

Easy purification of isomers with prepacked glass columns

Stereochemistry in the pharmaceutical industry

Since its discovery, stereochemistry remains important for development of pharmaceutical and biopharmaceutical substances. For the sake of drug safety and effectiveness, isomers need to be investigated closely. Therefore, the efficient separation both in analytical as well as in preparative scale of the isomeric forms is of high importance in the pharmaceutical sector. Chromatography is one of the key methods to obtain information regarding the different species [1,2].



Separation of isomers

Different methods are available for the separation of stereoisomers. Enantiomers are difficult to separate as they have exactly the same physical and chemical properties. They need special chiral phases.

In comparison, many stereoisomers, including E/Z isomers can be separated using conventional phases such as C18 as these isomers differ in their physical or chemical characteristics [1,2].

One major pharmaceutical company developed a very easy, straight-forward approach to transfer their analytical methods to preparative scale.

Their task was to collect, in a short time frame, information regarding cis-trans/EZ isomerism.

API purification from E/Z isomer mixture

In this recent comparison study, the scalability of two methods from analytical to semi-prep scale using a pre-packed glass column was investigated. The following columns were employed:

- 1. Analytical scale:** Pre-packed stainless steel column
150 x 4.6mm ID, packed with YMC-Triart Prep C18-S,
20µm particle size
- 2. Preparative scale:** Pre-packed ECO^{PLUS} glass column
220 x 35mm ID, packed with YMC-Triart Prep C18-S,
20 µm particle size

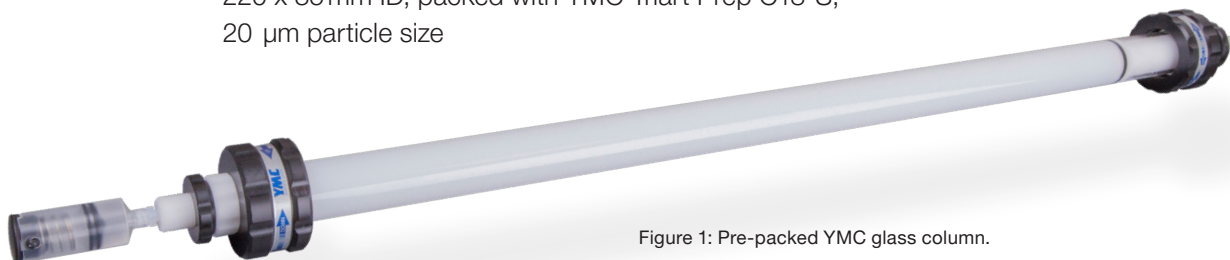
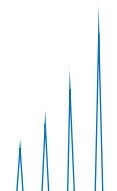
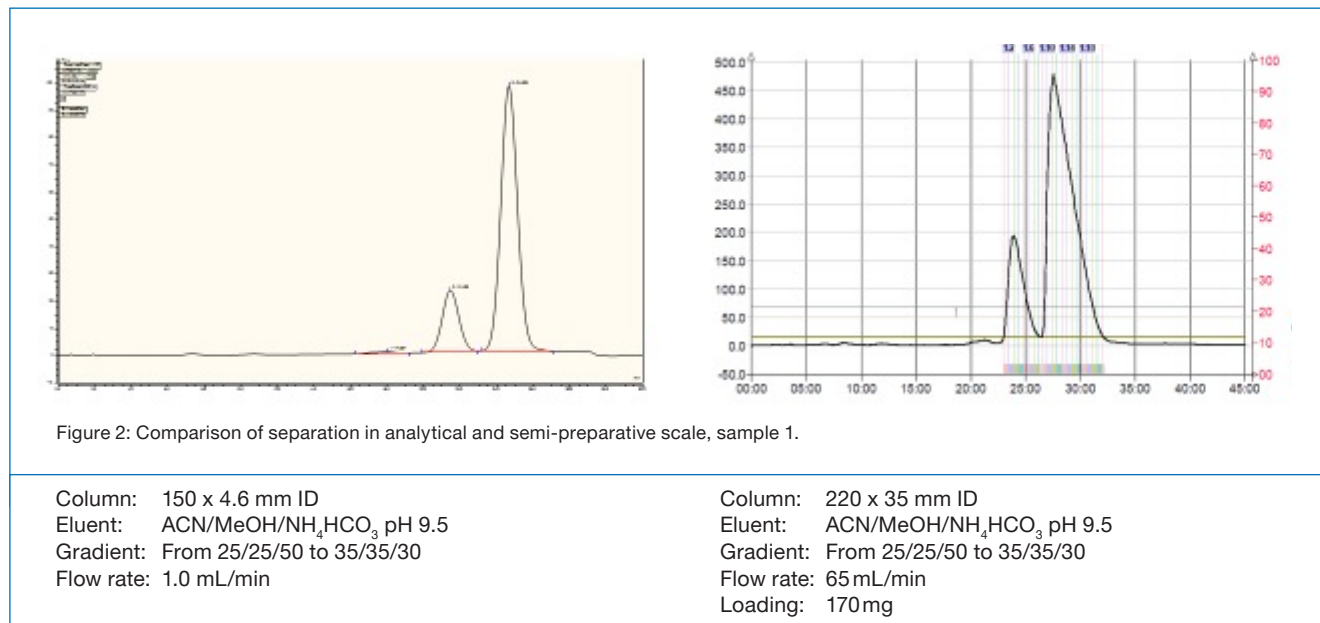


