

Chiral Adrenergic Drug Separations by HPLC

Utility of Chirex™ Chiral Stationary Phases

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Introduction

The sympathetic nervous system is responsible for the physiological responses that allow the body to interact with the environment and respond to stimuli. This is mediated by two hormones: epinephrine (Adrenaline) and norepinephrine (noradrenaline). Drugs that act to increase sympathetic activity by directly or indirectly (via epinephrine or norepinephrine) exciting Adrenergic receptors are called Adrenergic agonists. Those drugs that decrease sympathetic activity are referred to as Adrenergic antagonists (or adrenoceptor blockers).

Therapeutically, Adrenergic drugs can be divided into several types: vasoconstrictors, vasodilators (bronchodilators), cardiac β-blockers, antiglaucoma agents and mydriatics. Most contain an asymmetric carbon in their structures and exist as a pair of enantiomers. Usually only one enantiomer in the pair produces the desired therapeutic effect, whereas the other enantiomer is either less effective or more toxic.¹

Agonists	Therapeutic Use	Chirex CSP	Alpha Factor	App ID No.
Clenbuterol	Bronchodilator, Tocolytic	3022	1.27	13615
Epinephrine (Adrenaline)	Bronchodilator, Mydriatic, Antiglaucoma Agent	3022	1.10	13630
Etilefrine	Vasopressor (Antihypotensive)	3022	1.11	13867
Fenoterol	Bronchodilator, Tocolytic	3020	1.13	13847
Isoetharine	Bronchodilator	3020	1.21	13640
Isoproterenol (Isoprenalin)	Bronchodilator	3020	1.21	13644
Metanephrine	Vasopressor (Antihypotensive)	3022	1.12	13651
Metaproterenol	Bronchodilator	3020	1.24	5257
Methoxamine (Orciprenaline)	Vasopressor (Antihypotensive)	3022	1.16	13657
Methoxyphenamine	Bronchodilator	3017	1.10	13903
Midodrine	Vasopressor (Antihypotensive)	3020	1.10	13665
Norepinephrine (Noradrenaline)	Vasoconstrictor	3017	1.07	13868
Salbutamol (Albuterol)	Bronchodilator, Tocolytic	3022	1.33	5264
Synephrine (Oxydrine)	Vasopressor (Antihypotensive)	3022	1.12	13700
Terbutaline	Bronchodilator, Tocolytic	3020	1.28	13701

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 were 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 & Discussions

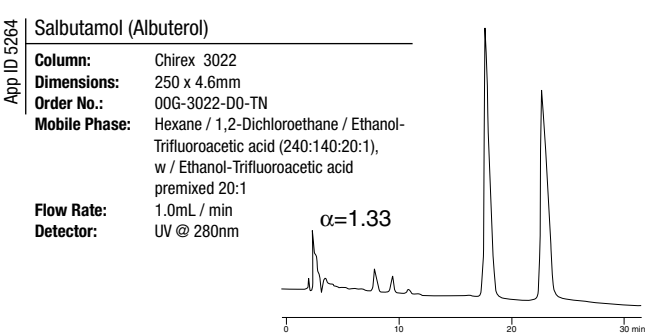
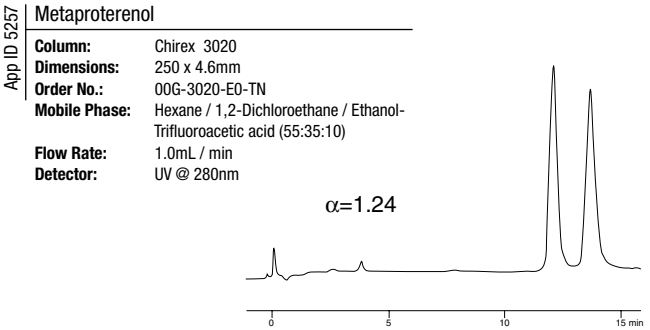
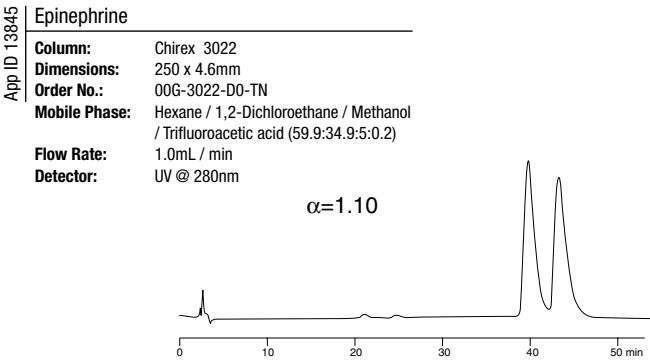
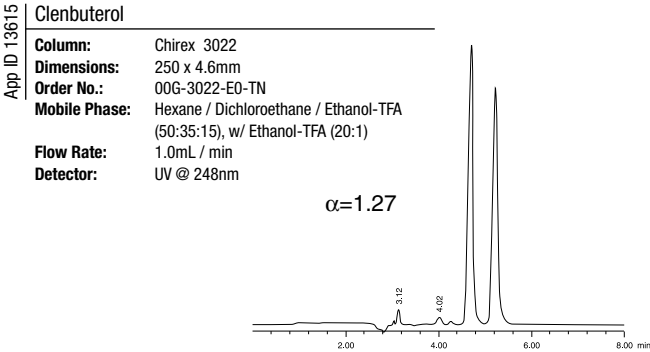
In the Tables below various Chirex™ chiral stationary phases (CSPs) were evaluated for their utility to directly resolve (without derivatization) enantiomers of some important adrenergic compounds.

