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

Part IV. Project Analysis and Next Steps

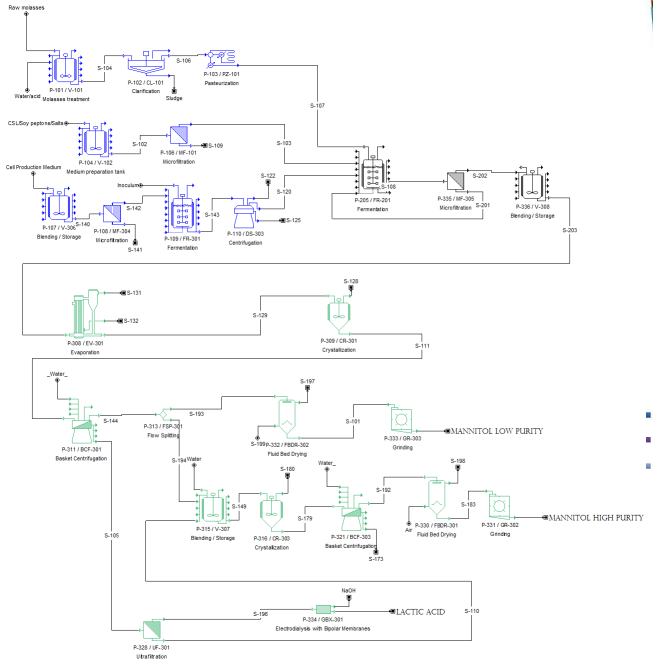
Bernat Coll, Ivette Parera, **Héctor Sangüesa**, Albert Serrano
Treball de Fi de Grau. Grau en Biotecnologia - Universitat Autònoma de Barcelona. June 2014

Universitat Autònoma de Barcelona

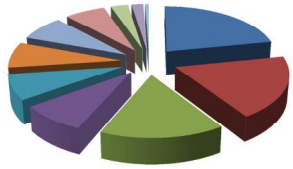
Introduction and Objectives

This project tries to demonstrate the feasibility of a plant destined to the biosynthesis of D-mannitol, a glucid type polyalcohol with important applications in the pharmaceutical and food sector. Its global production is 50,000 tones/year. The detailed project, located in the area of Tarragona (Spain), is a pioneer in the use of lactic acid bacteria to ferment molasses and produce mannitol. This represent an economical, environmental and social sustainable process in the production, facing traditional chemical synthesis of this sugar. Its challenge, however, is the achievement of a high product purity maintaining that economic profitability using a cheap source.

Process Flow Diagram and Cost Breakdown

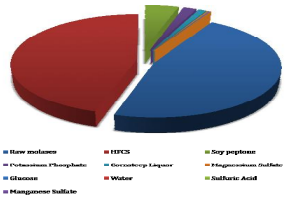


D-Mannitol Production Process Flow Diagram, created with *SuperPro Designer (R)*

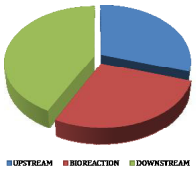


Fixed Capital Costs Breakdown

Annual Operating Costs Breakdown



Raw Materials Annual Cost Breakdown



Cost Breakdown, by Section

The upstream part consists of the clarification and sterilization of the beet molasses used as carbon source; and also it consists of the preparation of the media for the bioconversion of fructose into mannitol and the culture growth to generate the inoculum.

Cells producing mannitol work in resting state and are immobilized on a membrane. D-mannitol higher and lower purities are 99.4% and 97.8%, respectively.

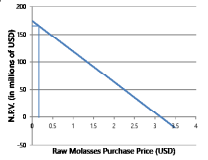
Downstream part comprises the crystallizations performed to separate the two kinds of D-mannitol; and, also, it consists of the part related to the purification of L-lactic acid by electrodialysis.