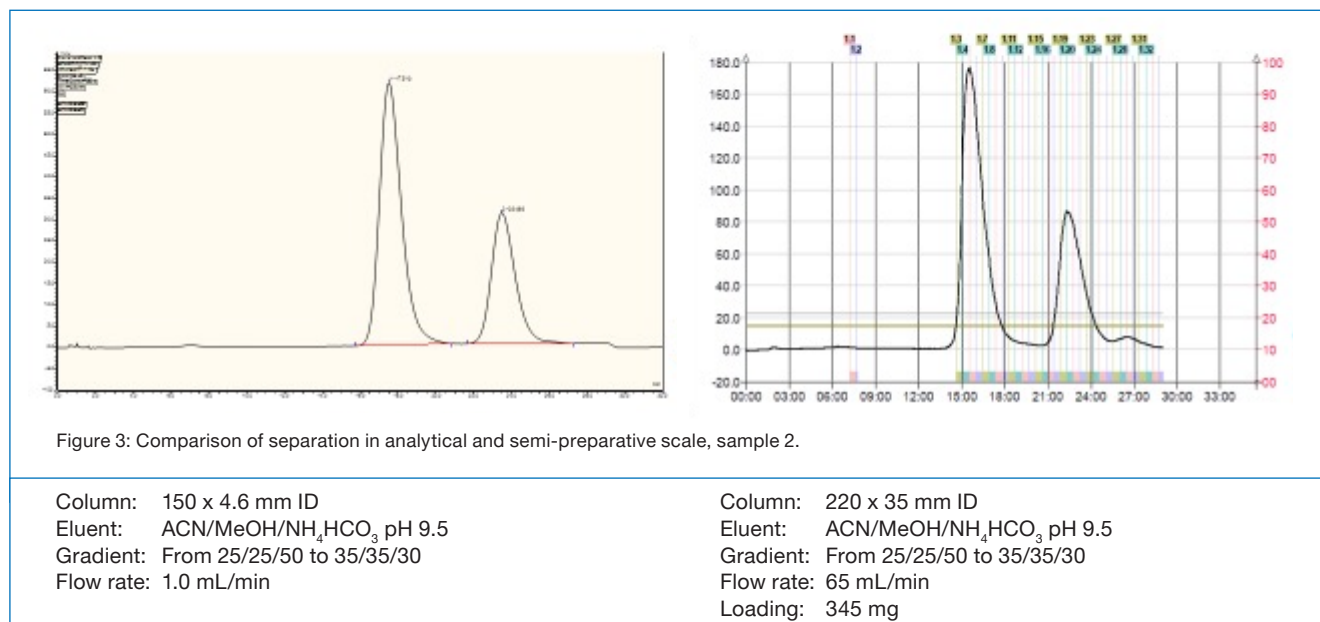
Figure 1: Pre-packed YMC glass column.



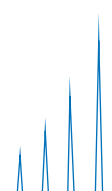
The API of interest, an E/Z isomer, turned out to be very challenging.
A successful separation was obtained at a high pH 9.5 with high organic modifier content.



The results in Figure 2 show that the method can easily be transferred from analytical to semi-preparative scale. Due to the same packing quality in the pre-packed glass column, the same separation could be achieved with a loading of 170 mg and a flow rate of 65 mL/min.



This easy method transfer was demonstrated using an alternative sample. Again, the approach showed successful results. Even with a loading of 345 mg, an efficient separation was achieved.



Single-use/Flash cartridges vs. pre-packed glass columns

In principle, single-use/Flash cartridges could be an option, too. Due to lower pressure limits and limited chemical resistance this approach was not investigated further. Additionally, a large number of samples needed to be

purified so the aim was to run the columns at the highest flow rates as possible. Due to the high pressure limit of the glass column, higher flow rates could be applied and the throughput was increased.

Pre-packed glass columns are the perfect solution for the purification of an API isomer in a crude mixture:

- Excellent chemical resistance: High pH and strong organic solvents can be used
- Higher pressure limits: Increased flow rates can be applied for improved throughput
- Full scalability: Due to excellent packing results, reliable scalability during scale-up
- Superior column performance: High resolution separation of the E/Z isomers

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- **New columns in standard and custom dimensions**

Depending on your required bed length, you can choose a column from our standard range. If you can't find a suitable standard product, we will gladly discuss with you the possibility of a customised column.

- **Refilling of your used column**

Do you need to refill your existing YMC glass column? This service can be combined with maintenance of your glass column (e.g. changing of frits and pressure testing), if desired.

- **Stationary phases from YMC or from other suppliers**

Is your method restricted to the use of a specific stationary phase? Of course, we can pack your glass column according to your needs, using stationary phases manufactured either by YMC or by any other producer.

Literature

[1]: Chhabra et al., A review of drug isomerism and its significance, Int. J. Appl Basic Med Res. (2013), Jan-Jun, Vol 3, Issue 1

[2]: Singh et al., Stereochemistry and its role in drug design, IJPSR (2014), Vol. 5(11): 4644-4659