Antagonists	Therapeutic Use	Chirex CSP	Alpha Factor	App ID No.
Acebuterol	Antihypertensive, Antianginal, Antiarrhythmic	3022	1.09	13584
Atenolol	Antihypertensive, Antianginal, Antiarrhythmic	3022	1.11	13824
Labetolol	Antihypertensive	3020	-	13649
Metoprolol	Antihypertensive, Antianginal	3022	1.08	13662
Nadolol	Antihypertensive, Antianginal	3022	-	13667
Oxprenolol	Antihypertensive, Antianginal, Antiarrhythmic	3020	1.06	13827
Pindolol	Antihypertensive, Antianginal, Antiarrhythmic	3022	1.12	13831
Propranolol	Antihypertensive, Antianginal, Antiarrhythmic	3020	1.10	13812

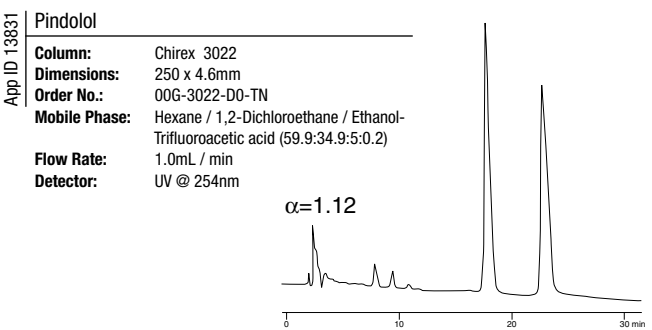
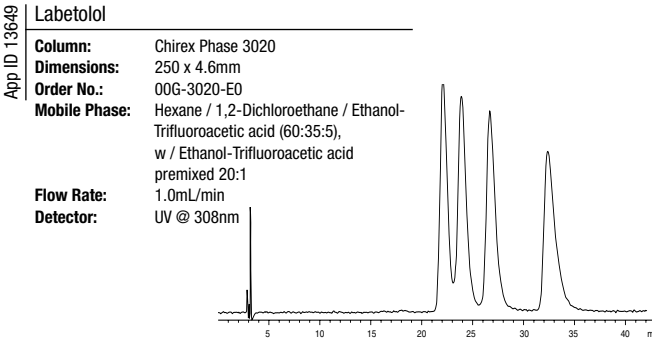
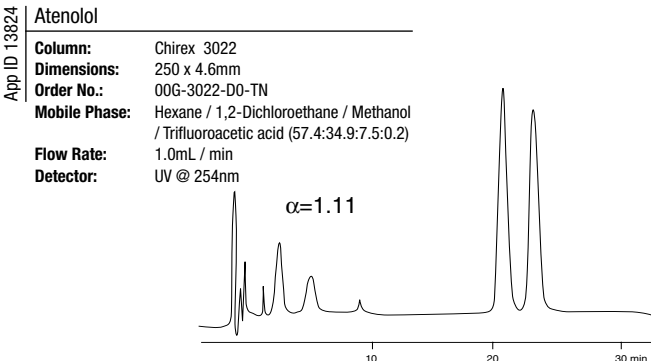
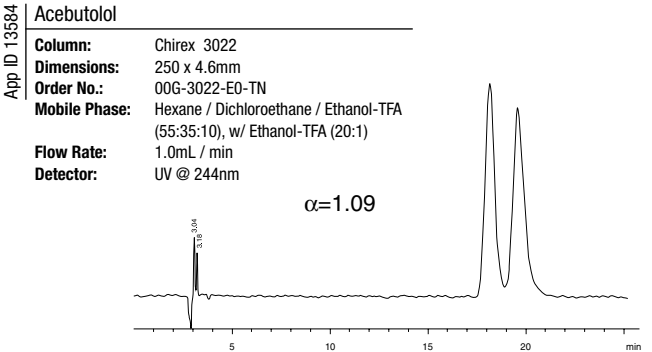
The capacity of these CSPs for separating an even wider variety of clinically important drug enantiomers has been previously demonstrated.² Compared with other, naturally-derived CSPs, these low-molecular weight phases demonstrate considerably higher efficiencies, are robust and long-lasting, and are often more suitable for quantitative work.³⁻⁴

2512_L

Agonists



Antagonists



Conclusions

Baseline separations for a number of racemic Adrenergic drugs are possible without the need for derivatization. Compounds in this class, such as salbutamol and atenolol, are directly separated with high efficiency and symmetrical peaks. The application of these phases to the areas of chiral drug synthesis, analysis in biological fluids and enantiomeric purity determinations make these CSPs an excellent choice for chiral separations and will aid in the development of superior therapeutics.

References

1. Mutschler, E., Derendorf, H., "Drugs Affecting the Sympathetic Nervous System" in Drug Actions Basic Principles and Therapeutic Aspects. Drugs Affecting the Sympathetic Nervous System, CRC Press, Boca Raton, Florida, 1995, pp. 217-240.
2. Cleveland, T., J. Liq. Chromatogr. 18(4): 649-671, 1995.
3. Allenmark, S.G., Chromatographic Enantioseparations: Methods and Applications. Wiley/Ellis Horwood, New York, 1988.
4. Krstulovic, A.M., ed., Chiral Separations by HPLC: Applications to Pharmaceutical Compounds. Wiley/Ellis Horwood, New York, 1989.

If you would like more information on these chiral columns or any of the applications 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		
Chirex Phases 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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