

Application of Core-Shell Technology for Pharmaceutical Analysis

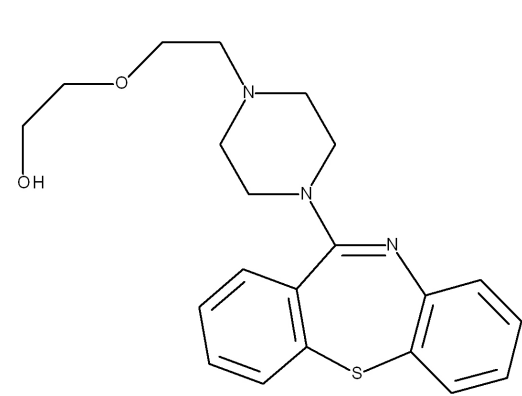
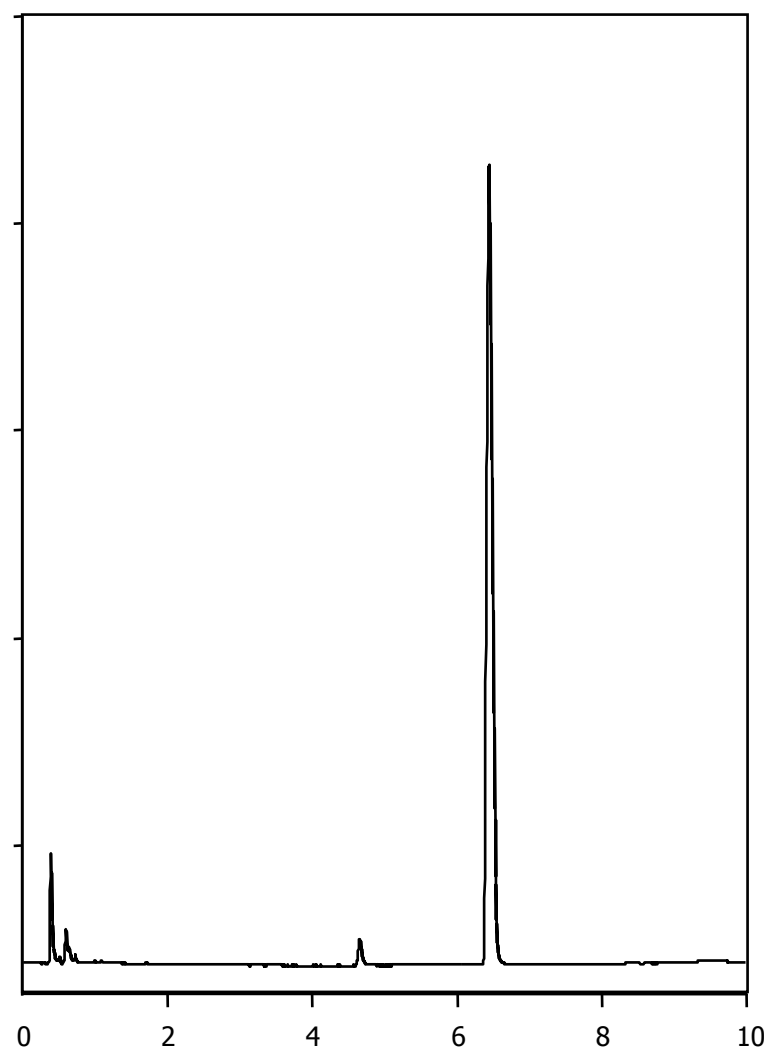
INTRODUCTION

In the world of separation science the pharmaceutical industry has many requirements, high throughput screening (HTS) of potential NDA candidates, highly selective methodology for separation of parent API from any potential interfering metabolites, chiral and genotoxic impurities. Sensitivity of analyte analysis to provide high LOD & LOQ limits to be achieved leading to robust qualitative/quantifiable results is also critical.

The introduction of core-shell particles into the separation sciences has led to potential improvements in all of the requirements above. In this work we look at the ability to achieve fast, selective, sensitive LC methods with these core-shell products for a range of pharmaceutical drugs.

