Effect of organic antifoam’s concentrations on filtration performance

S Mohamad Pauzi*, D Anak Halbert, S Azizi, N A A Ahmad, N Ahmad and F Marpani

Faculty of Chemical Engineering, Universiti Teknologi MARA

*syazana7932@uitm.edu.my

Abstract. The use of membranes is widely common in bioprocess industry to separate constituents of a liquid, especially during cell clarification process. Many has opted for normal flow filtration mode for this process due to the ease of handling of this technique as compared to tangential flow filtration. Meanwhile, antifoams are chemicals used in upstream process to eliminate the formation of foam throughout the course. It is normally used in conjunction with a nutrient rich broth that is used as a media to cultivate the cells. Some has claimed that antifoam may lead to premature membrane fouling, but some reported that the presence of antifoam may assist and improve the flux rate of the filtration process. This study investigates the effects of organic antifoam presence in a cell-free media on the performance of the filtration process, specifically normal flow filtration process. It was discovered that the presence of organic antifoam may be significant at 1.0% concentration of antifoam loaded in the sample which gives filtration capacity of 250L/m2 while filtration capacity was reported to be at 330L/m2 for samples containing 0.2% and 0.6% antifoam concentration. The flux rate profile has lower percentage reduction that ranges from 18% to 33% which resulted to final flux rate of approximately 700 – 800LMH for initial flux rate of 1000LMH and 27% to 46% reduction that lead to final flux rate of approximately 1000 – 1500 LMH for initial flux rate of 2000LMH.

1. Introduction

Bioprocess industry generally involves two main processes – upstream process and downstream process. Upstream process aims to obtain the product of interest while downstream process’s goal is to obtain high purity product while maintaining high yield. The characteristics of the cell culture and the operating parameters used to maintain the cell culture had increased the tendency for the formation of foam [1 - 2] which may cause an increase in the operating costs [3 – 4].

Foam is defined as a dispersion of gas in liquid and comprises of tiny bubbles generated inside a liquid. Foaming occurs when these bubbles accumulate at the top of the liquid at faster rate than they decay. Because the volume fraction of foam is mainly gaseous, the bulk density is more of gas than liquid. It is said that true foaming is achieved when the liquid in between bubbles does not rupture but it thins down to a lamella. The distance between adjacent bubbles is small therefore it differs from common gas-liquid dispersion. Foams are thermodynamically unstable due to its high specific surface area relative to separated gas and liquid phase [5]. Foam formation always accompanies processes with fermentation due to the high foaming tendencies of solutions containing biomaterials [6]. Therefore, a form of foam control that maybe known as antifoam agents or defoamers is used to combat the formation of foam. The solubility of the antifoams is important to ensure the efficiency of foam deformation and one has claimed that increasing the hydrophobicity of the solution able to destabilize the foam [2].
However, this condition may not be favorable for filtration process thus choosing the suitable antifoam for a process is important to reduce fouling potential [7].

Different type of antifoam agents has been widely in the bioprocess industry that mostly involves silicone-based antifoam and emulsion containing antifoam. Few studies have been done to assess their effects towards the cell culture [8]. Previous work has reported that a silicone-based antifoam agent may lead to negative effects on the flux profile and loading capacity of Polyether Sulfone (PES) filter [9]. Although organic non-silicone-based antifoam was introduced, the usage in the cell culture has not been widely discussed.

Upon maturity of the cell culture where targeted product concentration is achieved, the product will be separated from the unwanted culture components [10]. Filtration process has been widely used in the downstream process of a lot of biological products especially in the development of drugs. It has two different modes of operation that are normal flow filtration (NFF) and tangential flow filtration (TFF) [11].

Normal flow filtration runs with feed flow directly into the membrane and it does not allow any recirculation or backwashing option thus fouling event is irreversible [12 – 13]. The fouling of a filtration membrane can occur either because of concentration polarization or cake formation [14] where both may affect the membrane pore size due to physical/chemical interactions with the filtration liquid [15]. A combination of membrane properties, operating conditions, and suspension characteristics influences the fouling rate [16]. A method of fouling caused by protein adsorption on the membrane surface considerably surges resistance to flow henceforth causing a decline in flux rate and efficiency [17].

