CLEAN-IN-PLACE OPERATIONS FOR THIN-CAKE FILTRATION TECHNOLOGIES

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ABSTRACT & INTRODUCTION

In many chemical and pharmaceutical processes, solid-liquid separation, cake washing and drying steps directly impact the effectiveness of the production operation. Process engineers devote much of their time to analyzing these steps.

The solid-liquid separation step can be by pressure, vacuum or centrifugation as well as in a batch or continuous mode. In this separation step, there is a further choice both of the type of filter media and the thickness of the cake or the cake depth during which the separation occurs. Cake washing generally follows and the choices are displacement or reslurry options. Finally, drying may be necessary and there are many possibilities including vacuum, convection, spray, steam and a combination of techniques.

This article discusses the choice of thin-cake (2 – 25 mm) separation technologies and their benefits to optimizing the effectiveness of the production process. The paper continues with a discussion of clean-in-place operations to meet current Good Manufacturing Practices (cGMP) guidelines including riboflavin test and validations. ANSI/ISA S88 (and IEC 61512-1 in the international arena) batch process control system standards are also examined. Finally, factory and site acceptance testing is described.

IMPORTANCE OF THIN-CAKE FILTRATION

Thin-cake solid-liquid separation can be defined as the formation of a cake in the 2-25 mm thickness range. In this range, cake compressibility becomes less important in the cake building stage of a separation process. Compressible cakes or those cakes that have average or poor filtration characteristics can be better handled at thinner cake depths. For example, an amorphous crystal that does not centrifuge well can be filtered at 45 psig with a cake thickness of 2 – 3 mm. Thin-cakes also lend themselves to more effective washing and drying as there is less of a chance of channeling and the mechanism of "plug-flow" of liquids or gases is enhanced.

THEORY OF THIN-CAKE FILTRATION

Filtration

During the initial mechanism of cake forming in the filtration step, the filter cloth acts just to initiate filtration by capturing the first particles. These first particles form bridges over the pores of the cloth (bridging). As soon as a first layer of particles has accumulated on the filter medium, this cake will then act as the actual filter medium.

When plotting the amount of filtrate obtained at constant filtration pressure versus the filtration time, a filtration curve is developed, which represents a root function, V_F = Constant * $t_F^{0.5}$, as shown in Figure 1. .