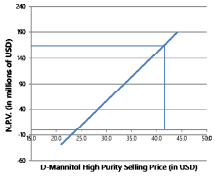
Profitability Analysis

The plant is located in Spain, so it would benefit from affordable prices to import beet molasses while allowing us to place the plant in a country where economy is expected to experience a high growth. Economic data, setting the payback period in less than 3 years, can ensure that the process will be able to generate profits during the next 9 years of operation. Sensitivity analysis confirms a strong process

Project Totals	
Investment	98,295,000 $
Annual Operating Cost	34,404,000 $
Main Annual Revenues	49,945,000 $
Other Annual Revenues	17,328,766 $
Total Annual Revenues	67,274,000 $
Unit Production Cost (*Mannitol Higher Purities*)	28.93 $/Kg
Unit Production Revenue (*Total*)	56.57 $/Kg
Project Indices	
Gross Margin	48.86 %
ROI	41.10 %
Payback Time	2.43 years
I.R.R. (after tax application)	25.23 %
N P V (at 4%)	169,764,000 $

Executive Analysis of the Plant and Economic Sensitivities to main bottlenecks



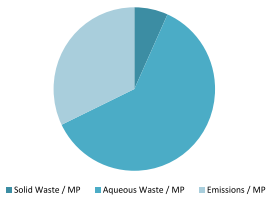


It could be concluded that the production of mannitol by fermentation of molasses is a viable process based on technologies sufficiently tested. The recommendation to possible investors is to proceed in the research of the necessary capital to build the plant.

Environmental Analysis

The environmental management plan is based on compliance with the hierarchy of practices regarding waste management established by the Directive 2008/98/EC of the European Union:

1-Prevention
2-Minimization
3-Reuse
4-Treatment



SOLID WASTE
The stream composition of the solids produced in the clarification of molasses makes the option chosen for its elimination is controlled direct discharge.

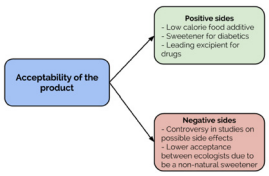
AQUEOUS WASTE
Liquid waste represent the majority of plant residues. They come from different streams. Those streams represent >80% of total waste. Given its high organic load, determined from the values of COD and TOC - will be treated in a municipal treatment plant.

GASEOUS WASTE
The emissions from the first evaporator contains water, acetic acid and ethanol. The last two are volatile compounds, and despite their low concentrations, they should respect the odorant limits.

Social Analysis

The sustainability of the plant in the social sphere is based on:

- Quality work respecting international standards
- Job creation respecting Spanish legislation
- Proper training of employees
- Student training offering internships and Industrial PhD programmes
- Potential technological innovation and business promotion
- Manufacturing a product that is used both as a sweetener and a therapeutic agent



Conclusions

- Production of mannitol by fermentation of molasses is a **viable process** based on technologies sufficiently tested.
- The project is economically, socially and environmentally **sustainable**.
- The plant is economically **strong** and resistant to fluctuations in pricing.
- Exploiting all the reaction products may be a challenge in the future.

Selected references

Saha, B. ; Racine, F. (2011) Biotechnological production of mannitol and its applications. *Appl Microbiol Biotechnol* 89:879–891

von Weymarn, N. ; Kiviharju, K. ; Jääskeläinen, S. ; Leisola, M. (2003) Scale-up of a new bacterial mannitol production process. *Biotechnol Prog* 19: 815–821

Sheelendra Mangal Bhatt, Anand Mohan, and Suresh Kumar Srivastava (2013), Challenges in Enzymatic Route of Mannitol Production, *ISRN Biotechnology*, vol. 2013, Article ID 914187, 13 pages.

What's Next?

METABOLIC FLUX OPTIMIZATION This technique is used to examine production and consumption rates of metabolites in the mannitol production metabolic system. With the determination in silico of the possible effect of changing several steps in the metabolism of *Leuconostoc mesenteroides* mannitol bioconversion pathway, it could be possible to decrease or even remove the non-profitable products appearing during the bioreaction.

POTENTIAL
- Simplification of the downstream processing of the product
- Reduction of aqueous and gaseous wastes
- Improvement of mannitol productivity in the bioconversion

DOWNSIDES
- Use of a non-GRAS bacterial strain
- Unexpected results might require further research

OTHER POSSIBLE IMPROVEMENTS

- Separation of acetic acid for less waste treatment costs
- Change the immobilization system