

## HPLC Analysis of Tramadol Using SPP Column Technology

### Introduction

Opiates, originally derived from the opium poppy, have been used for thousands of years for both recreational and medicinal purposes. The most active substance in opium is morphine which was first extracted from opium in a pure form in the early nineteenth century. Due to the problem of addiction of opioid drugs synthetic targets were developed that maintained therapeutic benefits but lessened the dependence for the user.

Tramadol, sold under the brand name Ultram among others, is an opioid pain medication used to treat moderate to moderately severe pain.<sup>1,2</sup> It was patented in 1963 Tramadol and launched under the name "Tramal" in 1977 by the West German pharmaceutical company Grünenthal GmbH.<sup>3</sup>

The scientific literature documents several different column chemistries used for the analysis of tramadol; from cyano columns to C18 and C8 alkyl phases and also with the addition of ion pair reagents.<sup>4</sup> With the application of modern phase chemistries, it is possible to eliminate the use of ion pair reagents. This application brief will illustrate the application of a superficially porous particles (SPP) column, with a polar embedded amide functionality, for the analysis of tramadol, Figure 1.

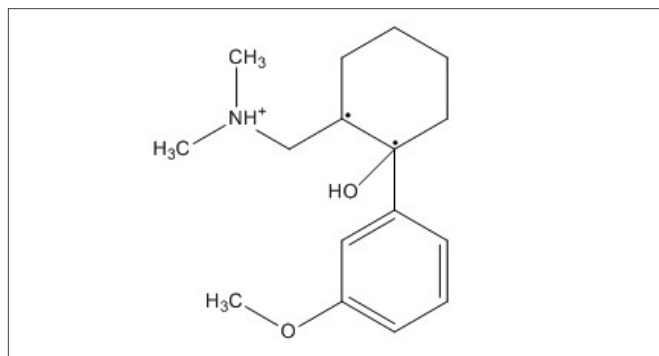


Figure 1. Chemical structure of Tramadol.

## Experimental Conditions

### Method Parameters

All HPLC method parameters are shown in Table 1.

Table 1. HPLC Method Parameters.

Quasar SPP RP Amide	150 mm	4.6 mm	2.6 $\mu\text{m}$	N9308946
Mobile Phase	A: 0.1% formic acid B: ACN 10-100% B in 10 minutes			
Flow Rate	1.0 mL/min			
Temp	25 °C			
Wavelength	270 nm			
Injection Volume	5 $\mu\text{l}$			
Analyte	Tramadol			

### Solvents and Samples

All solvents were HPLC grade and samples were filtered using a 0.45  $\mu\text{m}$  nylon filter, P/N 02542880.

## Results and Discussion

With the development and certification for medical use of tramadol being completed several decades ago, initial analytical methods used traditional porous silica C18 columns. And some methods also used the addition of ion pair reagents in the mobile phase to improve chromatography.

Superficially porous particles, SPP, (also called: shell, fused-core™, core-shell™, partially porous, pellicular) are made of a solid, non-porous core surrounded by a shell of a porous material that has properties similar to those of the fully porous materials conventionally used in HPLC. The terminology of “fused-core” was introduced by Jack Kirkland. As the name implies, fused-core particles are manufactured by “fusing” a porous silica layer onto a solid silica particle (Figure 2). Such phases can be used on standard HPLC instrumentation, without worrying about high backpressure or compromising column longevity.

With a shorter diffusion path with the SPP particle itself, coupled with a uniform packed bed and ultra-inert silica surface, short run times can be realised. The run time for Tramadol using the Quasar SPP RP Amide column is under 4 minutes, Figure 3. The embedded amide group within the alkyl chain of this stationary phase provides sites for interaction of polar functionalities within the analyte, tramadol. The addition of ion pair reagents, to afford retention, is not required. Consequently, this method is suitable for use with MS detection.

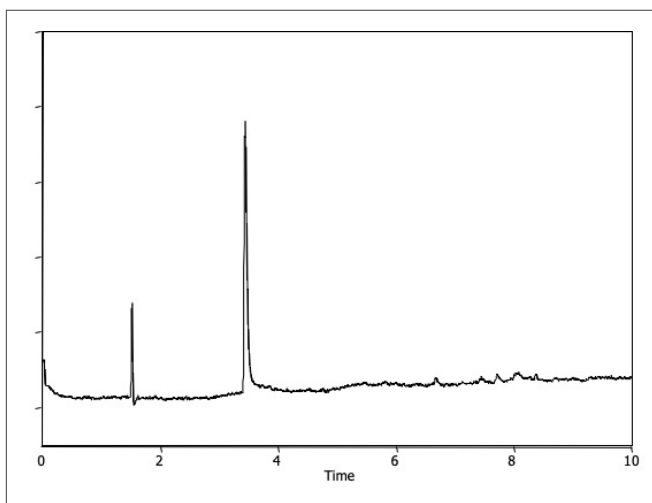


Figure 3. HPLC Analysis of Tramadol.

