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# Simulation Of Xylitol Production: A Review

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**Abstract:** This paper reviews a recent research development on simulations biological conversion of hemicellulosic biomass towards commercial scale production of xylitol by taking advantage of power of biotechnology. Xylitol is a five-carbon sugar alcohol that is found in small quantities in many fruits and vegetables. Xylitol is nearly as sweet as table sugar sucrose. Unlike sucrose, xylitol is well tolerated by diabetics and does not cause tooth decay. As a consequence, xylitol is in demand in sugar-free confectionery. In the present paper, a continuous enzyme-catalyzed xylitol commercial scale using the lignocellulosic biomass,was simulated by a commercial bioprocess simulator (SuperPro Designer®). In continuous mode, the objective is to maximize the amount of desired product per unit time, whereas in batch or fed-batch modes the goal is to maximize product at the end of each batch, leading to control challenges of a different nature. The development of computer-aided design tools for bioprocessing began in the mid 1980s. Mathematical modelling (in the subsequent text simply modelling) and simulation are widely used for optimally designing and operating production facilities in most industrial sectors such as the chemical and biotechnological process industries. Study of xylitol in continuous process using enzymes is too complex to be given tractable mathematical formulations. In the context of optimizing simulations, a "complex evaluation" refers to the execution of a simulation model (which can be extremely time-consuming). Established tool simulators for these processes include: Aspen Plus (from Aspen Technology, Inc.), ChemCAD (from Chemstations, Inc.), Aspen HYSYS (from Hyprotech, Ltd./AEA Engineering Software), and PRO/II (from Simulation Sciences, Inc.). The three bioprocess simulators, Aspen Plus, HYSYS and SuperPro Designer®, will be review and compared in this research. The proposed simulator; SuperPro Designer will be selected as the best simulator tool for production of xylitol in commercial scale.

**Key words:** *xylitol; bioprocessing; simulation; SuperPro Designer*

## INTRODUCTION

The low cost and renewable nature of lignocellulosic biomass such as sugarcane bagasse, wheat straw, rice straw, corn stover, etc. represent the ideal feedstock for their conversion into value-added products by biotechnological routes. This lignocellulosic biomass is the most promising feedstock considering its great availability and low cost; constituted primarily of lignin, hemicellulose(s) and cellulose (Cardona, 2007). The carbohydrate fraction (hemicellulose and cellulose) can be depolymerised into sugars which act as a primary carbon source for the microbial biocatalysts for the production of xylitol, ethanol, organic acids, industrial enzymes, etc (Chandel, 2007). Xylitol is a five-carbon sugar alcohol that is found in small quantities in many fruits and vegetables (Sirisansaneeyakul, 2009). It is one of the most expensive polyol sweeteners and has specific health claims in the world market. It is suitable for diabetes, recommended for oral health and paranteral nutrition. On an industrial scale, xylitol is currently produced through chemical reduction of xylose derived from saw dust and sugarcane baggase hemicellulose hydrolysate. It is relatively expensive by about \$7 $kg^{-1}$ comparatively with other natural sweeteners (Rao, 2006).

In the world of software development, systems often begin as simple and well understood, and normally contain elements such as creation of process flow diagrams, and generation of material and energy balances. To meet the ultimate requirements, models become more complex to include calculations such as equipment sizing, and capital and operating cost estimation. Simulation is becoming a requirement for all major process designs. Using simulation, bioprocess engineers can identify potential problems ahead of time and take corrective action. A common use for bioprocess simulation is for process mapping and cost analysis. Process mapping enables investigators to analyze or predict the action of organisms in response to certain specific inputs. Cost analysis

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identifies the expensive process steps and other cost items that have major impacts overall process economics. In addition, one of the challenges for users when using such simulation tool is accumulation of the appropriate data. Simulation can only be run until all the data is collected and put into the system (Thien, 2011). The first step in building a simulation model is collection of information about the process.

