Application Note
Drugs & Pharmaceuticals

Olanzapine

The most reliable LC-EC applications for Drugs & Pharmaceuticals analysis

Antipsychotic drugs
Clozapine
Olanzapine
Risperidone

PET imaging tracer
Fluorodeoxyglucose (FDG)
FDG impurities

Pharmaceuticals, API
Acetaminophen
Artemether
Artemisinin, Dihydro-artemisinin
Betadex sulfobutyl ether sodium
Etoposide
Epinephrine
Heparin
mesna BNP7787
8-OH-DPAT
Vincristine
Sulfides
Glutathione
Aminothiols
Disulfides

Aminoglycoside drugs
Amikacin
Framycetin sulphate
Gentamicin sulphate
Kanamycin
Netilmycin
Neomycin sulfate
Spectinomycin
Lincomycin
Tobramycin

- **Electrochemical detection of antipsychotic drugs**
- **Wall-jet flow cell with HyREF™ (Pd/H_2) electrode**
- **Reproducible & sensitive**

Introduction

Olanzapine (trade name Zyprexa) belongs to the class of atypical antipsychotic drugs for the treatment of schizophrenia and bipolar disorder. Olanzapine is structurally similar to Clozapine, but is classified as a thieno-benzodiazepine. In 2011 the drug went generic.

To measure olanzapine levels in human plasma, different HPLC methods with electrochemical detection were developed [1-2]. Due to its reversible oxidation potential, olanzapine can be detected in oxred mode, requiring two serially placed electrochemical flow cells [1]. Olanzapine is also detectable in amperometric mode with a single flow cell [2]. Due to it being easily oxidizable, a low and selective working potential can be applied.

In this application note a proof of principle is presented for the analysis of Olanzapine standards using an ALEXYS LC-ECD system with a DECADE II detector and amperometric wall-jet flow cell.

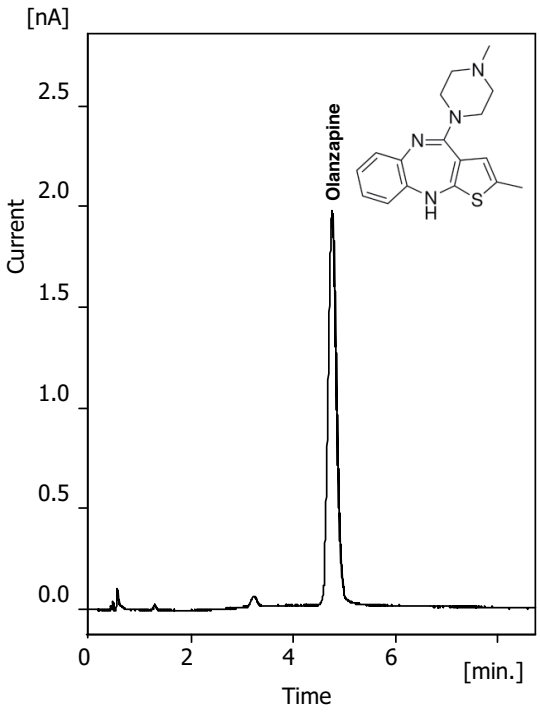


Figure 1: Analysis of 50 ng/mL olanzapine standard in mobile phase. Measurement conditions as given in Table 1.

Method

For the analysis of olanzapine a C18 column was used in combination with a mobile phase containing 50% organic modifier followed by electrochemical detection using an amperometric wall-jet flow cell. Olanzapine standards in the analytical relevant range of 0-100 ng/mL were prepared in mobile phase and used to determine the optimal working potential and assess linearity, repeatability and detection limit.

Conditions

In table 1 the conditions are listed that were used for the analysis of Olanzapine standards. For real sample it might be necessary to optimize the LC conditions for separation. The experiments in this application note were performed using a 1 mm ID C18 column, but the described method can be easily up scaled to standard bore LC (2 – 4.6 mm ID columns).

Table 1

Conditions	
Mobile phase	Phosphate buffer 50 mM set to pH 6.5, 25% methanol, 25% acetonitrile
Column	C18, 50 x 1 mm ID, 3 µm particle size
Flow rate	50 µL/min
Injection volume	1 µL
Needle wash	100% acetonitrile
Temperature	35 °C
Flow cell	SenCell 2 mm GC HyREF, spacing position 1
Detector	DECADE II
E-cell	300 mV vs. HyREF
Range	50 nA/V
I cell	about 0.25 nA
ADF	0.01 Hz
Pressure	about 65 bar

Results

Working potential

In figure 2 a hydrodynamic voltammogram for Olanzapine is shown. For Olanzapine under the specified conditions the optimal working potential was 0.3 V. The relatively low working potential can be beneficial with respect to detection selectivity. At higher working potentials more components will be detected, resulting in more complex chromatograms with possible interfering peaks.

Detection limit, repeatability and linearity

The detection limit (S/N=3) for Olanzapine was about 0.1 ng/mL using the settings listed in Table 1. The linearity of the method was determined in the concentration range of 20-100 ng/mL. The method showed a good linear detector response with correlation coefficient > 0.999. The repeatability in peak area was RSD<0.5%

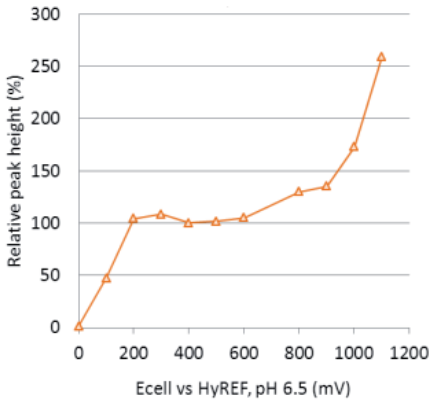
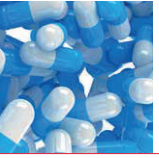


Figure 2: Hydrodynamic voltammogram of Olanzapine under the LC conditions specified in Table 1.

Conclusion

Measurement conditions are presented for the analysis of Olanzapine standards using an ALEXYS HPLC/ECD system. The method is reproducible and sensitive, and can be used for assay validation with real samples.



References

1. Raggi, M. A., Mandrioli, R., Sabbioni, C., Ghedini, N., Fanali, S., Volterra V., Determination of olanzapine and desmethylolanzapine in the plasma of schizophrenic patients by means of an improved HPLC method with amperometric detection, *Chromatographia*, 54 (2001) 203-207.
2. Sabbioni, C., Saracino, M. A., Mandrioli, R., Albers, L., Boncompagni, G., & Raggi, M. A., Rapid analysis of olanzapine and desmethylolanzapine in human plasma using high-performance liquid chromatography with coulometric detection, *Anal. Chim. acta*, 516 (2004) 111-117.

Recommendation

The advised configuration for this application is the ALEXYS Analyzer using an auto sampler with sample cooling option.

Ordering information

180.0035C	ALEXYS Analyzer – cooled
116.4320	SenCell 2 mm GC HyREF

For research purpose only. The information shown in this communication is solely to demonstrate the applicability of the ALEXYS system. The actual performance may be affected by factors beyond Antec's control. Specifications mentioned in this application note are subject to change without further notice.