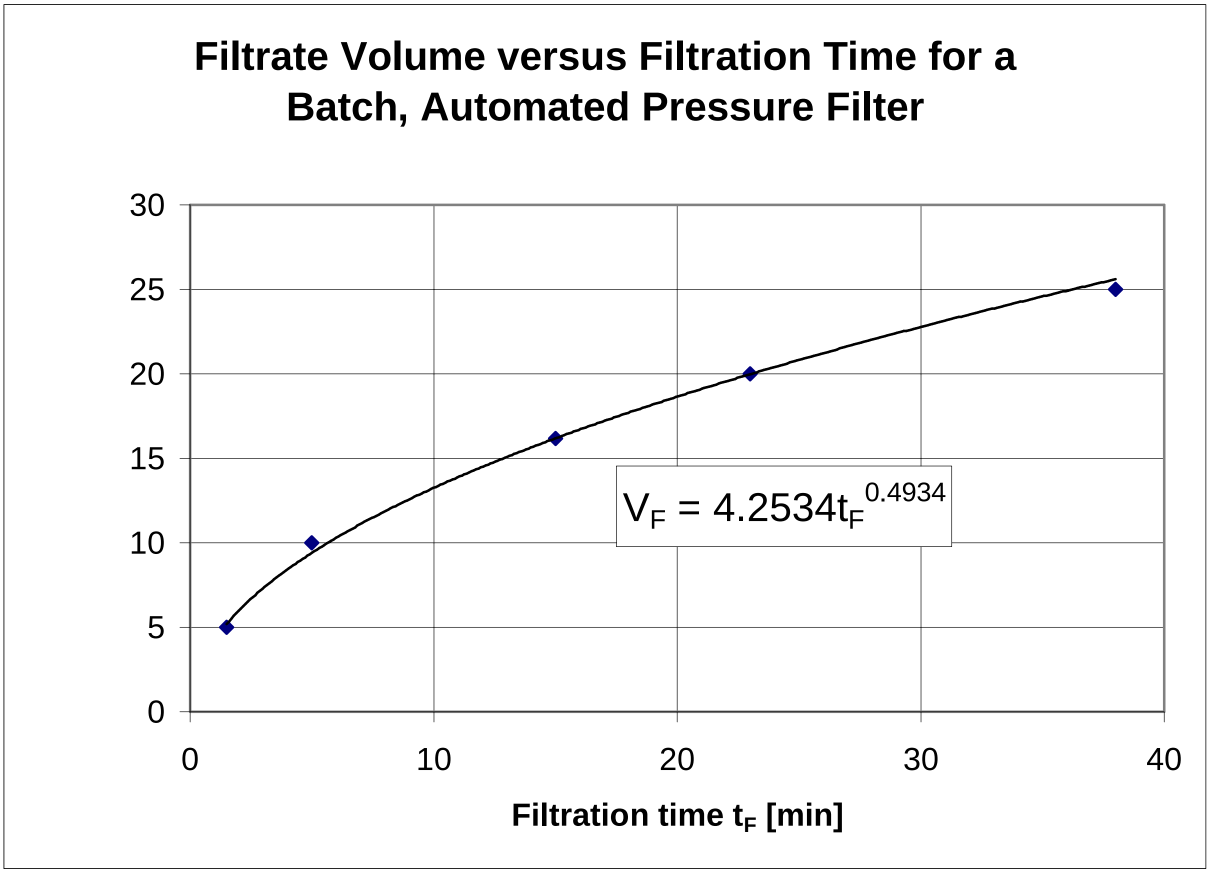


Figure 1: Example of a Typical Filtration Curve

The equation of the trend line for this specific chemical product was calculated by Excel. The exponent of 0.4934 almost exactly corresponds to the root function and the constant, in this case, equalled 4.2534. Accordingly, the filtrate flow rate is at its maximum in the beginning and then declines as a result of the constantly increasing filtration resistance (as the cake thickens).

Parameters that Influence Filtration Performance:

Filtration pressure

The higher the filtration pressure, the higher the filtration performance for a non-compressible cake. In case of a compressible solid matter, an increase of pressure will often not result in an increased performance because the filter cake gets more impermeable due to the compression. Thinner cakes reduce the impact of compression.

Temperature
The higher the temperature of the slurry, the lower its viscosity. The lower the viscosity, the higher the filtration performance. As a general rule, therefore, increasing the filtration temperature will result in an increase in the filtration performance.

Particle Size / Particle Size Distribution (PSD)
The particle size and particle size distribution are important parameters, which can influence the filtration performance. As the filter cake begins to form, channels (capillaries) are formed between the particles. The smaller the capillaries, the higher the capillary pressure and thus the resistance of the filter cake. Small particles and a wide particle size distribution result in a densely packed filter cake and reduced filtration performance. In cases such as these, a thinner cake will mitigate this impact and allow for successful filtration.

Particle Shape
The type and shape of the particles also impact the filtration performance. Hard, spherical particles will form a permeable cake with increased void volume leading to high rates. Irregularly shaped crystals, platelet-type or flat crystals as well as needles and amorphous crystals can pack together and result is a dense and low-permeable cake. In cases such as these, once again, thin-cake filtration or low filtration pressures mitigate the impacts of the particle shape.

Washing of the Filter Cake
When washing the filter cake, there are two mechanisms that occur: displacement washing and diffusional washing. With displacement washing, a large part of the void volume (which is still filled or saturated with mother liquor before washing starts) is replaced by the washing liquid.

For bound moisture, diffusional washing is the preferred mechanism. These liquids are removed by the diffusion washing, i.e. the liquid to be washed out diffuses into the washing liquid. The driving force is the concentration difference.

Depending upon the cake formation, generally, a thinner cake would require less wash liquid (maximized wash ratio efficiency) and less handling of solids. This would allow for a more "plug-flow effect" for the displacement washing. For the bound liquids, there would be a lower concentration of bound liquids, which would also require less diffusional wash liquids and less contact time.

Finally, in terms of the parameters that impact washing, these would generally fall in the same category as the influences on filtration.

