JBAT 8(2) (2019) 124 – 132

p-ISSN 2303 0623
e-ISSN 2407 2370

Jurnal Bahan Alam Terbarukan

Accredited by Directorate General of Strengthening for Research and Development - SK No.: 36b/E/KPT/2016
http://journal.unnes.ac.id/nju/index.php/jbat

Antifungal Lotion as Value-Added Product for Harvested BSFL Processing: Simple Process Design and Economic Evaluation

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DOI: https://doi.org/10.15294/jbat.v8i2.22794

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Article Info

Article history:
Received
September 2019
Accepted
November 2019
Published
December 2019

Keywords :
Antifungal lotion;
BSFL;
Economic evaluation;
SuperPro Designer

Abstract

Advancing the value of products derived from insect biomass is a potential way to increase the demand of processing insect as renewable and sustainable resources. Among several species of insect, black soldier fly larvae (*Hermetia illucens*) is promising biomass source because of its favorable characteristics such as easy cultivation, fast-growing, and worldwide distribution. One problem that could limit the development of insect-based bioproduct is the low market price and displeasing uses for edible food. To overcome this problem, value-added product development is necessary to carried out. Thus, establish an antifungal lotion using extracted materials from BSFL biomass was discussed in this report followed by the economic evaluation and sensitivity analysis. The result reveal that equipment availability in market and raw material readiness espouse the production expediency. From the economic aspect, the direct fixed capital cost (DFC) for a plant of this capacity is around US$3.6 million, or approximately 6 times the total equipment cost. Thus, the net profitability will remain stable even the market price of BSFL might fluctuate in the range of 20%. In contrary, the change in main product price was impactful to the rate of return (ROI), internal rate of return (IRR) and, payback time (PBT) value. The overall result suggests that this project is worthy to being built.

INTRODUCTION

Agriculture and food sector are significantly producing large amount of organic waste in the form of biosolids or livestock. Roughly one-third of food produced for human consumption is lost, equivalent to an annual economic loss of about USD 1 trillion or wasted globally which amounts to about 2.3 billion tons per year (FAO, 2019).Thus, collection, processing and disposal of organic wastes become costly and troublesome along with the increasing volumes of waste streams and their complex bio-physico-chemical composition. Furthermore, organic wastes can release biological agent, chemicals, and emission which disrupt the natural ecosystem when left untreated. The worst, if not managed properly, these organic wastes can cause environmental pollution and become potential health hazards (Li et al., 2011).

In past years, several insect species, such as *Hermetia illucens*, have attracted increased interest as a sustainable alternative to convert organic waste become valuable protein, oil, and fertilizer (Li et al., 2015; Kim et al., 2016; Wang et al., 2017). In the other hand, *Hermetia illucens* known many advantages as high fat content, rapid reproduction rate, and short life cycle (Yu et al., 2019). These insects consume various waste materials and efficiently convert organic waste into biomass that is rich in protein and fat (Nguyen et al., 2018; Manurung et al., 2016; Surendra et al., 2016; Gao et al., 2019), which can be defatted and used for the preparation of biodiesel, while the

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remainder of the defatted meal could be used as an alternative sustainable protein rich ingredient for the feed industry (Wang et al., 2017). Furthermore, the methanol compound extract from BSFL significantly decreases the proliferation pathogenic bacteria and have unique properties which effectively block the viability of the gram-negative bacteria (Lalander et al., 2013; Choi & Jiang, 2014).

From those advantages, the oil and chitin extracted from BSFL was used to develop an emulsion which loaded with polyene to form antifungal drug for pets. The polyene antifungal drugs consist primarily of amphotericin B and nystatin which demonstrate an antifungal activity against several deep fungal infections, such as candidiasis, aspergillosis, mucormycosis, and cryptococcosis (Yagiela et al., 2010). According to the report of (Khosravi et al., 2009), the risk of fungal infections of the skin during the whole life is predicted in the range of 10–20%. Thus, the attempts of this research directed no only developing antifungal drug to decrease the infection rate of fungi but also to increasing the value of harvested BSFL final product.

From the economic aspect, the global edible insect market is expected to reach USD 7,956.7 million by 2030, supported by a CAGR of 24.4% during the forecast period of 2019 to 2030. Also, in terms of volume, this market is poised to grow at a CAGR of 27.8% during the forecast period to reach 732,684.1 tons by 2030. Additionally, the global Antifungal Drugs market generated $14.23 billion in 2017 and is estimated to reach $17.72 billion by 2023, growing at a CAGR of 3.7% from 2017 to 2023 (Allied Market Research, 2019).