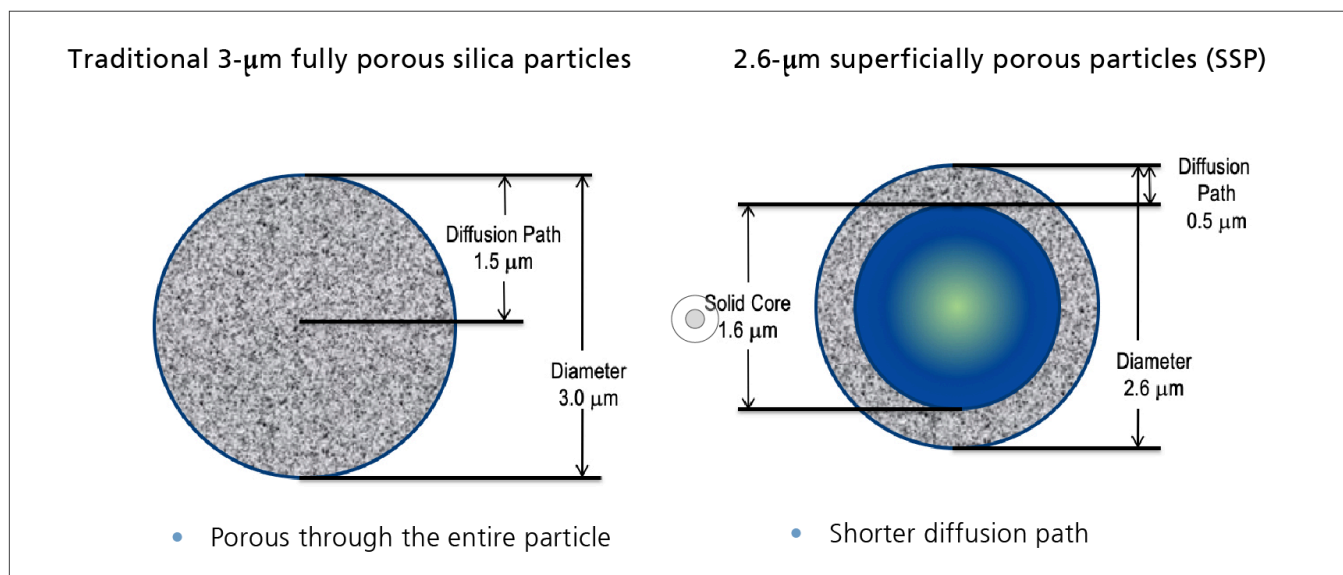


Figure 2. Schematic of porous silica particles and SPP particles.

## Conclusion

- The Quasar SPP RP Amide HPLC phase offers high efficiency separation of this opioid drug.
- The embedded amide group within the alkyl chain of the Quasar SPP RP Amide stationary phase provides sites for interaction of polar functionalities within the analyte, tramadol.
- With a solid core and outer porous silica layer you can realise up to a 50% improvement in cost and efficiency over traditional porous silica columns.

## References

1. "Tramadol". Drugs.com. Retrieved December 22, 2018
2. Tramadol Hydrochloride". The American Society of Health-System Pharmacists. Retrieved Dec 1, 2014.
3. Fischer, Jnos; Ganellin, C. Robin (2006). Analogue-based Drug Discovery. John Wiley and Sons. p. 528. ISBN 9783527607495.
4. <https://www.sciencedirect.com/science/article/pii/S0021967303020910>

## Consumables

	Part Number
Nylon filters	02542880

Phase	Length (mm)	I.D. (mm)	µm	Part
Quasar SPP RP Amide	150	4.6	2.6	N9308946
Quasar SPP RP Amide	100	4.6	2.6	N9308947
Quasar SPP RP Amide	50	4.6	2.6	N9308948
Quasar SPP RP Amide	150	3	2.6	N9308949
Quasar SPP RP Amide	100	3	2.6	N9308950
Quasar SPP RP Amide	50	3	2.6	N9308951
Quasar SPP RP Amide	150	2.1	2.6	N9308952
Quasar SPP RP Amide	100	2.1	2.6	N9308953
Quasar SPP RP Amide	50	2.1	2.6	N9308954
Quasar SPP RP Amide	250	4.6	5	N9308971
Quasar SPP RP Amide	150	4.6	5	N9308972
Quasar SPP RP Amide	100	4.6	5	N9308973
Quasar SPP RP Amide	50	4.6	5	N9308974
Quasar SSP RP Amide Guard Cartridge (3/pack)	10	3	2.6	N9306888
Quasar SSP RP Amide Guard Cartridge (3/pack)	10	3	5	N9306889
Quasar Guard Cartridge Holder	-	-	-	N9306876