Bioprocess design for D-mannitol production from low-cost substrates

Part III. Product recovery

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Introduction and Objectives

D-Mannitol is a naturally occurring sugar alcohol with applications in the food, pharmaceutical, medical and chemical industries. Biological production of mannitol is receiving increasing attention due to the several drawbacks associated to the current chemical production. In the present project, we have designed a cost-effective bioprocess for the production of D-mannitol using beet molasses as carbon source. Mannitol can be easily recovered from the fermentation broth by crystallization; nevertheless, a proper design of the entire downstream procedure is key to achieve a viable and sustainable process.

The purpose of this project is to design an efficient and optimized procedure for the recovery of D-mannitol from bioconversion medium in two purity grades, in order to supply the market demand. A sustainable process design also includes the recovery and revaluation of the main by-product, lactic acid.

Downstream Input Stream

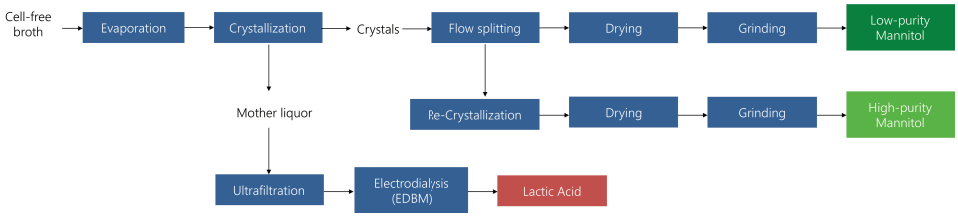
Mannitol is produced in a 21.8 m^3 (wv) MCRB by *Leuconostoc mesenteroides* ATCC-9135 as an extracellular product (see Part II: Upstream and Bioreaction). The main by-products in the cell-free broth are lactic acid, acetic acid and ethanol.

Cell-free broth

Component	kg/batch	g/L
Mannitol	2036.60	99.69
Lactic acid	568.14	27.81
Acetic acid	370.06	18.11
Ethanol	20.68	1.01

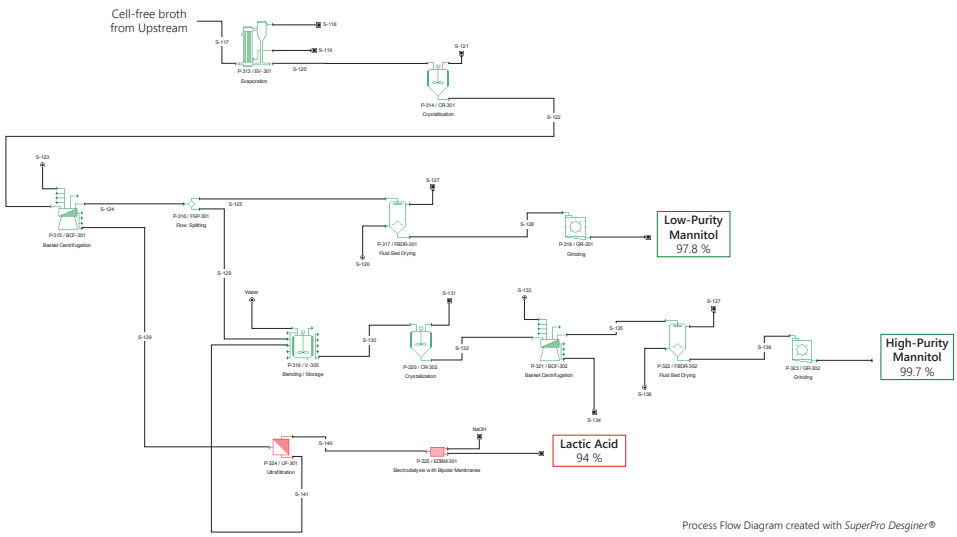
Note that lactic acid represents almost a 30% of mannitol production. For this reason, a strategy to recover it has also been designed.

Block Flow Diagram



Recovery of mannitol is based on its low solubility on water, which is about 180g/L (25ºC). This property allows to separate it from the other compounds by crystallization. The process is designed to obtain two categories of mannitol: 75% low-purity and 25% high-purity. Electrodialysis with bipolar membranes (EDBM) is used to obtain lactic acid from the side stream.

Process Flow Diagram



Process Flow Diagram created with *SuperPro Desginer®*

Mannitol recovery

Main Operations	Yield (%)
Crystallization	80
Basket Centrifugation	92
Re-Crystallization	95
Overall downstream	96

Lactic acid recovery

Main Operations	Yield (%)
Ultrafiltration	91
EDBM	96
Overall downstream	82

Quality by Design (QbD) and Process Analytical Technologies (PAT) implementation

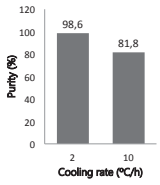
Product and process undertanding are the key elements when establishing a QbD approach. For this purpose, control strategies by means of PAT are implemented to ensure product quality and operation efficacy in every stage of the development:

- Purity of crystals: HPLC
- Multi-Effect Evaporation: pressure and temperature
- Crystallization: supersaturation and cooling rate
- EDBM: current efficency and membrane fouling
- Integration of EDBM operation and pH control in the bioreactor

Mannitol Recovery: Crystallization

Two crystallization procedures are performed in which a supersaturated solution of mannitol is cooled down to form crystals. In the first operation, low purity crystals for bulk purposes are obtained and a small fraction is separated to be re-crystallized, eventually isolating crystals of high purity.

Cooling rate and filtration time are the main factors affecting purity.

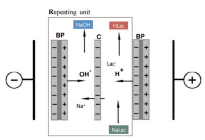


As a compromise between purity and productivity, cooling rates of 10ºC/h and 8.5 ºC/h have been chosen, improving purity with longer filtration times.

Lactic Acid Recovery: EDBM

Lactic acid exists in the fermentation broth as sodium lactate. In order to obtain the acid form, an electrodialysis technology is used. EDBM produces organic acids via water splitting in bipolar membranes.

The two-compartment configuration with H^+/M^- substitution has been chosen for its effectiveness when producing weak acids and its low energy consumption.



EDBM Operation Details

Energy consumption	0.88 kW·kg⁻
Conversion ratio	96 %
Membrane life	20,000 h
Membrane cost	0.09 $/kg

The alkali liquor is used for the pH adjustment in the bioreactor. To this end, current density must be carefully arranged in order to meet the demand of the bioreactor.

Integration between the bioconversion process and EDBM becomes productive, economically favorable and environmentally

Results and Conclusions

Product details

Product	kg/batch	tpy	Purity (%)
Mannitol low purity	1,453.97	3,016	97.8
Mannitol high purity	506.47	1,051	99.7
Total mannitol	1,960.44	4,067	-
Lactic acid	467.51	970	94

Crystals of mannitol can be efficiently recovered from the bioconversion broth by performing the designed downstream procedure. Mannitol is recovered with a 96% yield and reaching the two target crystal purity grades. The design also allows the recovery of lactic acid from the side stream with a 82% yield.

Two aspects are worth to conclude: (1) re-crystallization is necessary to obtain high purity crystals and (2) an strategy for the recovery of lactic acid is key to make the process sustainable. A future approach to the design may include the addition of a ion-exchange column to increase purity of lactic acid.

Selected references

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