To carried out the whole process, SuperPro Designer Software used to simulate the extraction process of BSFL and several processing steps to gain the final product as crude protein and lotion. SuperPro Designer is higly versatile and exhibits many of the desirable attributes required for project developments. It can be considered to analyze individual basic unit operations, yet has the flexibility of combining these unit operations for integrated analysis of a complex processes (Flora et al., 1998). To get a better understanding about the reliability of this production process and the eligibility in economic aspect, performing economic evaluation process comparison to get the optimum condition is necessary to accomplished.

PROCESS DEVELOPMENT

Biomass processing is a promising outcome that can be facilitated by the use of simulation tools. SuperPro Designer (SPD) software is a comprehensive simulator due to its large database of unit operations and chemical compounds compared to the other various simulation tools (Petrides et al., 2014). The provided database is very useful to facilitate the estimation of several properties such as: physical, chemical and biological processes. The SPD as modeling tool widely used for processes evaluation and optimization in a pharmaceutical, biotechnology, biofuels, and consumer goods industries. Thus, simulating BSFL extraction and processing using SuperPro Designer hoped can provide estimation and several evaluations toward its appropriateness.

Process description

Adopted from (Caligiani et al., 2018), the proximate composition of BSFL V instar larvae are expressed on dry matter basis in the Table 1 below. Thus, 75% water content use to represent the total composition of BSFL.

Table 1. Proximate composition of BSFL V instar

Compound	Formula	Percentage	Amount (ton)
Water	H_2O	75	1.986
Amino acid	$C_5H_9NO_4$	4.6	0.121808
Protein	$C_6H_{13}NO_2$	4.125	0.10923
Chitin	$C_8H_{13}O_5N$	2.25	0.05958
Crude lipid	$C_{12}H_{24}O_2$	9.275	0.245602
Ash	$CaCO_3$	4.75	0.12578
Total		100	2.648

The extraction and production process were simulated in SuperPro Designer v8.5 (Intelligen Inc., MIT) to evaluate a large-scale production of polyene loaded black soldier fly larvae oil as an antifungal drug for pets. The simulation process was mainly divided into 3 major part:

1. Extraction section,
2. Separation and purification section,
3. Emulsion manufacturing section.

Based on the framework above, the block flow diagram (BFD) was built, as shown in Figure 1.

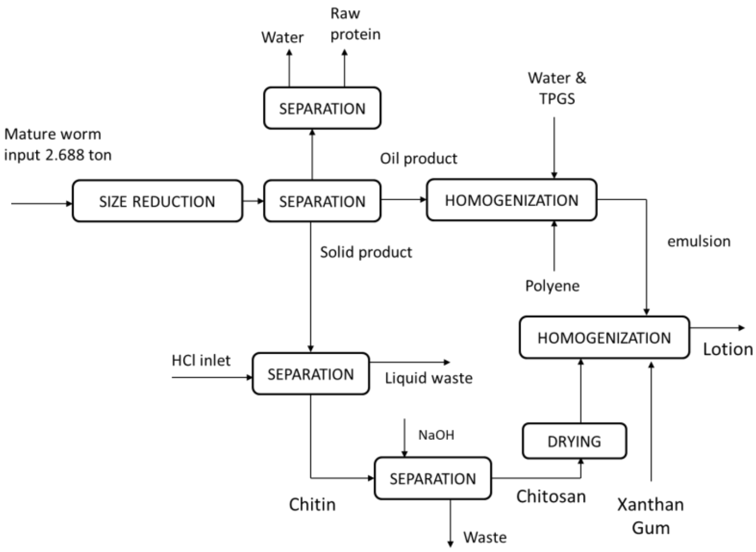

Figure 1. BFD of polyene loaded BSFL oil emulsion production for antifungal drug.