Process simulation and modelling is the application of a range of software tools to analyse individual unit operations (or process stages) and their relationships within the overall process. Process simulation is defined as the utilization of computer software resources to develop mathematical models for the construction of an accurate, representative model of a chemical process in order to understand its actual behavior during regular plant operations (Diwekar, 2005). These tools can be used at all stages of process development, from conceptual design, through process operation and optimization. Process simulation of xylitol using enzymes in continuous production will study. Today the largest supplier of simulation software to the biotech and pharmaceutical industry is Microsoft, which offers several basic software tools that can be used for simulation: Visio® - Constructs flow sheets with a drawing package; Excel® - Process calculations are performed with spreadsheets and reported graphically; and Project® - Constructs process schedules and labor assignments. The disadvantage of these tools is that they are not designed for bioprocess simulation.

A bioprocess is a special type of chemical process that produces biochemical products (e.g. antibiotics, xylitol, amino acids, etc.) from microorganisms or enzymes. Bioprocesses share some common features with general chemical processes, but differ in their kinetics of product formation, process structure (unit operations and procedures) and operating constraints (Brunet, 2012). Most biochemical products are produced by fermentation. In fermentation, the products are formed by catalysts that catalyse their own synthesis. Enzymes are biological catalysts and are produced as secondary metabolites of enzyme fermentation (Saarel.U., 2003). Study of xylitol in continuous process using enzymes is too complex to be given tractable mathematical formulations. As research by (Barradas, 2010), where biological production of xylitol from xylose it has been demonstrated that a low-level supply of oxygen to the culture (~0.1 volume of air per volume of culture medium per minute) yields an increase of extracellular accumulated xylitol up to 0.65 $g_{xylitol}\ g_{xylose}^{-1}$ by using software Matlab© Release 12 (Math Works, Inc.). Mathematical function contains multiple nonlinearities, combinatorial relationships and uncertainties inaccessible to modeling except by resorting to more comprehensive tools like computer simulation (Fernandez. J. A., 2008). The complexities and uncertainties in these systems are the primary reason that simulation is often chosen as a basis for handling the decision problems associated with them.

Process simulators offer the opportunity to shorten the time required for process development. They allow comparison of process alternatives on a consistent basis so that a large number of process ideas can be synthesised and analysed interactively in a short time (Tochampa, 2005). Simulation of integrated processes also enables the study of interactions that exist between upstream and downstream processes (Rouf, 2001). To assess the technological feasibility and obtain material and energy balances for a preliminary economic analysis, complete process simulations were performed. Despite some expected differences between a process simulation and real-life operation, process simulators are commonly used to provide reliable information on process operation, owing to their vast component libraries, comprehensive thermodynamic packages and advanced computational methods.

***Aspen Plus:***

Advanced System for Process Engineering (ASPEN) is a process modelling software suite designed for batch and continuous simulation (Farid, 2007). For continuous processes, it is possible to use the conventional Aspen Plus simulator but this requires customization for many bioprocess operations (Gosling, 2005). Aspen Plus (developed by Aspen Technology Incorporated), is a steady-state sequential modular simulation package used as a tool to simulate and design chemical processes. It offers the possibility to simulate various combinations of unit operations such as reactors, distillation towers, heat exchangers and compressors using the built-in process models (Verhoef, 2008). The steady-state is a characteristic of a condition, such as value, rate, periodicity, or amplitude, exhibiting only negligible change over an arbitrary long period of time (infinite). It is one of the most important process simulators in the chemical industry and oil refining process, includes standard, ideal unit operations, such as Gibbs reaction and heat exchange models (Ye, 2009).

Essentially, the Aspen Plus simulator is made up of: i) a rich databank with pure components, binary parameters, reactions constants, etc; ii) a vast number of thermodynamic models for the physical and transport properties calculation; iii) a unit operation model (U.O.M). It overall model consists of 33 unit operation blocks, one design specification and five Fortran Calculator blocks (Cimini, 2005; Somers, 2011). It also includes a library of standard unit operation blocks (eg. pumps, heat exchanger, reactors, splitters), which represent process taking place in an actual chemical plant (Yun, 2013). Aspen Plus includes many basic units, such as distillation towers, drums, pumps, and heat exchangers. It does not include many specialty unit operations that are used for particular industries, such as conveyor belts or equipment necessary for the pre-treatment of solids (Bowen, 2010). Aspen Plus includes a wide variety of thermodynamic packages, which gives the user many options as to

which will most accurately model any process (Haydary, 2009).

