XPURE
innovative continuous chromatography

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Target Ingredients for Adsorption Chromatography in Whey and Milk

This blog focuses on useful and valuable proteins in both milk and whey that can be recovered with chromatographic separation.

Milk and its derivatives contain various proteins that are useful as human nutrition. Milk proteins are especially rich in amino acids that stimulate muscle synthesis. In addition, some proteins and peptides in milk have positive health effect e.g. on blood pressure, inflammation, oxidation, and tissue development [1]. Some people suffer from a deficiency of specific proteins, In order to to find a solution for this, manufacturers produce balanced, composed (semi-)synthetic milk products, e.g. baby food, by adding those proteins in the manufacturing process.

This blog describes a few examples where adsorption chromatography can serve as a separation technology to isolate useful milk and whey proteins.

Minor Milk Proteins

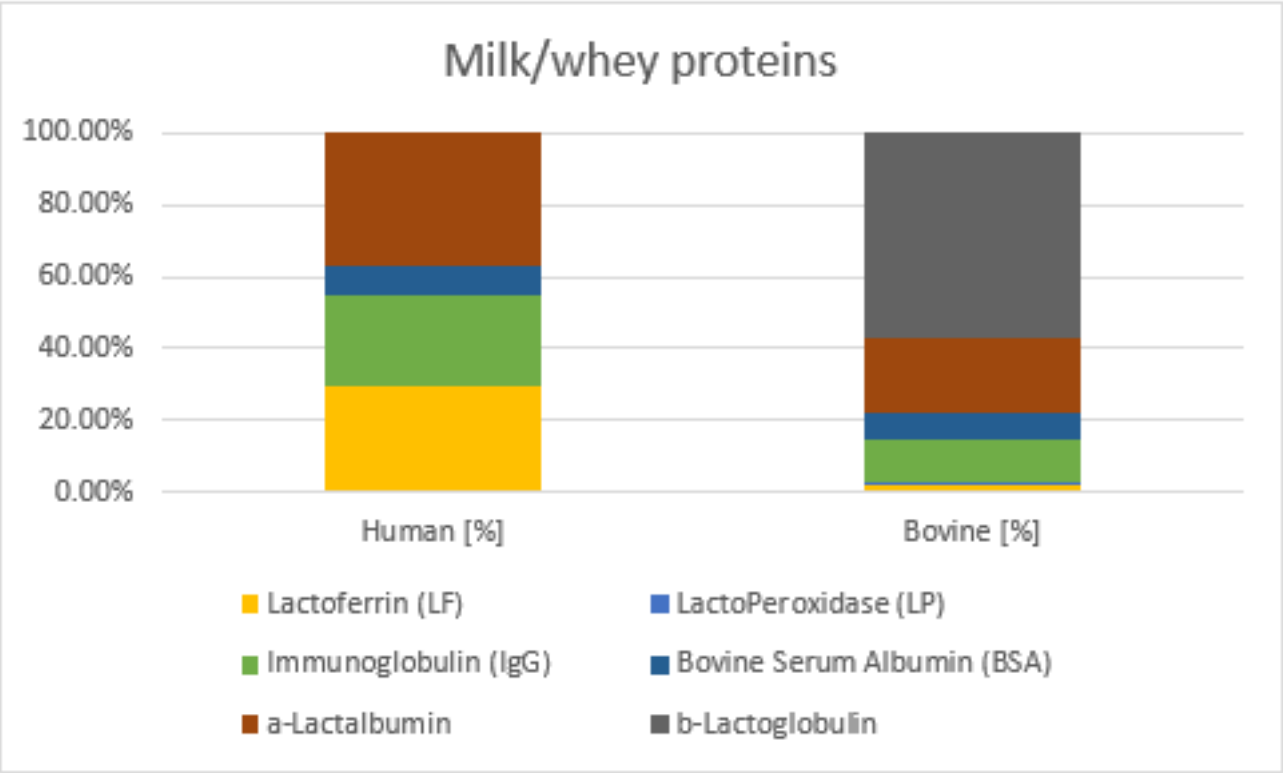

Figure 1. Human versus bovine minor milk protein composition [2], [3], [4].