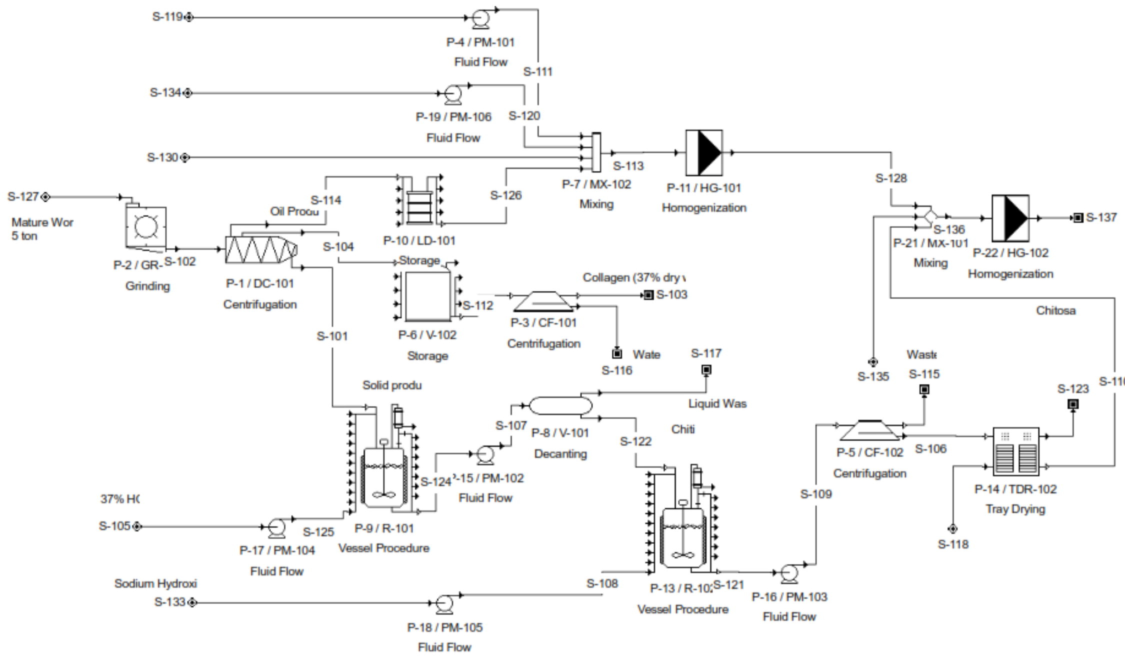

Figure 2. Process flow diagram of modelled antifungal batch process production

Several presumptions were used to define the process boundary in SuperPro Designer software simulation which are:

1. Processed capacity loading set by 100 ton/year dry larvae,
2. Fresh larvae were 75% water content,
3. Fresh larvae purchase price for 5 NTD/kg,
4. The factory was run in 300 days per year.

These presumptions were adopted by considering the production and availability or raw materials provided by Wormax Inc., Taiwan. Thus, the production process was modelled as a batch process shown in Figure 2. From the PFD, thus we got overall process data such as number batch per year and recipe cycle time to calculate the processed materials per batch which is 151 and 47.38 hr, respectively. Thus, the capacity per batch was found to be 2,648 ton/batch wet larvae.

The wet larvae of Black Solder Fly are processed in several steps, depicted in Figure 2. The initial process begins with feeding the wet larvae into biomass crusher to get fine piece in slurry form. This step processed for 1 hour and continued to centrifugal decanter separator. This separator will separate oil, water and solid by the centrifugal force and the specific design of this equipment.

Table 2. Major equipment specification and purchase cost

Name	Type	Model	Capacity	Purchase Cost ($)
HG-101	Homogenization	6000lph	6000lph	9,800
NM-101	Biomass crusher	SFSD78*125	3450mm*1400mm*1690mm	10,000
DC-101 & V-101	Decanter	LW450-1800	3-30m^3/h	45,000
CF-101	Centrifuge	XP1320-N	900kg	30,000
R-101	Stirred tank reactor	3000L	3000L	2,000
R-102	Stirred tank reactor	FYS-500	500L	4,000
TDR-102	Tray dryer	JK03RD	300kg	10,000

Recently, this separator become popular and used in many industries because of its feasibility and reliability. Passing this process, the flow will divide into 3 streams, which the oil and protein will temporary store to the liquid storage, and the solid product will directly be fed to the reactor to further processed become chitosan.

The second stream was belonging to protein purification, where the water-rich protein fed into the centrifuge to separate protein and water. In the third stream, oil product was fed into the mixer together with the polyene then continued to the second mixture which contain surfactant and deionized water to form a coarse emulsion. To gain fine-emulsion, then the mixture further processed into the homogenizer. Until this step, the emulsion still in the form of water like solution. Increasing stability of the emulsions can be done by mixing a thickener to get a tuneable viscosity of lotion. The solid product which is rich of mineral $CaCO_3$ was fed into reactor and reacted with 37% HCl to get the demineralization process following this condition and reaction shown in Eq. (1).

$$CaCO_3 + HCl \longrightarrow CaCl_3 + CO_2 + H_2O \qquad (1)$$

The process condition, reaction, and the ratio of HCl was adapted from (Tanasale et al., 2016).

