Introduction

Higher productivity is the new catch phrase in pharmaceutical and other industries. One way to meet this demand is utilizing Superficially Porous HPLC columns such as Poroshell 120 into Compendial methods. These 2.7 um particles show comparable efficiency to sub 2 micron particles with about half the back pressure. Columns packed with these materials can be used in older HPLC instruments or in new higher pressure instruments for high resolution in longer column format. In this work USP (United States Pharmacopeia) and (European Pharmacopeia) methods for generic pharmaceuticals will be adjusted to use Superficially Porous Columns. The examples show that adjustments are easy and time savings of 50% or more can be realized.

Experimental

With improvements in HPLC column technologies such as sub-2 micron packing materials and superficially porous packing materials, opportunities are available for method improvements. Reducing cost while providing a high quality product is a goal of innovator and generic pharmaceutical companies throughout the world. By taking advantage of new technologies cost and time savings can be met. A high-use method can be modified to save $500,000 per year, based on physical time savings, solvent savings and reduced instrument usage.

The USP provides an opportunity to take advantage of new technologies through use of “method adjustments”. These modifications are allowed changes to a method that logically follow the original method. They allow for slight differences in column chemistry, but also provide a chance to improve the original method (within limits) as long as system suitability testing (SST) requirements are met. Two examples will demonstrate application of method modifications for an isocratic and gradient example. In this work an Agilent 1200 SL Rapid Resolution System with a binary pump and a diode array detector are used.

Allowable Method Modifications (Adjustments) under USP Chapter 621.

- Column length: ± 70 %
- Column id: ± 25 %
- Column material particle size: Reduction of up to 50 %, if increase
- Flow rate: ± 50 %
- Injection volume: Changes are allowed as long as system suitability testing (SST) criteria are met.
- Column temperature: ±10 %
- pH of mobile phase: ± 0.2
- 20% increase in column efficiency or decrease in average tailing factor

Flowchart of Poroshell 120 Method Modification

- Choice of column: using similar chemistry (C18/L1)
- Use diode array detector (DAD)
- Increase flow rate ±50 %
- Increase column length ± 20 %
- Use diode array detector (DAD)
- Increase injection volume ±25 %

USP Method for Naproxen – 4.5X Faster

Analysis on Poroshell 120

USP Naproxen Method Demonstrated on 4.6 x 100 and 4.6 x 50 mm Poroshell 120 EC-C18 at 50 % increased flow rate.

Gradient Method

Gradient methods are frequently found in USP impurity methods. These methods require nearly one hour to run, but are used primarily to qualify incoming raw materials. Even if not used frequently, the delay caused by waiting for the typical 6 SST runs can lead to substantial delays in production. The path for method adjustment is similar to isocratic methods with the addition of adding a gradient. The gradient is scaled geometrically with the size of the column in order to maintain the separation (k’). In this example, column diameter is not changed but an adjustment of mobile phase composition is used.

The original USP/EP method for the antibiotic Cefepime is demonstrated on a 4.6 x 250 mm 5 micron Eclipse Plus C18 column and two other columns. Each of these columns requires at least 20 minutes run time plus equilibration time.

Conclusions

• Converting Methods to Superficially Porous Columns can be easily accomplished by following a simple plan and the allowable method modifications as listed under USP Chapter 621.
• Substantial solvent savings can be realized, while allowing faster analyses.
• Laboratories performing Compendial analyses with fully porous LG columns can benefit from the increased speed resolution and resolution that superficially porous columns provide.