to these two compounds is now widespread throughout the tropics.

Similar drug resistance has rapidly developed to other, more potent, and sometimes more toxic, drugs such as primaquine and quinacrine, Amodiaquine, Mefloquine, and Halofantrine. Recently, new and important contributions to treating malaria have come from China, with the development of qinghaosu or artemisinin. Other synthetics, such as piperaquine, lumefantrine, and pyronaridine are also providing clinicians with a new generation of effective, and in some cases, affordable antimalarial drugs.

An active area of investigation involves possible combination therapies, where two or more of these drugs are administered in tandem. Since many of these old and new compounds are chiral, there is growing interest in determining the therapeutic efficacy of individual enantiomers and the potential development of drugs in optically pure form.

Chirex HPLC columns offer superior tools to analyze and purify these new medicines for use in the war against malaria. In this Technical Note, simple and direct chiral HPLC methods for the resolution of racemic antimalarial drugs are described.

Instrumentation & Equipment

Analyses were performed using an HP 1100 LC system (Agilent Technologies, Palo Alto, CA, USA) equipped with a quaternary pump, in-line degasser, multi-wavelength detector, and autosampler. HP Chemstation software was used for the data analysis. The HPLC columns used for the analysis are Chirex™ brand (Phenomenex, Torrance, CA, USA, see Ordering Information). Standards were purchased from Sigma (St. Louis, MO), Aldrich (Milwaukee, WI), or Fluka (Ronkonkoma, NY), depending on availability.

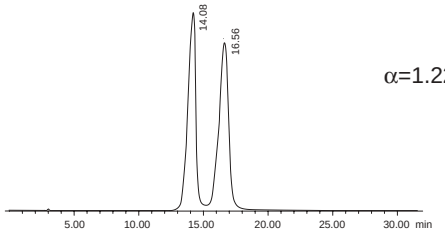
Results & Discussion

Various Chirex™ chiral stationary phases (CSPs) were evaluated for their utility to directly resolve (without derivatization) enantiomers of some important antimalarial compounds.

App ID 13603

Chloroquine

Column:	Chirex 3014
Dimensions:	250 x 4.6mm
Order No.:	00G-3014-E0-TN
Mobile Phase:	Hexane/Dichloroethane/Ethanol-TFA (50:35:15), with ethanol-TFA (20:1)
Flow Rate:	1.0mL/min
Detector:	UV @ 346nm

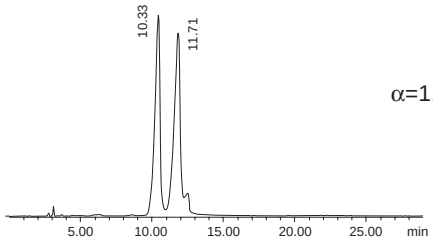


α=1.22

App ID 13682

Primaquine

Column:	Chirex 3014
Dimensions:	250 x 4.6mm
Order No.:	00G-3014-E0-TN
Mobile Phase:	Hexane/Dichloroethane/Ethanol-TFA (50:35:10), with ethanol-TFA (20:1)
Flow Rate:	1.0mL/min
Detector:	UV @ 268nm

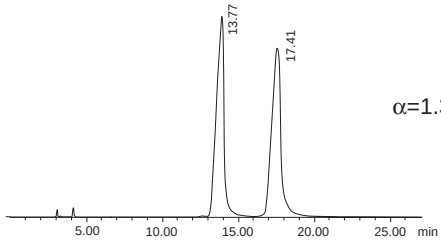


α=1.18

App ID 13695

Quinacrine

Column:	Chirex 3022
Dimensions:	250 x 4.6mm
Order No.:	00G-3022-E0-TN
Mobile Phase:	Hexane/Dichloroethane/Ethanol-TFA (40:35:25), with ethanol-TFA (20:1)
Flow Rate:	1.0mL/min
Detector:	UV @ 282nm



α=1.33

Table 1. Enantioresolution of three antimalarial drugs using Chirex CSPs

Antimalarial	Chirex CSP	Resolution (Rs)	Separation Factor (alpha)	Retention Time Second peak (min)	App ID
Chloroquine	3020	3.78	1.21	14.32	13604
	3014	3.41	1.22	16.56	13603
	3022	2.86	1.13	16.51	13605
	3018	4.49	1.20	25.94	13606
Primaquine	3014	3.54	1.18	11.71	5248
	3020	3.27	1.16	18.07	13683
Quinacrine	3022	6.12	1.33	17.41	13695
	3017	2.71	1.38	8.21	13694
	3020	2.10	1.10	26.99	13696

References

1. Cleveland, T., J. Liq. Chromatogr. 18(4): 649-671, **1995**.

If you would like more information on these columns or any specific application listed, please contact Phenomenex. Also, if you are new to chiral HPLC or are doing method development work call us today to reserve your ***FREE*** copy of our 70-page ***Guidebook to Chiral HPLC Method Development***.

Ordering Information:
Chirex is available in a wide range of phases and column sizes, from analytical to preparative. All phases are also available in bulk (15 and 30µ particle size).

The columns discussed in this Note are listed below.

5µ Analytical Columns (mm)

Chirex Phase and Bond Linkage, 250 x 4.6mm ID

Phase	Description	Order No.
3001	(R)-PGLY and DNB Covalent Amide	00G-3001-E0-TN
3014	(S)-VAL and (R) NEA Covalent Urea	00G-3014-E0-TN
3017	(S)-PRO and (S) NEA Covalent Urea	00G-3017-E0-TN
3018	(S)-PRO and (R) NEA Covalent Urea	00G-3018-E0-TN
3019	(S)-LEU and (S) NEA Covalent Urea	00G-3019-E0-TN
3020	(S)-LEU and (R) NEA Covalent Urea	00G-3020-E0-TN
3022	(S)-ICA and (R) NEA Covalent Urea	00G-3022-E0-TN

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