The membranes used for filtration processes are semipermeable that it is selective to a certain constituent in a mixture [18]. The usage of Polyether Sulfone (PES) membranes are common due to its impressive stability [3] that is due to the alternating linkage of repeated ether and sulphone between aromatic rings giving the membrane good rigidity and excellent strength [19]. PES does have its drawbacks and a major one is that it is due to its hydrophobicity nature which has an affinity to fouling by protein rich mediums [20]. Nevertheless, increasing the hydrophilicity of the membrane may overcome the problem [21].

2. Methodology

In this study, the Lysogeny Broth (LB) broth used was from Merck. 10g of the broth was dissolved with 400 mL of distilled water to prepare fresh LB broth which was used immediately. The antifoam used was Antifoam 204 from Sigma Aldrich which is an organic non-silicone antifoam. To prepare media with 0.2%, 0.6% and 1.0% antifoam, 0.8, 2, and 4 mL of antifoam was added respectively to the fresh LB broth. A polyethersulfone (PES) membrane by Cobetter with a pore size of 0.2µm and a diameter of 47mm that make up to surface area 15.2cm² was used. The pump used was a Masterfrex peristaltic pump (Easy-Load II Head) with tubing of size 15.

Constant-flow method where the initial flow rate based on specific operating flux rate was set on the pump. The time taken and differential pressure were recorded at certain filtrate interval to obtain the flux rate profile and the loading capacity of the membrane. Four sets of data were collected at initial flux rate of 1000LMH and 2000LMH at 0% v/v (control), 0.2% v/v, 0.6% v/v, and 1.0% v/v antifoam.

The membrane resistance was calculated based on resistance-in-series model as follows;

\[ R_{Tot} = \frac{\Delta P}{\mu J} \]  

Where \( R_{Tot} \) is the total membrane resistance, \( \Delta P \) is the differential pressure, \( \mu \) is the viscosity of the solution and \( J \) is the flux rate.
3. Results and Discussion

3.1 Flux rate profile

Figure 1 shows the flux rate profile for process run at initial flux rate of 1000LMH. The graph illustrates that there were noticeable decreases of flux rate for control sample and sample containing 1.0% antifoam where the calculated reductions of flux rate were 18% and 33% respectively. However, the were almost insignificant reduction of flux rate for samples containing 0.2% and 0.6% antifoam agent as it can be observed from the graph that the flux rate remain constant throughout the process. Meanwhile, Figure 2 displays the flux rate profile of 2000LMH initial flux rate. Similar patterns were detected as compared to the initial flux rate of 1000LMH where the flux rate reduction for sample containing 0.2% and 0.6% were almost insignificant although sample with 0.6% antifoam agent might have shown a more decremental effect as compared to sample containing 0.2% antifoam. The control sample and sample with 1.0% antifoam implicated approximate flux rate reductions of 27% and 46% respectively. Both results show that the flux rate reductions were almost 1.5 times higher than that of 1000LMH initial flux rate. Previous study [9] shows similar behavior higher flux rate when compared to lower flux rate. Nevertheless, the results of this study might have been better in terms of flux rate reduction where only control sample and sample with 1.0% antifoam have shown substantial effects for both initial flux rates – at 9% difference. Although one claimed that both silicone and organic non-silicone antifoam agent may pose similar attribute with regards to the decrease of flux rate [22], this study shows that organic non-silicone antifoam may lead to flux rate reduction at high concentration used. The components of the organic non-silicone antifoam agent consist of polypropylene based polyether dispersions that may interact with the hydrophobic components of the PES filter and indirectly increase the hydrophilicity of the membrane. Yet, higher concentrations of the antifoam agents possibly will increase the free hydrophobic components in the solution leading to sharp decrease in flux profile. It is also likely that the more organic interaction between the antifoam component and the PES filter membrane will accelerate the cake formation on the filter membrane. Apart from that, fouling may be minimized and properly controlled by maintaining the operating temperature above the cloud point which can be attained by using organic non-silicone antifoam as it is temperature-dependent while silicone-based antifoam may not have inverted cloud points that reported to have caused the fouling in filtration using polysulfone filters [7].

