Student Project Paper for Final Class

University of Baghdad	Al-Khwarizmi college of Engineering	Biochemical Engineering Dept.	Project index:1	Date 25-6-2012
Project Name	Production of Tissue Plasminogen Activator (tPA)			
Student Name	Faten Khalid	Ghuffran Muafaq		
Supervisor Name	Dr. Khalid W. Hameed			

Aim of the work

Plant Design of Manufacturing of Tissue Plasminogen Activator, Including: Material balance, Energy balance, layout of plant and design of some equipment in the plant.

Summary

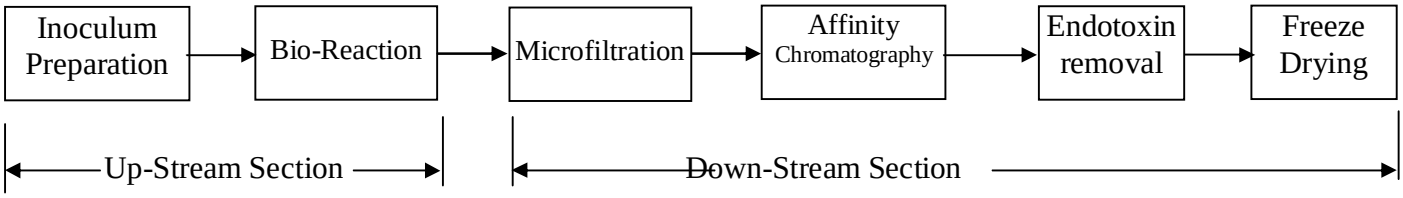
Tissue plasminogen activator (tPA) is a recombinant, therapeutic protein comprised of 562 amino acids. tPA activates plasminogen – **t**o plasmin (an enzyme), plasmin dissolves fibrin formations that hold blood clots in place blood flow is re-established once the clot blockage dissolves. Important for patients with heart attacks (myocardial infarction) or stroke. The production capacity of plant is 40 kg/year where the dose required for patient is 100 mg. The plant consists of two sections; upstream section which is split into two sub-sections, the inoculum preparation section and the bio-reaction section, and downstream section. It has calculated the material balance and energy balance and design of some equipments in the plant. The plant operates around the clock for 350 days a year. A new batch is initiated every 14 day resulting in 25 batches per year. In addition to the production bioreactor, a seed train is necessary to provide the needed amount of cells.

The inoculum is prepared in laboratory as follows: tPA-DNA sequence + CHO cells → selected tPA-CHO cells

The Inoculum used for bio-reaction: tPA-CHO cells + HyQ PF-CHO media + O2 → Increased cell nos. + tPA

tPA protein must be recovered from other proteins, cell debris, media, water, and gas emissions. Proteins lose activity (denature) at temperatures above ~ 0°C. Hence - entire separation process designed to operate at 4°C, slightly above freezing point of water.

The plant can be represented by the following block diagram:



Discussion

It can be seen that the production capacity of the plant is relatively low (40 kg/year), that is because of low needed for patient (100 mg/dose) , i.e. each 1 kg of product is enough for 10000 patient. The media of fermentation is at 4^{o}C and must be raised to fermentation temperature, and the fermentation broth result is at 37^{o}C and must be reduce to 4^{o}C, so the energy of fermentation broth is used to raised the temperature of media and at the same time the fermentation broth temperature is reduced, that can achieved by inserting a heat exchanger in the plant. There is another way to produce tPA using *E.Coli* bacteria with less time than the present method, but the product is intracellular and lower than the present.

Future Work

- Construct the foundation and piping system of the plant.
- Design the remaining of the equipments which not considered in this project.
- Suggest treatment the waste of the plant.