Aspen Plus can be a difficult program to learn and work with because it contains so much information. This makes the program complicated, but also an incredibly valuable resource. When given inappropriate information about a system Aspen Plus will sometimes give nonsensical results, but more often it will simply give an error message. This often catches user mistakes, which is helpful, if sometimes frustrating. Considerable knowledge of thermodynamics, chemical equipment and processes is necessary to successfully work with Aspen Plus, or the user will end up with many errors and little information. A Microsoft Excel VBA tool has been developed to help the engineer when performing energy and thermoeconomic analyses of processes that have been simulated using Aspen Plus. The application is needed because Aspen Plus does not have an integrated function to calculate the energy of the streams presented in a process, nor to evaluate thermoeconomic costs, although it gives enough thermodynamic data and can also estimate capital costs (Querol, 2011).

After the completion of process modelling and calculations of mass and energy balances, the simulation results can be generated and sent to another Aspen utility, Aspen Icarus Process Evaluator or Aspen IPE, which is specialized for further economical evaluations (Kumar, 2010). Aspen IPE is designed to automate the preparation of detailed designs, estimates, investment analysis and schedules from minimum scope definition, whether from process simulation results or sized equipment lists (Yu, 2011; Magnusson, 2005). From study of (Posada, 2011), the economic analysis of poly-3-hydroxybutyrate (PHB) production from glyceol was estimated by using Aspen Icarus. In economic terms the best technological scheme for PHB production from crude glycerol includes three important features as follows: (i) purification of crude glycerol up to 98 wt%, (ii) a two continuous fermentation stages, with operating times of 21 and 22.5, h respectively and finally (iii) the PHB recovering performed with the Downstream Process I, which is similar to the BIOPOL flow sheet.

Other disadvantages of Aspen Plus are the kinetic and models must define for simulation and in some cases it is hard to converge. The model library of Aspen Plus is limited in type and number of models of process unit operations (Larrson, 2011). The properties for components not included in the Aspen Plus database were obtained from a custom property database developed by National Renewable Energy Laboratory (NREL). Heat, work, and material stream flows, as well as process conditions from Aspen Plus simulations are imported into Excel for use in the economic analysis.

Some research had used Aspen Plus for conversion of glycerol to added-value components. Because of both the petrochemical character of Aspen Plus and its modular-sequential approach, there are not available kinetic models describing the biotechnological processes such as fermentations or enzymatic reactions. Therefore, it is required to work with the available interface between Aspen Plus and Excel. The specific compounds involved in the different processes of raw glycerol conversion to added-value products such as: free fatty acids, alkyl esters, proteins, salts, cell mass strains, enzymes, and other complex molecules produced by reactive-extractive process are not available on the Aspen Plus Database (Duque, 2011).

Same study also by (Limniyakul, 2007), where due to unavailable structure of reactants and products in the library of Aspen Plus, the major components of Jatropha which were triglyceride, diglyceride and monoglyceride of oleic and linoleic acid were draw by GaussViewW. After drawing, the structures were optimized by GAUSSIAN 03W in order to obtain the stable structure. All of these structures were used in Aspen Plus for finding the parameter such as boiling point, molecular weight, heat capacity, coefficients for antoine equation. The simultaneous production of bioethanol and xylitol from rye straw is investigated by (Franceschin, 2011) that was then implemented using the software Aspen Plus. The optimization of the process energy duties is carried out by means of the pinch technology analysis. Mass balances from the simulation are used in order to size the equipment and calculate the capital investment. As a result, 736 kg/h of xylitol, 82 kg/h of cells, 52 kg/h of ethanol are obtained; in the product also arabitol, $CO_2$, unreacted xylose and arabinose are present, according to the yields reported.

***Aspen HYSYS:***

Aspen HYSYS (HYprotech SYStem) by Aspen Technology is one of the major process simulators that are widely used in chemical and thermodynamic process industries today. It also specializes on steady state analysis same as Aspen Plus (Dash, 2008). Aspen HYSYS is designed specifically for a continuous process of multiple process units. It is not designed to handle batch, semi-batch, or semi-continuous process units (Hanyak, 2012). Aspen HYSYS had to advantage to export the process design to Aspen Icarus Process Evaluator (Aspen IPE) for cost estimation. The cost estimation was based on equipment costs given by Aspen IPE, raw material costs provided by user and utility costs from Aspen IPE database. Otherwise, the thermodynamic packages incorporated in Aspen HYSYS had limited thermodynamic data on the biomass components.