PHARMACEUTICAL APPLICATIONS

1. ANTIPSYCHOTICS - QUETIAPINE

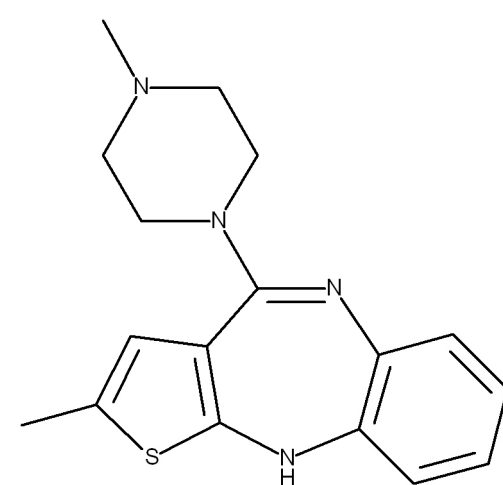
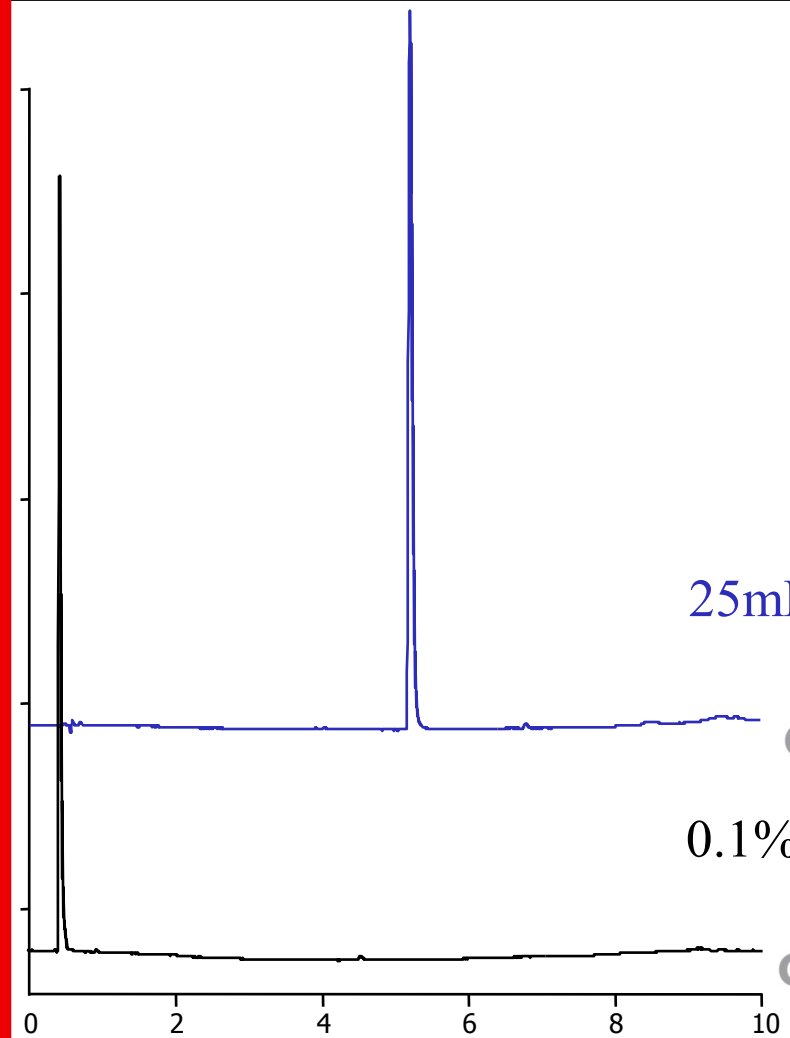


2.6µ SpeedCore[®] C18 100x2.1mm

A: 25mM NH₄OAc
B: ACN
10-90% B in 10mins
0.4ml/min, 254nm

Quetiapine (branded as Seroquel, Xeroquel, Ketipinor) is a short-acting atypical antipsychotic approved for the treatment of schizophrenia, bipolar disorders, and along with an antidepressant to treat major depressive disorder.