Above Figure 1 represents the average milk protein composition in both human and bovine milk (note that only the "high-value" minor proteins are represented in this figure, because the majority (i.e. > 80%) of cow milk proteins consists of different types of casein. For human milk approximately 40% of total protein consists of casein).

Total bovine milk protein content amounts to 30-34 g/l.

PROTEIN ADSORPTION

Protein adsorption has been applied on batch scale utilizing dedicated functionalized resins, e.g. agarose-based cation exchange resin [5].

In expanded bed mode, suited to direct the fermentation broth to the adsorption process, without having to clarify the crude broth first, it has been found that the feed flow rate can be substantially higher (~10 m/h or even higher) without significant backpressure [6].

Before loading milk on a chromatography column the fat (components) need to be skimmed first in order to prevent blockage of the adsorption phase and reduce viscosity to attain higher bed flow rates.

Dairy Characteristics

Milk is a complex medium; in addition, the composition of milk is subject to seasonal influences. and further pooling prior to processing is quite common in the dairy industry. Volumes to be processed lie in the range up to 100's of m^{3}'s per day.

Since the proteins are utilized in food supplements, regulatory and hygiene rules apply.

Pasteurization is a common step in milk processing, temperature largely affects the adsorption characteristics and may also pose additional demands on the adsorption materials in terms of thermosensitivity.