Drying of the Filter Cake
When dewatering the filter cake, the liquid remaining in the pores shall be replaced by gas (mechanical dewatering by blowing) with the objective of obtaining a residual moisture content as low as possible. During blow-out operation, the capillary pressure of the pores must be overcome. The smaller the capillaries, the higher the capillary pressure. As soon as the first

capillaries are blown through, the gas consumption rises and reduction of the residual moisture becomes more ineffective. When this point occurs on the drying curve, there are two further approaches that are undertaken. First, the cake can be slowly compressed to allow for reduced gas consumption during this mechanical dewatering stage. Secondly, vacuum drying can be employed as well as thermal drying.

During the blowing phase, one of the most important factors for a low residual moisture is a high blow out pressure rather than gas flow. Depending upon the product characteristics, time, temperature and cake thickness will also impact the drying curve.

CLEAN-IN-PLACE (CIP) OPERATIONS

Thin-cake filtration technologies can be batch or continuous, pressure or vacuum, and for high-solids or clarification of slurries.

High-Solids Slurries-Batch Pressure Operation

In some production plants, the process is a batch operation. This is important in the pharmaceutical industry whether batch – to – batch integrity is critical. For these applications, the crystals can be processed with a deep bed nutsche filter or centrifuge. However, some crystals, due to the factors previously discussed, are more easily managed using thin-cake pressure filtration. This technology, shown in Figure 2, consists of circular filter plates that are sealed in a movable housing. The filter plate design allows for forward and reverse flow operations and can be automatically cleaned to less than 1 ppm residual cross contamination. Riboflavin tests document this performance as shown in Figures 3 and 4.

Figure 2: Internal Features of an Automated, Batch Pressure Filter Technology

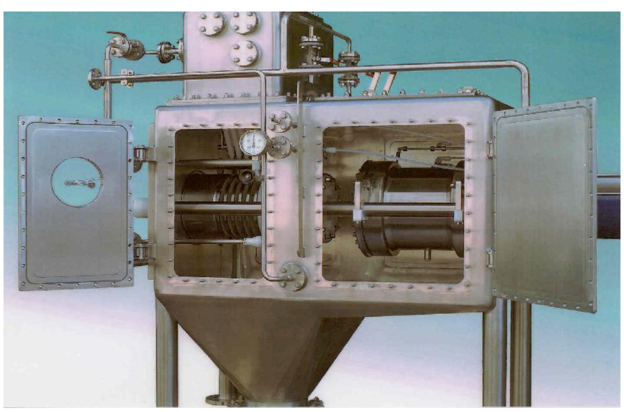


Figure 3: Before Riboflavin Test (Contaminated Areas shown in green /purple)

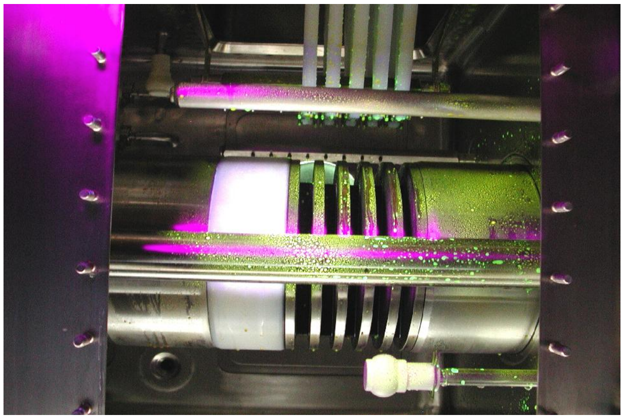
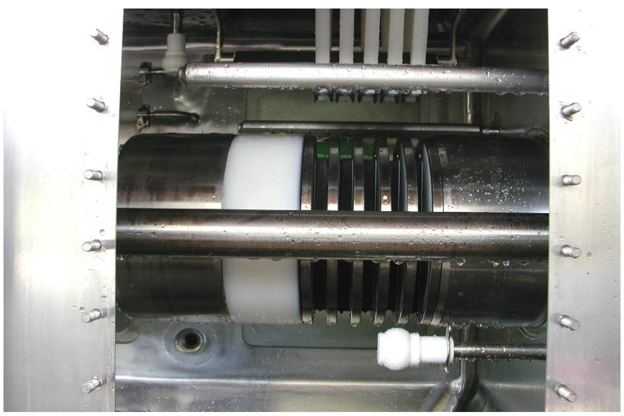