2. ANTIPSYCHOTICS - OLANZAPINE



25mM NH₄OAc

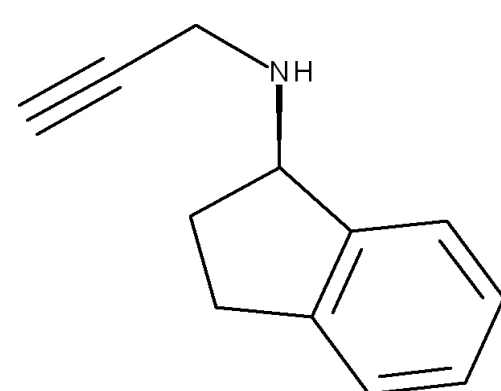
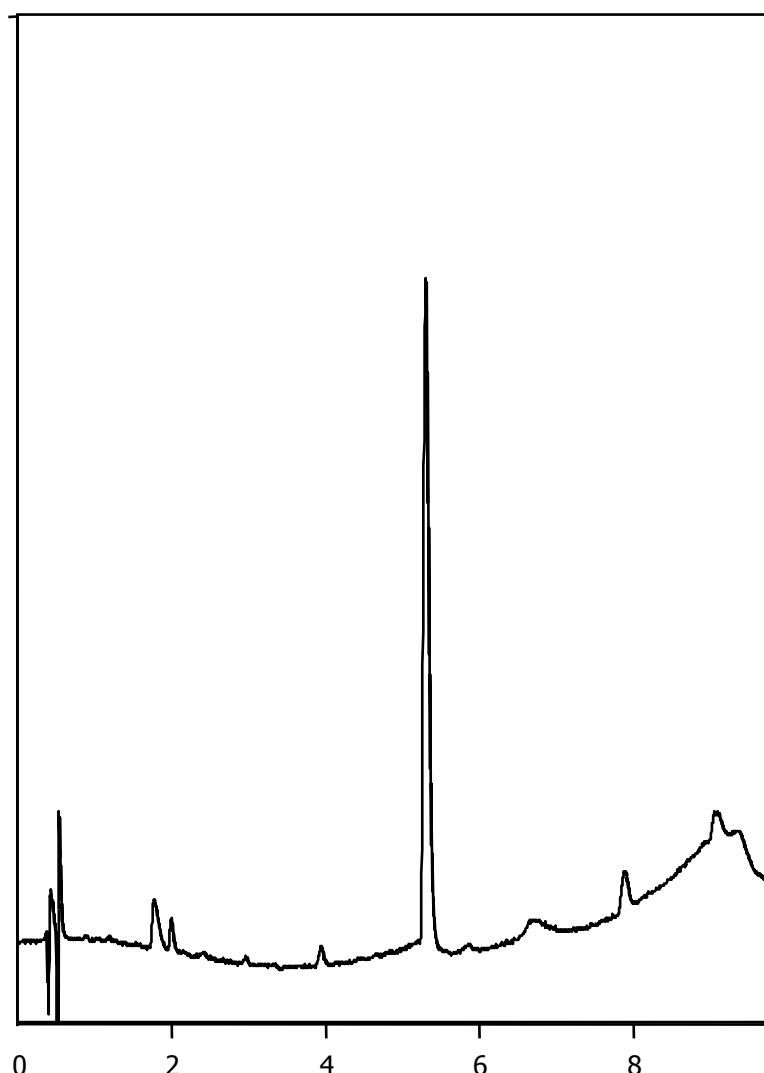


0.1% Formic acid



Olanzapine is structurally similar Quetiapine, but is classified as a thienobenzodiazepine and mobile phase buffer selection is therefore important for achieving separation/retention as seen in figure 2.

