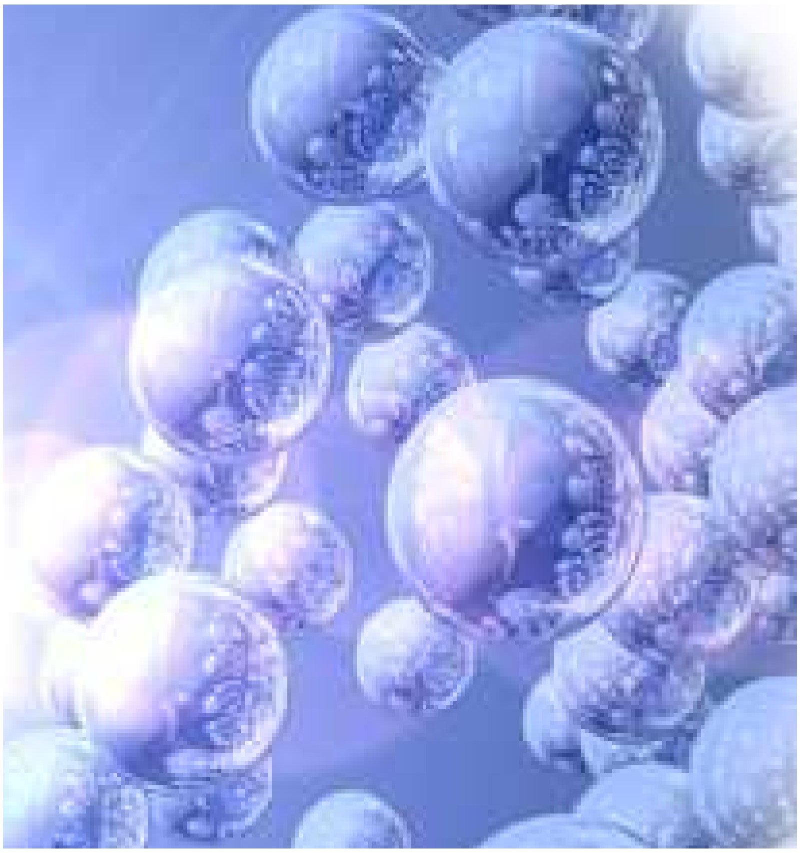

Cellufine Sulfate Packing Update

Dynamic Axial Packing in Pall 80 cm Resolute Column

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Cellufine

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Executive Summary

This report summarizes column packings with Cellufine Sulfate using a Pall 80 cm Resloute column. The Packing Study was performed to provide packing data using state-of-the-art production scale columns. Three packs were run to confirm that a packing method employing a combination of pack-in-place delivery of a 50-60% (gravity-settled) slurry and a DAP (dynamic axial packing) hydraulic-assist finish is appropriate to pack Cellufine Sulfate. This method is optimal for consistent packing of large-scale columns over a range of bed heights.

Objective

Confirm a packing protocol for Cellufine Sulfate using state-of-the-art large scale columns. In this case it is an 80 cm diameter Euroflow Resolute Column with Hydraulic Assist was used.

The proposed packing method employs a combination of pack-in-place delivery of a 50-60% (gravity-settled) slurry – starting with the adjuster above the ultimate packed bed height -- and a DAP hydraulic-assist to achieve the desired final bed height. The target compression factor (C_f = gravity-settled volume / packed bed volume) is approximately 1.15 – 1.20 X and an ultimate target bed height of approximately 22 cm.

Packing Protocol

1. Downward pack-in-place delivery of the resin with the adjuster starting above the ultimate packed bed height, so as to allow retraction of the nozzle prior to contact of the adjuster with the packed bed.
2. Downward pack-in-place with hydraulically-assisted adjuster movement to apply the final compression of the bed utilizing the Hydraulic Power Unit (HPU) in the pressure mode of control (i.e., at constant pressure up to 2.0 bar).
3. Packing will first be done in 0.1 M NaCl to limit the use of high salt concentrations. A packing in 1 M NaCl will be done to show that use of high salt concentration is not required. The end user's preference will always be to reduce the salt consumption to save expense and corrosion potential.

Packing Study at Pall Euroflow Technical Center, Portsmouth, NH
Euroflow 80 cm SS Resolute Column

One hundred sixty (160) liters of media was available for packing. This was placed in slurry vessel at approximately 50 % slurry. A sample of ~ 20 L was removed for a pump attrition study. [After settling the container was found to have 11 L of Cellufine Sulfate.] The attrition study is conducted by circulating a volume of media through the packing pump and periodically taking samples for examination. The size distribution is checked to determine if there is any particle damage. If damage is found, it can be related to the time of pumping to provide guidance on minimizing potential shear damage.

The upper adjuster is set at ~ 5 cm above settled bed height and the column is fully primed before the media, as the slurry is added to the column at a rate of 750 cm/hr using the upper valve. Once the proper media volume has been added, the upper slurry valve is closed prior to engaging the hydraulics of upper adjusted to move it downward until adjuster meets the top of the bed.

Pack 1

The actual column setup used was to set the starting height at 27.1 cm and aim for a finished bed of 22 cm. For this column condition the volume of media required is (27.1 cm x 5 L/cm = 135.5 L)

The target bed height was not achieved because the slurry concentration was higher than anticipated. With 53 % slurry concentration the packing stopped at 23.4 cm vs. the target of 22 cm. The packed bed had a compression factor of 1.12. At end of pack the exit flow was minimal and there was some concern about possible local over-compaction of the bed.