Figure 4: After CIP Cleaning



High-Solids Slurries-Continuous Vacuum Operation

High-solids slurries can be defined as up to 50 – 55% solids in the slurry feed. In some cases, for high solids applications, the slurries can be better handled using vacuum filtration rather than pressure filtration. An example of a continuous, thin-cake technology is a Continuous – Indexing Vacuum Belt Filter. This technology consists of fixed vacuum trays, continuously feeding slurry system and indexing or step-wise movement of the filter media. The filter media is indexed by pneumatic cylinders located on the exterior of the unit. CIP operations for this technology consists of spray balls, spray nozzles and circulation techniques. Due to the design, there are no internals that can trap crystals or that cannot be swabbed. Figures 5 and 6 show photographs of the external and internal designs.

Figure 5: External Design with Rounded Corners and Gap-Free Construction

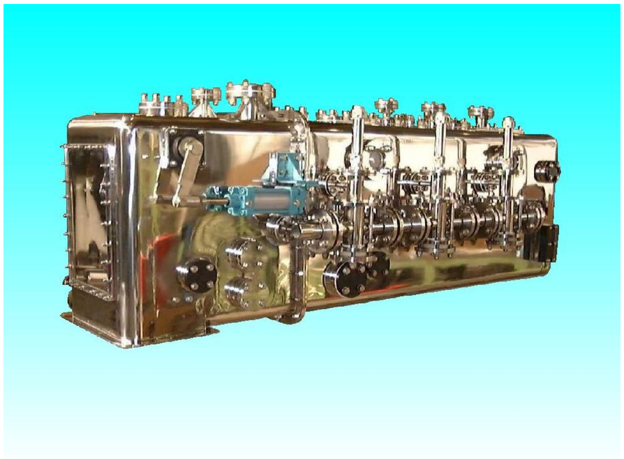
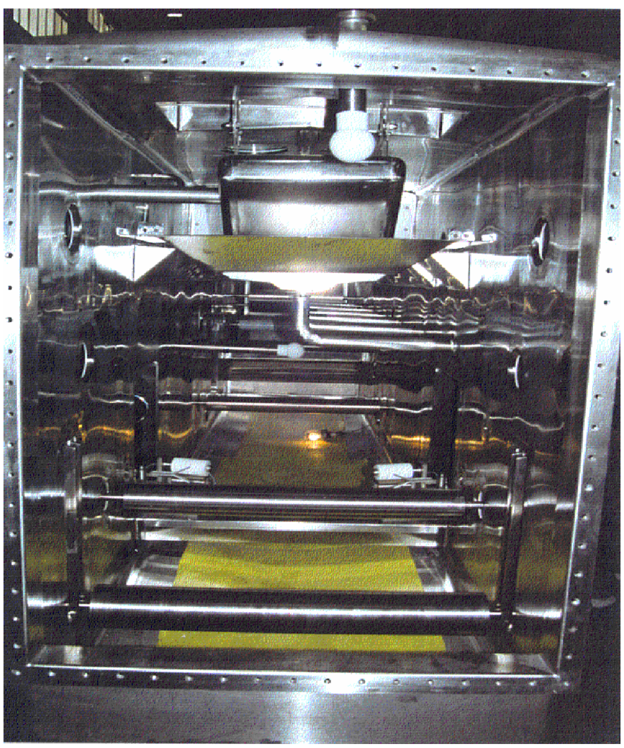


Figure 6: Internal Design with Spray Balls and Fully Drainable Surfaces



Clarification & Recovery of Slurries-Pressure Operation

Candle Filters and pressure plate filters are installed for clarification and recovery applications from liquids with low solids content. The candle filters are vertical candles while the pressure plate filters are horizontal plates. The major difference between the two units depends on the cake structure that is formed. Some cakes are better handled in the horizontal and some in the vertical. Both units conduct CIP operations in identical manners by filling and circulating cleaning fluids while blowing gas in the reverse direction to the filtration direction, which crates a turbulent mixture or a quasi-ultrasonic cleaning effect. The pressure plate filter further enhances this operation with plate vibration.