3. MONOAMINE-OXIDASE-B INHIBITOR – RASAGILINE (Azilect)

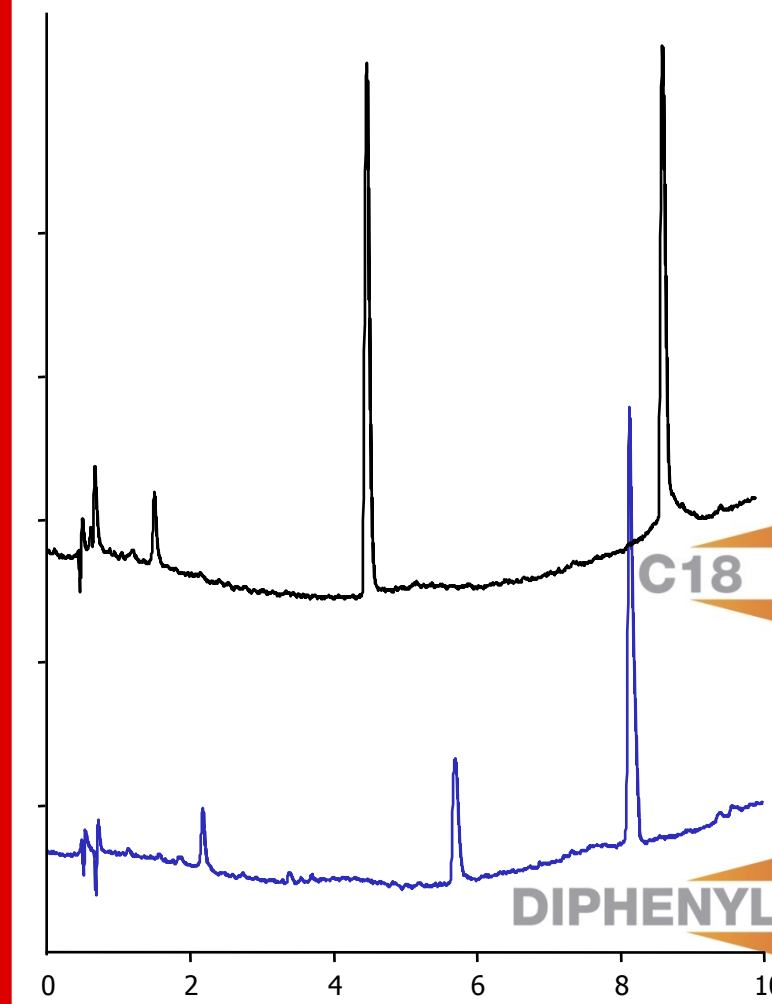


2.6µ SpeedCore[®] C18 100x2.1mm

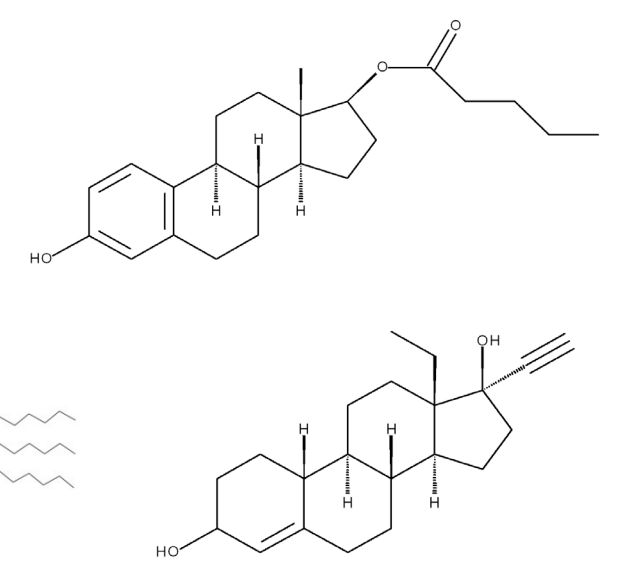
A: 0.1% Formic acid
B: ACN
10-90% B in 10mins
0.4ml/min, 254nm

Rasagiline (figure 3) is a selective monoamine-oxidase-B inhibitor (MAOI-B), which increases the levels of dopamine in the brain and is used in the treatment of Parkinson's disease.

