Grace Discovery Sciences

Reveleris® X2 Flash System

RevealX™ Technology Can be Used in the Impurity Isolation of Valproic Acid from Cyclodextrin During Encapsulation

Introduction

Valproic acid is one of the major antiepileptic drugs used in the treatment of different kinds of epilepsy.[1] The drug has shown to be effective in treating cancer due to its antitumor properties. Although water is usually used as the reaction medium for enzymes, organic solvents or cyclodextrins have been added to improve the solubility of poorly soluble compounds. To increase its water solubility and bioavailability, the drug can be linked chemically by physical entrapment with polymers such as cyclodextrin or to polymeric carriers such as dextran.

Flash Chromatography Conditions:

Cartridge: Reveleris® C18 12g
Flow Rate: 36mL/min
Equilibration: 3.0 min
UV1 Wavelength: 220nm
UV2 Wavelength: 254nm
Solvent A: Water
Solvent B: Acetonitrile

Gradient Table		
Step	**Time (min.)**	**%B**
1	0.0	30
2	7.0	80

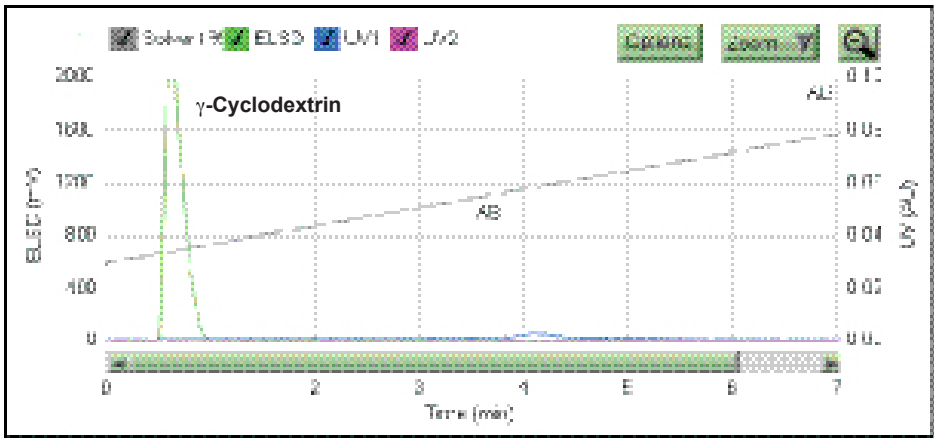
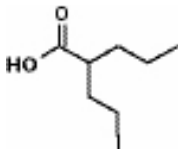
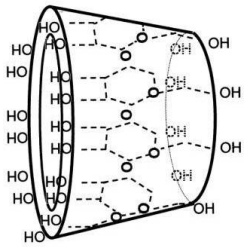


Figure 1: In this application, the separation of valproic acid from its entrapment-carrier, γ-cyclodextrin, has been shown using the Reveleris® flash cartridge with the RevealX™ detection technology. Using a linear gradient with acetonitrile and water mobile phase, cyclodextrin is poorly retained on a reversed phase cartridge.



Valproic acid



γ-Cyclodextrin

Flash Chromatography Conditions:

Cartridge: Reveleris® amino 12g

Flow Rate: 36mL/min

Equilibration: 6.0 min

Run Length: 12.0 min

UV1 Wavelength: 212nm

UV2 Wavelength: 254nm

Solvent A: Water with 0.1% TFA

Solvent B: Acetonitrile

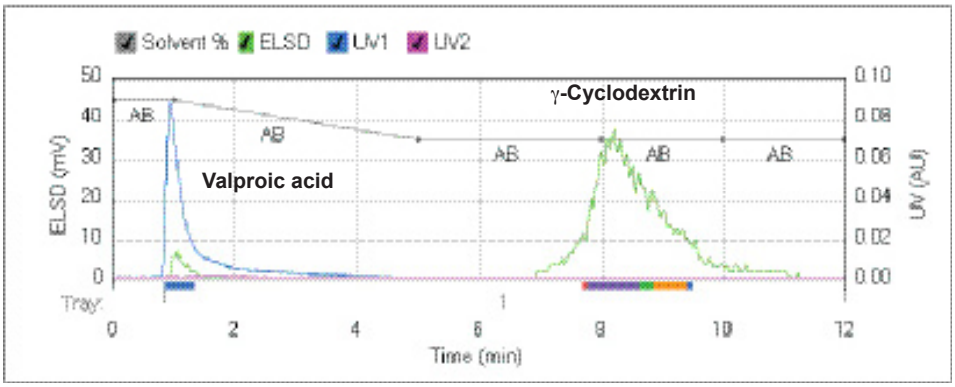


Figure 2: Compared to a reversed phase cartridge separation as shown where the retention is based on the hydrophobic interaction, the water-soluble cyclodextrin has been retained and separated from the free valproic acid using an amino phase media cartridge.

Gradient Table		
Step	**Time (min.)**	**%B**
1	0.0	90
2	1.0	90
3	4.0	70
4	7.0	70

Conclusion

Polymer nanoparticles allow proper drug delivery and targeting with a wide range of properties under controlled conditions.[2] As polymer technology plays a key role in overcoming drug delivery challenges for those undeliverable molecules, nanospheres and nanocapsules designed as drug carriers can be synthesized with drugs linked through encapsulation or conjugation for better target delivery. There needs to be a better purification technique for isolation of these compounds when the drug is poorly soluble in water while its carrier is a polar molecule. Hence such a method helps medicinal chemists isolate water based encapsulated drug from its impurity either as free or degraded and unbound compounds from the reaction mixture.

References

1. Praveen, B., Shrivastava, P., Shrivastava, S. K.; In-Vitro release and pharmacological study of synthesized valproic acid-dextran conjugate; Acta Pharmaceutica Sciencia, (2009), 51, pp. 169 – 176.

2. Vauthier, C. and Bouchemal, K.; Methods for the preparation and manufacture of polymeric nanoparticles; Pharmaceutical Research, (2008), 26, No. 5, pp. 1025 – 1058.

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