Figure 7: Candle Filter Cleaning

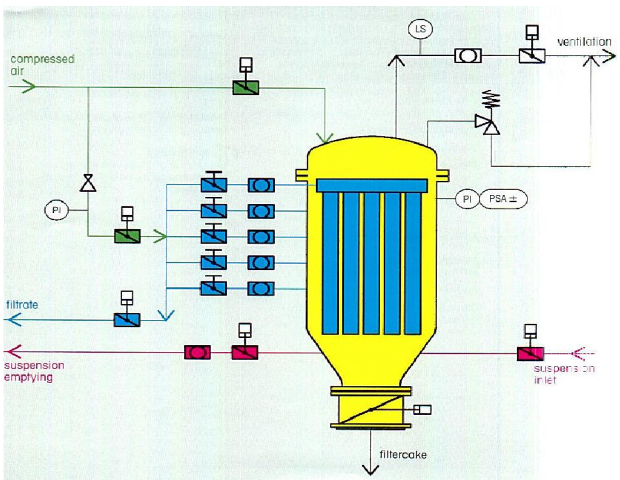
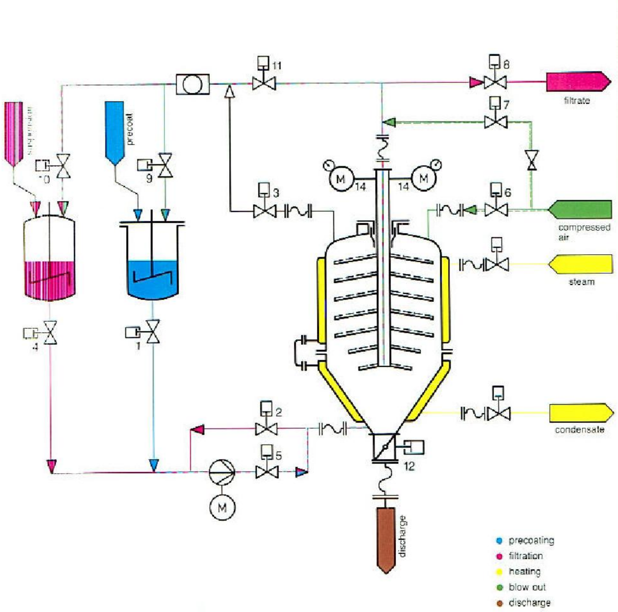


Figure 8: Pressure Plate Filter Cleaning



PROCESS CONTROLS & TESTING

The final step of the process is controls and factory (FAT) and site acceptance (SAT) tests. The Batch-S88 standards allows for modular control system operation. It defines the process and cleaning operations in steps so that operators can perform certain tasks reliably and without variation to ensure a unit that is defined as clean. A typical sequence would be as follows:

- Idle – In Semi-Automatic/Automatic mode sequence is not running
- Running – Main Operation is running without any active sequences
  - Purging – Fast Purge Sequence Active
  - Setup – Setup Sequence Active
  - Filling – Filling Sequence Active
  - Wash 1 – Wash 1 Sequence Active
  - Wash 2 – Wash 2 Sequence Active
  - Blowing – Blow Sequence Active
  - Discharging – Discharge Sequence Active
  - Clean-In-Place
- Complete – Main Operation Sequence is complete
- Aborted – Sequence aborted.
- Holding – Holding Sequence Active
- Hold – Holding Sequence completed
- Restarting – Sequence is restarting from Hold state
- Grounding – Ground sequence is active

FAT and SAT tests are then performed using the S-88 standards and formats and repeating the procedures and riboflavin tests, as necessary.

SUMMARY

Thin-cake filtration operations provide many benefits to the production process in terms of higher filtration flux rates, improved wash ratios and drying cycles and an overall improvement in production rates. By selecting the optimum thin-cake technology of pressure or vacuum, batch or continuous, engineers can realize a more efficient process approach including solids handling and cleaning of equipment with minimal operator involvement for improved safety and environmental concerns.