After equilibration at 200 cm/hr with 100 mM NaCl, an HETP test was conducted by injecting of 2% BV of 1 NaCl salt solution (2.3L) at 100 cm/hr. The testing showed Asymmetry = 0.91 (fronting); HETP = 0.037 mm; N = 2702 p/m. The result was quite promising.

Further compression was applied, and some improvement in peak symmetry was achieved.

Run	Bed Height cm	Bed Volume Liters	Compression Factor C_f	HETP mm	Plates/m	Asymmetry
Pack-1	23.4	117	1.12	0.037	2702	0.91
Pack-1b	22.9	115	1.15	0.037	2677	0.94

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Pack 2.

After unpacking the column, the slurry was re-suspended and the column was packed again.

Pre-Pack Calculations:

Volume for 22 cm [22(5)1.2]/0.54 = 243.9 L @ 54%.

Settled volume: 131.8 L Packed Volume: 110.6

C_f = 131.8/110.6 = 1.19

This packing proceeded smoothly. Column testing showed that while the plates per meter were high, the chromatogram was still fronting. Post-pack HETP: As = 0.87; HETP = 0.032 mm; N = 3130 p/m

To correct the fronting, column conditioning by flow reversal was attempted. The brief conditioning consisted of 2 CV upflow followed by 1 CV downflow followed by equilibration and HETP testing. The increase in fronting suggested that flow conditioning did rearrange something in the bed. Even with worsening symmetry, there was slight improvement in efficiency (plates/m).

The bed was further compressed to 21.7 cm. Retest of the HETP showed: As = 0.84; HETP = 0.034 mm; N = 2966p/m. The improvement in symmetry was encouraging. The combination of flow conditioning and hydraulic packing was effective in creating a better bed.

When the packing material balance was rechecked it appeared that there was an additional 4 L of media in the column. The recalculated compression factors increased the compression to 21 and 23 %. It is felt that this degree of compression is excessive for the Cellufine media.

Run	Bed Height	Bed Volume Liters	Compression Factor C_f	HETP mm	Plates/m	Asymmetry
Pack-2	22.0	110	1.21	0.032	3150	0.87
Pack-2a	22.0	110	1.21	0.031	3193	0.75
Pack-2b	21.7	109	1.23	0.034	2966	0.84

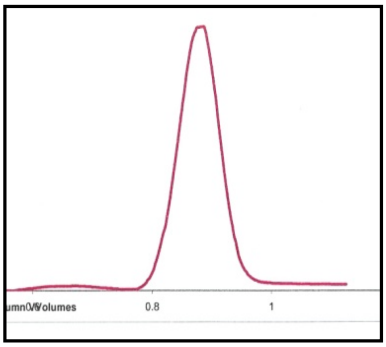

Figure 1.
The curve to the left shows the Pack-2 salt injection peak. It is typical of the chromatograms for most of the injections. It shows slight fronting (As = 0.87), but the efficiency is very good (3150 p/m).

Pack 3.

Objective:
Based on the results of Pack 1 and 2, the plan was to pack to 10 % compression to see if column tailing can be induced. Ideally, at the lower compression, salt injection should exhibit tailing. If that is the case, the packing will be followed by further DAP compression to between 17-20%.

The pack was first made to 24.3 cm to achieve 10.9 % compression. The salt injection results were: As = 1.04.; HETP = 0.036 mm; N = 2762 p/m. The salt peak showed slight tailing and thus confirmed the observed fronting in Pack 1 and 2 was related to over-compression. At 10.9 % compression there was no fronting. As expected, the resultant flow/pressure data was slightly higher than the flow/pressure curve for the 20 % compaction beds.

DAP compression was used to lower the upper adjuster was lowered to 22.2 cm to achieve 20 % compression of the bed. The HETP data showed: As = 0.94; HETP = 0.034 mm;
N = 2945 p/m. The greater compression improved the efficiency (plates/m), but the symmetry reverted to just slightly fronting.

Run	Bed Height cm	Bed Volume Liters	Compression Factor C_f	HETP mm	Plates/m	Asymmetry
Pack-3	24.3	121	1.11	0.036	2762	1.04
Pack-3a	22.2	111	1.21	0.034	2945	0.94

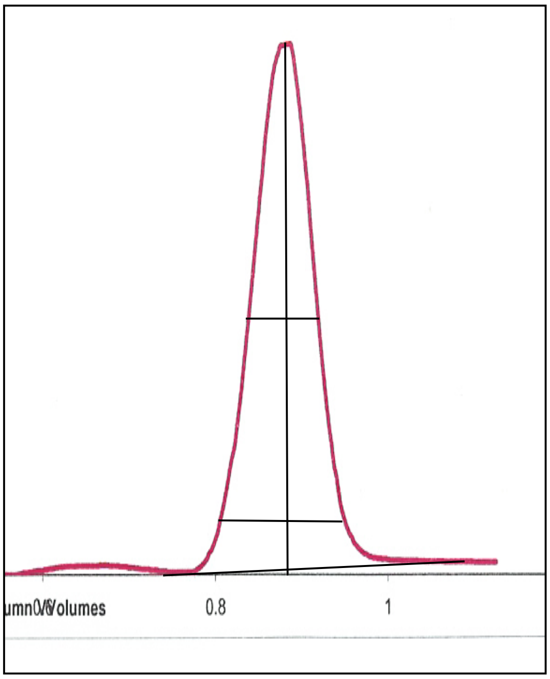

Figure 2.
Typical HETP data for Cellufine Sulfate packed in 80 cm column and tested by 1 M NaCl injection.

HETP = 0.034 mm
N = 2900 plates/m
As = 1.1