A difficulty in modelling the bioprocesses using HYSYS process simulation software was to obtain the thermodynamic package that incorporated biological materials in the design. The fermentation, anaerobic digestion and transesterification processes had least thermodynamics properties available for modelling. Most of the biomass components were manually entered using the user-defined method and the structures of each compound were constructed using standard software (SYMYX Draw 3.2). Property estimation methods for

HYSYS were used to predict the interaction parameters. Conversion reactors were used for single reactions. Tanks were used for multiple reactions, as conversion reactors in HYSYS were incapable of handling multiple reactions.

Study by (West, 2008), continuous biodiesel processes by using waste vegetable oil feedstock were designed and simulated in HYSYS. HYSYS was selected as a process simulator for both its simulation capabilities and its ability to incorporate calculations using the spreadsheet tool .Components not available in the HYSYS library was specified using the ‘‘Hypo Manager” tool. However, specification of a component requires input of a number of properties, such as normal boiling point, density, molecular weight, as well as the critical properties of the substance were obtained from the ASPEN Plus component library. The initial cost estimations of the processes were also exported to ICARUS Process Evaluator (IPE). As study by (Sengupta, 2010), the economic analysis was also performed in ICARUS for process for fermentation of biomass to ethanol. The design has three sections, a pre-treatment section, a fermentation section and a purification section. The total project capital cost was $20 million. The operating cost was $81 million per year which included raw material costs of $54 million per year. A minimum product selling price computed from the operating cost was set at $1.52/gallon for ethanol.

For process economics, Aspen In-Plant Cost Estimator was used. It has been used for over 30 years in commercial plants and engineering designs, and provides more accurate estimation. Aspen In-Plant Cost Estimator provides specifications for detailed design, estimation and economic data, allowing quick modifications of the process equipment and sensitivity analysis. The alkali-catalyzed process using fresh vegetable oil had the lowest total capital investment, but the supercritical process was the most economically feasible overall, providing a lower manufacturing cost and higher net present value and a discounted cash flow rate of return (Lee, 2011).

***SuperPro Designer:***

SuperPro Designer is a professional process simulator developed by Intelligen Incorporated, which facilitates modeling, evaluation and optimization of integrated processes in a wide range of industries such as in pharmaceutical industries, agrochemicals, food processes, water purification and end-of-pipe treatment processes. It is also designed specifically for processes including biological components (Athimulam, 2006). It combines the drawing, calculation and scheduling features of the three Microsoft packages; Excel, Project and Visio into a single, moderately priced package (Gosling, 2003). SuperPro Designer can handle batch and continuous processes equally well; whereas the other three tools are practically limited to batch or continuous processes. (Petrides, 2002). Besides process modeling, Superpro Designer has many advanced convenient features such as material and energy balances calculations, extensive databases for chemical component and mixture as well as equipment and resource, equipment sizing and costing, thorough process economics, waste stream characterization, etc (Ernst, 1996). This program is also capable of providing equipment cost used for the plant (Qureshi, 2013). All these features are quite useful when analysing the process models (Yu, 2011).

SuperPro Designer includes unit operations specific to biological operations, such as fermentors and strainers that Aspen lacks. As study by (Malakahmad, 2013; Vucˇurovi, 2012), the biodegradation process of a small-scale anaerobic bioreactor was simulated using SuperPro Designer® and process simulation flow sheet, materials registration and process reactions were conducted during model setup However, SuperPro Designer has significantly less rigorous thermodynamic packages and far less information about components in databases. This often forces the user to research outside of the program in order to gather enough information for a successful simulation. SuperPro Designer enables an easy and user-friendly approach than Aspen Plus (Biwer, 2004). However, much more care is required of the user to successfully run a simulation in SuperPro Designer because it will give physically impossible results. SuperPro Designer also includes a costing feature that certain versions of Aspen Plus lack. It is very helpful to get an approximate cost of equipment and plant operating cost as the simulation is completed (Bowen, 2010).