![Figure 1: Flux Rate Profile (Initial Flux rate: 1000LMH)](image-url)
3.2 Filtration capacity

Both Figure 3 and Figure 4 demonstrate the final filtration capacity for all runs are at approximately 330L/m² – the maximum filtrate volume that can be processed by the filter. However, sample with 1.0% antifoam agent for both initial flux rates poses filtration capacity at approximately 250L/m² that is about 24% reduction as compared to control sample. This result agrees with the resulted flux rate profile where the same samples have significant reduction of flux rate. This shows that the usage of high concentration of antifoam agent may not be favorable to filtration process. In addition to that, all samples with higher concentration that are of 0.6% and 1.0% of the antifoam agent resulted in higher membrane resistance. In Figure 3, the trendlines for filtration of samples containing 0.6% and 1.0% of the antifoam agent depict a sharp increase in the membrane resistance. This means that the fouling occurred continuously throughout the process. Although there is no sharp increase in membrane resistance for samples run at initial flux rate of 2000LMH in Figure 4, the membrane resistance of sample containing 0.6% and 1.0% antifoam agent is already high at the start of the process run which is around 0.015psi/LMH that is close to three times higher than that of control sample and sample containing 0.2% antifoam agent. While samples run at initial flux rate of 2000LMH do not have significant change throughout the process run, the risk of fouling is higher for samples containing 0.6% and 1.0% due to high starting membrane resistance. This can be seen from the result of sample containing 1.0% antifoam agent where the membrane resistance rapidly increases after about 250L/m² filtrate volume processed. The control sample in Figure 3 may display a contradict result as compared to Figure 4, but the membrane resistance has insignificant difference – approximately 0.001psi/LMH throughout the process run. It is important to assess the filtration capacity of a filter for scale up purpose to avoid wrong filter area selection and cost increment in the large-scale manufacturing process [23].

![Figure 2: Flux Rate Profile (Initial Flux rate: 2000LMH)](image_url)
Figure 3: Filtration Capacity Profile (Initial Flux rate: 1000LMH)

Figure 4: Filtration Capacity Profile (Initial Flux rate: 2000LMH)

4. Conclusion
The study evaluates the performance of normal flow filtration by assessing the flux rate and the filtration capacity profile; the most important parameters to avoid fouling occurred during the process run. Due to the nature of this mode of operation where the fouling is irreversible, proper selection of filter area and operating parameters are important as it can lead to high operating cost. This study verifies that there is a reduction of flux rate with control sample and with sample containing 1.0% of organic non-silicone antifoam agent concentration where the flux rate reduction ranges from 18% to 33% for initial flux rate of 1000LMH and 27% to 46% for initial flux rate of 2000LMH. Meanwhile, the flux rate for sample containing 0.2% and 0.6% organic non-silicone antifoam agent is maintained throughout the process. In addition to that, the membrane resistance pattern for sample containing 0.6% and 1.0% organic non-silicone antifoam agent with initial flux rate of 1000LMH shows a significant increase while it maintains at high membrane resistance at initial flux rate of 2000LMH. The membrane resistance for control sample and sample containing 0.2% organic non-silicone antifoam agent maintain the same throughout the process regardless of the starting membrane resistance for both initial flux rates.
Finally, the reported filtration capacity for sample containing 1.0% organic non-silicone antifoam agent is approximately 250L/m² and the other sample may pose approximately 330L/m² filtration capacity. In conclusion, the results demonstrate that the usage of organic non-silicone antifoam agent may affect the overall filtration performance, depending on the concentration of antifoam agent loaded in the culture.

**Acknowledgement**

Authors are highly thankful to the Ministry of Higher Education, Malaysia and the Faculty of Chemical Engineering, Universiti Teknologi MARA for the research grant (ID: 600-IRMI/MyRA 5/3/LESTARI (016/2017)) and the research facilities.

**References**

[1] Routledge S J 2012 Beyond de-foaming: productivity the effects of antifoams on bioprocess *Comput Struct Biotechnol J.* 3, p. 1-7.

[2] Pugh R J 1996 Foaming, foam films, antifoaming and defoaming *Adv. Colloid Interface Sci.* 64, Supplement C p. 67–142.

[3] Shi Q, Su Y, Zhu S, Li C, Zhao Y and Jiang Z 2007 A facile method for synthesis of pegylated polyethersulfone and its application in fabrication of antifouling ultrafiltration membrane *J. Membrane Sci.* 303, 1 p. 204 - 212.

[4] Soddell J A and Seviour R J 1990 Microbiology of foaming in activated sludge plants *J. Appl. Microbiol.* 69, 2 p. 145 - 176.