Adsorption Technology

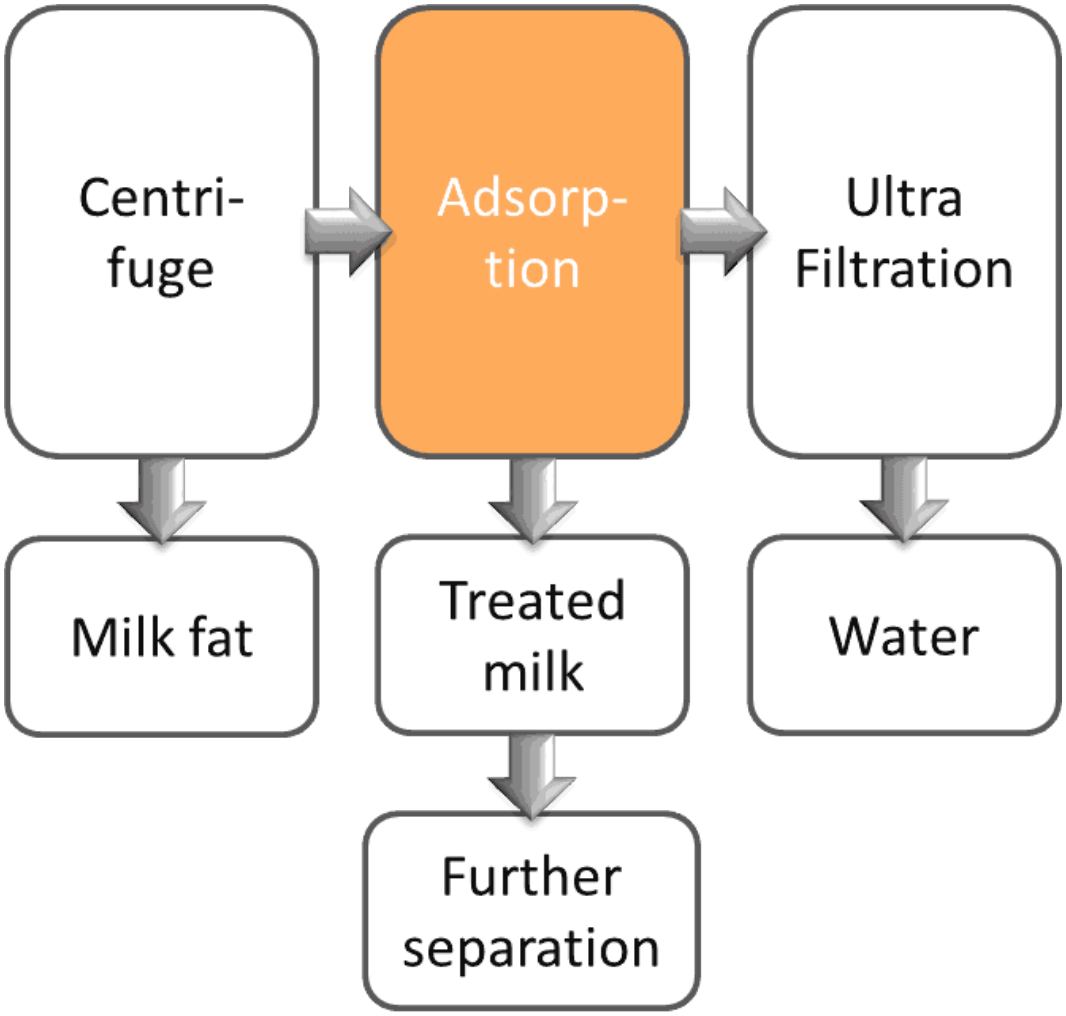

Figure 2. Part of flow scheme to recover milk proteins, including chromatographic adsorption

Figure 2 conveys part of a typical milk process where fat and protein are separated.

The Adsorption step comprises the capture of specific proteins to a specific, selective resin, and the elution with a proper salt buffer.

Depending on the magnitude of the process, as well as process control requirements, the adsorption step may be operated in a continuous mode. A well established continuous chromatography mode is based on simulated moving bed technology (SMB). This technology features a multiple (typically 4-16) column process that smartly accommodates all distinct process steps –running simultaneously- that is part of the bind and elute process, including wash/rinse/equilibration and regeneration.

XPure has developed an SMB system that can be operated both in fixed and expanded bed mode, so-called Expanded Bed Adsorption (EBA). This EBA mode features all individual steps of the SMB process cycle, operated in upflow / expanded bed mode, refer

to Figure 3.