4. SEX HORMONES - CYCLO-PROGYNOVA



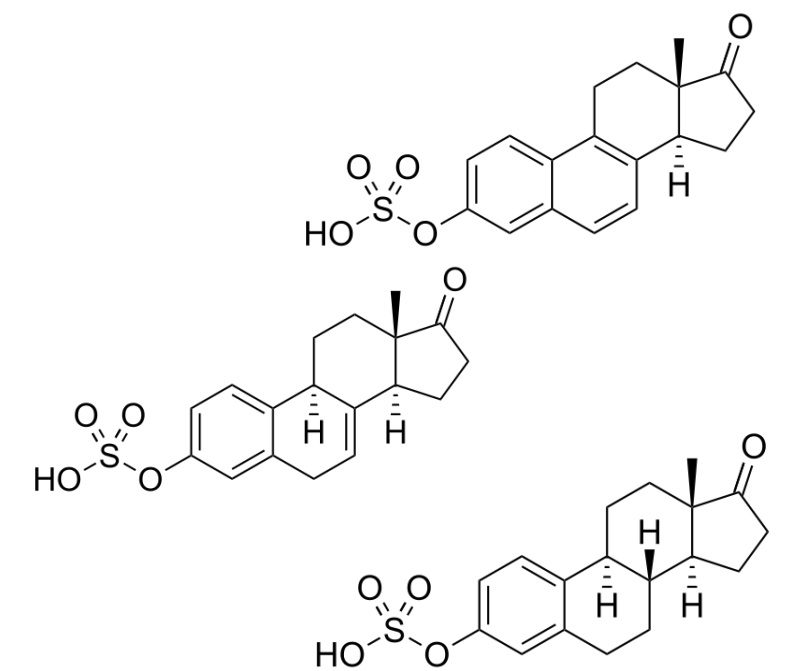
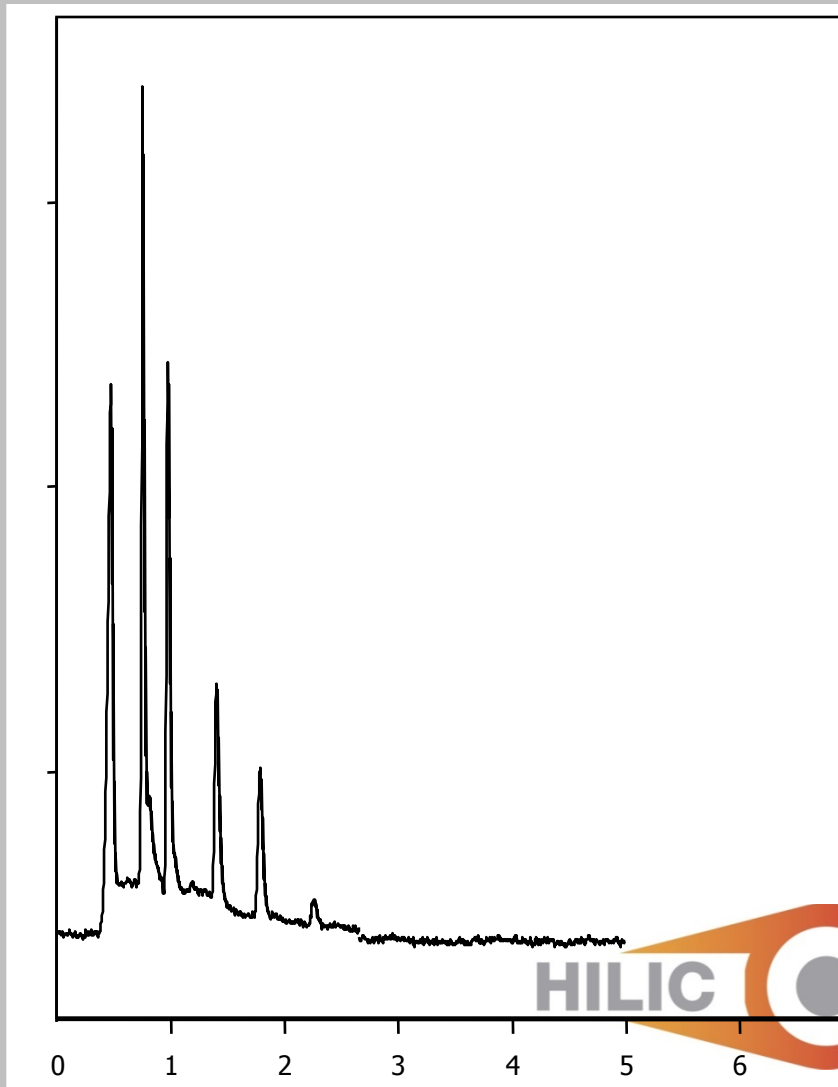
1. Estradiol Valerate
2. Norgestrol



A: 0.1% Formic Acid B: ACN,
10-100% B in 10mins
0.4ml/min, 254nm

Cyclo-Progynova is a hormone replacement therapy (HRT) preparation containing estradiol valerate in combination with norgestrel. Estradiol valerate and norgestrel are forms of the main female sex hormones, oestrogen and progesterone. The resolution of the two compounds present can be increased or decreased by stationary phase selection as shown in figure 4.

5. CONJUGATED ESTROGENES (Premarin)



2.6µ SpeedCore[®] HILIC 100x2.1mm

99:1 ACN : Water
0.3ml/min
210nm

Premarin is the commercial name for a medication consisting primarily of conjugated estrogens. The major forms of estrogen in Premarin are estrone(>50%), equilin(15-25%) and equilenin. The estrogens in Premarin are often called "conjugated equine estrogens" (CEE) because the estrogen molecules are generally present with hydrophilic side-groups attached such as sulfate. This makes the product suitable for analysis using HILIC stationary phase as shown in figure 5.

Conclusion

2.6µm Fortis SpeedCore[®] provides higher efficiency than 3µm or 5µm particles

Application of core-shell technology provides improvements in speed of analysis, this will be especially useful in both method development screening (HTS) as well as adapting new procedures within a QC environment to significantly decrease overall production time.

When undertaking method development selectivity is still an immensely important variable, we should not be reliant upon efficiency of these new particles alone.

One of the main advantages of these core-shell particles is the ability of the particles to operate on both 'traditional 400bar LC' and on the newer UHPLC systems. This allows the transfer of methods to be potentially simplified between various labs and organisational units, as well as outsourcing to CRO's. However one caveat on this is the necessity for well optimised systems, since dead-volume will rapidly decrease the available plate count and therefore compromise the expected efficiency gain.