SuperPro Designer also offers a database feature to log equipment and utility capacities. This package has the added advantage that it was specifically developed for simulation of bioprocess unit operations and processes. It is user friendly and set up to capture the unique unit operational data requirements of biological processes (Gosling, *et. al.*, 2003). SuperPro Designer is relatively simple and fast to set up a flowsheet for an entire process where it does not require integration of differential equations (Kawachale, 2011). This shortens the computation time and enables the user to evaluate a larger number of scenarios in a shorter period (Trifkovic, 2000). It also had default values for many of the input data required for simulation that could be used when experimental data were not readily available or as a reference to check against. However, one of the key disadvantages was that it could not capture the desired dynamic behaviour capabilities related to time-dependent operations (Farid, 2007). The main advantages of this simulator consist in a large data base of specific chemical compounds and unit operations, and the evaluation of economical and ecological process performance indexes (Taras, 2011). The unit operation models in SuperPro Designer are not very complex. If more accurate results are desired, the solutions obtained with SuperPro Designer at the large scale of the entire process can be refined

at the small scale of unit operations. Most of all chemical and biochemical engineering simulators are not equipped with optimization tools. In very few simulators (e.g. Aspen Plus) there are some optimization tools, but the formulation of optimization problems and techniques are severely imposed. SuperPro Designer doesn't contain any optimization tools for optimization purposes; this was linked with Matlab using automation Client-server of Matlab Component Object Module (COM) technology (Woinoraso, 2009).

A study by (Rouf, 2001), production of tissue plasminogen activator (t-PA) from Chinese hamster ovary (CHO) cells are using Aspen BPS$^{TM}$ and SuperPro Designer®. However, the economic evaluator of Aspen BPS$^{TM}$, which has been derived from the chemical process simulator AspenPlus$^{TM}$, is geared more towards chemical processes. Its calculation mode is rigorous and requires a lot of data from a real project to make appropriate use of the available options. SuperPro Designer® on the other hand, has an economic evaluator that is specifically developed for bioprocesses. It is simple and easy to use. (Vlysidis, 2011) have design and simulation in HYSYS of biodiesel processes involving two different feedstocks (virgin vegetable oil and waste cooking oil) catalysed by two different catalysts (alkali and acid catalyst). It has technically and economically assessed and compared these schemes. They have performed sensitivity analysis and they have indicated that the capacity and the prices of feedstock and products have a great impact on the plant's profitability. A similar study has studied and compared the economic viability of three biodiesel scenarios that use different catalysts by using the process simulation software SuperPro.

Research by (Kawachale, 2011), the membrane based processes for the recovery of isoflavones from red clover flowers shows purchasing cost of $3/kg and $0.75/kg was assumed for dry flowers and ethanol respectively. Also, in order to keep the equipment costs lower, the ultrafiltration modules in the membrane based processes were modelled to be constructed out of plastic, which was appropriate for moderate pressure operations (550 kPa). The processes were evaluated for a 15 year project life time, assuming the plant to be operational for 330 days/year. Alternatively, in a fed-batch process a constant substrate concentration can be maintained during the fermentation. C. boidinii NRRL Y-17231 fermentations achieved 75% theoretical xylitol yield in a fed-batch process compared to 53% theoretical yield in batch process. The maximum productivity (0.46 g/l.h) in the fed-batch process was twice the maximum productivity observed in the batch process (Rangaswamy, 2003).

***Conclusions:***

Process simulation is an important tool in bioprocess industry. The benefits of simulation for bioprocess improvement, assessment and expand have been realized previously. Basically, process development is shortened by application of process models and simulators. In simulation, the tasks provided such as; represent the entire process on the computer, perform material and energy balances, estimate the size of equipment, estimate the cycle time of the process and perform cost analysis. SuperPro Designer®is windows-based software which can be used to design and assess manufacturing of the product and decide on treatment methods, pollution prevention and waste minimization approaches, at the same time. Application of SuperPro Designer® has been reported for process simulation in production of xylitol, pyruvic acid, monitoring of biopharmaceutical facility, fuel ethanol production and biodiesel production costs analysis. As a conclusion, Super Pro Designer can provide sophisticated modeling for bioprocess for a batch and continuous processes.

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