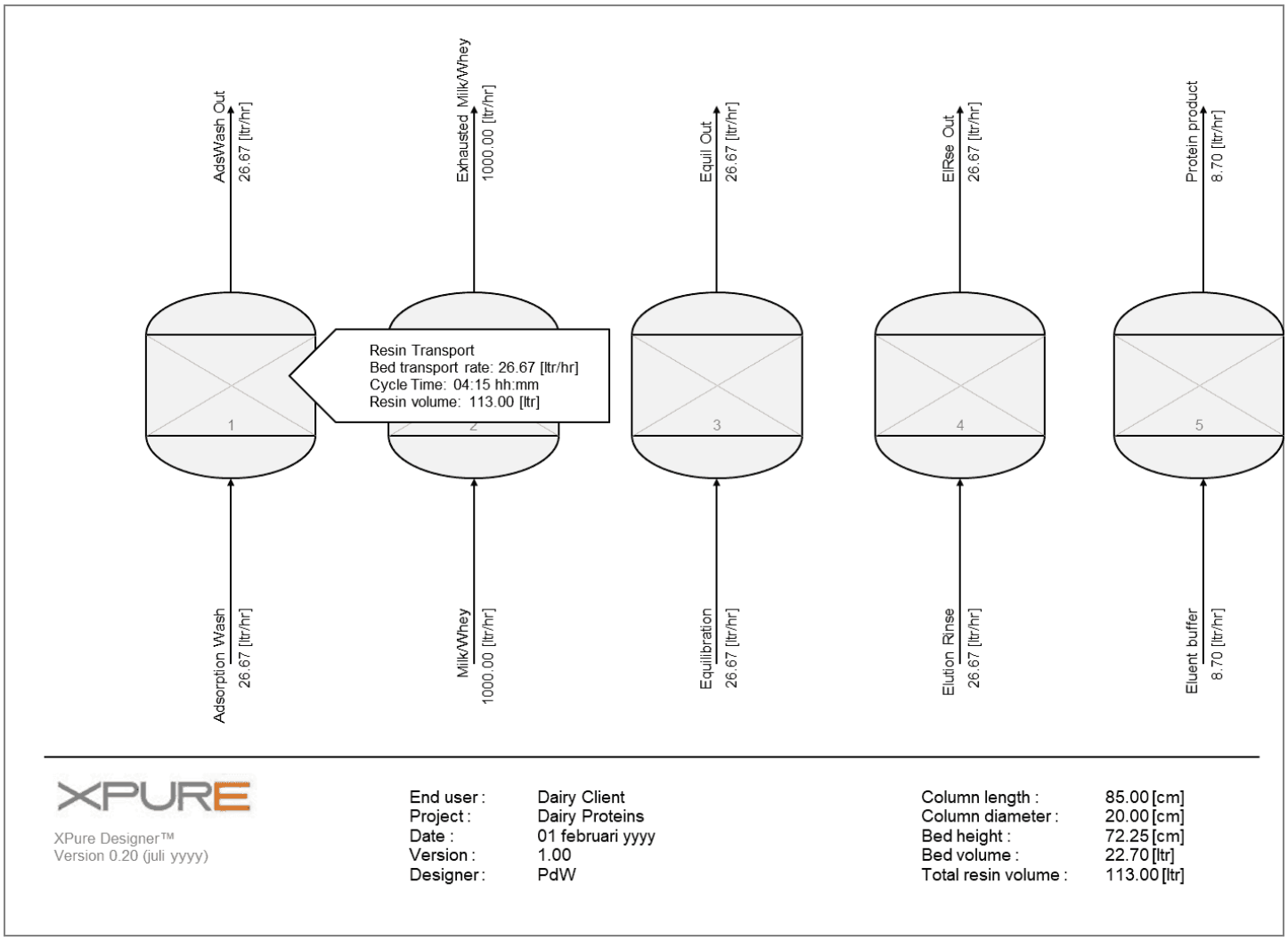

Figure 3. Typical SMB flow scheme for protein isolation/purification from dairy

Note: Regeneration has not been included, every column can be read as a zone consisting of multiple columns, either in series or parallel

Process cycle time and specific residence time in certain zones may be adapted to changing input parameters, e.g. protein content and composition.

Case studies have been done both for lacto-peroxidase and lactoferrin. Based on packed bed mode for daily milk production of 70 m^3 a continuous process for lactoferrin would result in significant cost reduction in cost of goods, refer to Figure 4. A significant part of the cost reduction in SMB-mode in relation to batch-mode chromatography can be related t0 consumables. It has further been found that skimming is necessary to reduce the residual fat content below 0.1 w-%, prior to applicable chromatography processes.