[5] Vardar-Sukan F 1998 Foaming: Consequences, prevention and destruction *Biotechnol. Adv.* 16, 5 p. 913 - 948.

[6] Liew M K H, Fane A G and Rogers P L 1997 Fouling effects of yeast culture with antifoam agents on microfilters *Biotechnol. and Bioeng.* 53, 1 p. 10 - 16.

[7] McGregor W C, Weaver J F and Tansey S P 1988 Antifoam effects on ultrafiltration *Biotechnol. and Bioeng.* 31, 4 p. 385 - 389.

[8] Routledge S J, Poyner D and Bill R M 2014 Antifoams: the overlooked additives? *Pharm Bioprocess.* 2, 2 p.103 - 106.

[9] Mohamad Pauzi S, Ahmad N, Yahya M F and Ariffin M A 2018. The Effects of Antifoam Agent on Dead End Filtration Process *IOP Conf. Ser.: Mater. Sci. and Eng.* 358, p. 1-6.

[10] Jena A K, Mahalakshmi D K and Sridhari G 2011 Integrated application of bioprocess engineering and biotechniques for quality and bulk drug manufacturing *J. of Bioequivalence Bioavailab.* 3, 11 p. 277 - 285.

[11] Shukla A A, Hubbard B, Tressel T, Guhan S and Low D 2007 Downstream processing of monoclonal antibodies – application of platform approaches. *J. of Chromatogr.* B 848, p. 28-39.

[12] Abdelrasoul A, Doan H and Lohi A 2013 Fouling in membrane filtration and remediation methods mass transfer *Mass Transfer - Advances in Sustainable Energy and Environment Oriented Numerical Modeling* p. 195-218.

[13] Modise C M, Shan H F, Neufeld R D and Vidic R D 2005 Evaluation of permeate flux rate and membrane fouling in dead-end microfiltration of primary sewage effluent *Environ. Eng. Sci.* 22, 4 p. 427-439.

[14] Park K, Kim P, Kim H G and Kim J H 2019 Membrane fouling mechanism in combined microfiltration – coagulation algal reach water applying ceramic membranes *Membranes* 9, 33 p. 1-11.

[15] Le-Clech P, Chen V and Fane T A G 2006 Fouling in membrane bioreactors used in wastewater treatment *J. Membrane Sci.* 284, 1 p. 1-53.

[16] Vera L, González E, Díaz O, Sánchez R, Bohorque R, Rodríguez-Sevilla Juan 2015 Fouling analysis of a tertiary submerged membrane bioreactor operated in dead-end mode at high-fluxes *J. Membrane Sci.* 493, p. 8-18.

[17] Marshall A D, Munro P A and Trägårdh, G 1997 Influence of permeate flux on fouling during
the microfiltration of β-lactoglobulin solutions under crossflow conditions *J. Membrane Sci.* **130**, 1-2 p. 23 – 30.

[18] McCabe W, Smith J and Harriott P 2005 *Unit Operations of Chemical Engineering*: McGraw-Hill Education.

[19] Rahimpour A and Madaeni S S 2007 Polyethersulfone (PES)/cellulose acetate phthalate (CAP) blend ultrafiltration membranes: Preparation, morphology, performance and antifouling properties *J. Membrane Sci.* **305**, 1-2 p. 299 – 312.

[20] Ahmad A L, Abdulkarim A A, Ooi B S and Ismail S 2013 Recent development in additives modifications of polyethersulfone membrane for flux enhancement *Chem. Eng. J.* **223**, p. 246 – 267.

[21] Wang C, Li Q, Tang H, Yan D, Zhou W, Xing J and Yinhua W 2012 Membrane fouling mechanism in ultrafiltration of succinic acid fermentation broth *Bioresour. Technol.* **116**, Supplement C p. 366 – 371.

[22] Lecomte J 2006 n.d. The Effects of Antifoams on Ultrafiltration Membranes Retrieved from https://www.yumpu.com/en/document/view/8688825/the-effects-of-antifoams-on-ultrafiltration-membranes-dow-corning.

[23] Juang R S, Chen H L and Chen Y S 2008 Membrane fouling and resistance analysis in dead-end ultrafiltration of Bacillus subtilis fermentation broth *Sep. Purif. Technol.* **63**, p. 531 – 538.