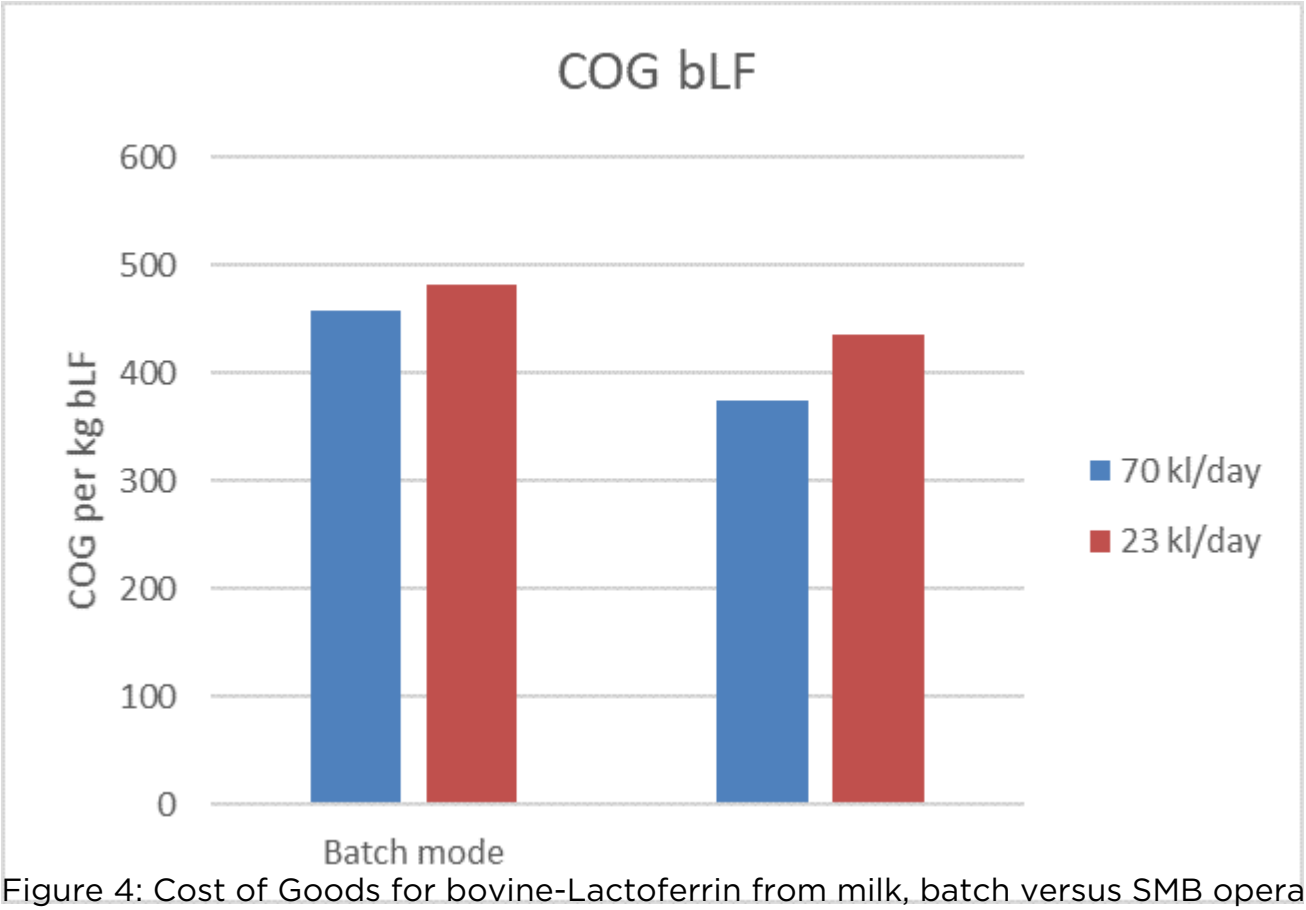

Figure 4: Cost of Goods for bovine-Lactoferrin from milk, batch versus SMB operation

XPure EBA-SMB has been successfully run on amino-acid containing fermentation broth without prior clarification or filtration. This process design can directly be translated to the milk protein application and could flexibly be fit in any process step that the skimmed milk goes through.

Conclusion

For large-scale dairy processes, cost reduction can be attained by a continuous operating mode. For the adsorption process, simulated moving bed chromatography (SMB) is a state-of-the-art technology that contributes to a high level of process automation, product quality and yield.

The XPure SMB-EBA offers the additional feature to process the unclarified (skimmed) milk directly, and so reducing operational and capital costs. For further information, you are invited to contact us or read more information about XPure's product portfolio and services.

References

[1] A. Haug, "Bovine milk in human nutrition – a review," Lipids in Health and Disease, vol. 6, no. 25, 2007.
[2] M. Malacarne, F. Martuzzi, A. Summer and P. Mariani, "Protein and fat composition of mare's milk," International Dairy Journal, vol. 12, no. 11, pp. 869-877, 2002.
[3] J. Billakanti, "Extraction of high-value minor proteins from milk," University of Canterbury, Christchurch, 2016.
[4] S. Séverin and W. Xia, "Milk Biologically Active Components," Critical Reviews in Food

Science and Nutrition, vol. 45, pp. 645-656, 2007.
[5] General Electric Health Care – Pharmaceuticals, “GE Health Care – Pharmaceuticals,” 2019. [Online]. Available: www.ge-healthcare.com.
[6] R. Noël, “Industrial processing and biotherapeutics,” Filtration+Separation, vol. 44, no. 3, pp. 26-28, 2007.