After the demineralization process finish, stream was fed into decanter to separate the bulk amount of water and liquid waste from solid product. From this process, we get rich chitin slurry product and fed into 2nd reactor and let the chitin react with NaOH to form chitosan by following the reaction in Eq. (2).

$$\text{Chitin} + NaOH \longrightarrow \text{Chitosan} + NaCOOH \qquad (2)$$

After the process was finish, the product will be rich of chitosan and high-water content. To get the pure chitosan, then we fed the stream into moderate speed centrifugation. From this process, we get the high concentration of chitosan, but still in wet condition. So, we fed this stream into tray dryer to get dry powder of chitosan and remove the liquid impurities like sodium acetate, sodium hydroxide, and calcium chloride. Finally, we got the high purity of chitosan (91%).

To improve the stability of the emulsion, then we add the chitosan from the solid purification process and xanthan gum from purchasing to reach concentration of 1 wt%. This chitosan was performed as thickener and known have a good pharmacological activity. Then we fed this stream into homogenizer to get better dispersion of emulsion. Finally, we get an end product of emulsion which uses as antifungal lotion.

Equipment Customization

The equipment was customized based on the commercial's availability through the website which provide the most relevant and suitable equipment for the simulation requirement. Table 2 provides a list of the major equipment items in this project, along with their purchase costs.

According to the equipment availability, the design of process was adjusted to gain the ideal condition. For example, the purification process of protein is design to divide the stream become 3 times centrifugation because of the total stream was 2137.28 kg/batch but the available equipment in market only for 900 kg/batch, Thus, before this process need to put a temporary storage tank which dived the amount of stream become 712.5 kg/batch.

Material Balances

Table 3 provides a summary of the materials balance at several major stream to give an additional sight about how the process was running. These results were calculated by the

Table 3. Mass balance at major streams.

Component Flowrates (kg/batch)	S-127	S-114	S-104	S-101	S-128	S-116	S-110	S-137
CaCl3	-	-	-	-	-	-	0.018	0.018
CaCO3	125.78	-	1.258	124.52	-	-	1.220	1.220
Chitin	59.58	-	0.596	58.984	-	0.232	2.891	2.891
Chitosan	-	-	-	-	-	-	43.73	56.161
Glutamic Acid	109.23	1.092	107.045	1.092	-	1.070	-	1.093
Polyene	-	-	-	-		-	-	2.419
Lauric Acid	245.60	241.9	2.456	1.228	-	0.958	-	-
Leucine	121.80	1.218	119.3	1.218	-	1.194	-	-
Sodium Acetate	-	-	-	-	-	-	0.030	0.030
Sodium Hydroxide	-	-	-	-	124.3	-	0.150	0.150
TPGS	-	-	-	-		-	-	240.62
Water	1,986.0	19.860	1,906	59.580	58.3	1,887	-	11,794
TOTAL (kg/batch)	2,648.0	264.0	2,137	246.6	182.7	1,891	48.04	12,098
TOTAL (L/batch)	2,176.3	228.9	2,060	168.3	123.6	1,942	22.5	12,156

Table 4. Estimated material entering demand and material exiting revenue.

Component	Price ($/kg)	Demand (kg/yr)	Output (kg/year)	Total cost ($/yr)
Chitosan	20	1,876.18	-	37,523.50
HCl	3	20,566.20	-	61,698.60
HL	13	3,633.06	-	47,229.78
ketoconazole	250	365.27	-	91,317.25
Mature Worm	0.32	399,848.00	-	127,951.36
NaOH	1.12	18,779.87	-	21,033.45
TPGS	8	32,709.62	-	261,676.96
Water	1	2,821,954.53	-	2,821,954.53
Lotion	6.5	-	3,206,635.40	-
Raw Protein	1.59	-	34,886.74	-

process simulator, based on the input parameters and operations procedure such as stream configurations. Process simulators calculate the amounts and compositions of each individual stream (inputs, intermediates and outputs) in addition to calculate the overall mass balance. This information provides a useful data for verifying results related to material transformations and separations, liquid and solid waste generation, emissions, equipment capacity requirements, etc (Petrides et al., 2014).

COST ANALYSIS AND ECONOMIC EVALUATION

During late-stage of development and commercialization of a product, proper analysis of project cost and economic evaluation are an important aspect. To accomplish this, the software estimated the equipment cost using built-in cost correlations that are based on data derived from a number of vendors and literature sources (Parjikolaei et al., 2016). Thus, equipment costs and various multipliers used to estimate the fixed capital investment.

Economic Evaluation Parameters

To get economic evaluation, several parameters are necessary to customized based on the available data and reliability such as the amount and type of employees, material purchasing price, and material exiting price. Thus, Table 4 shows the estimated material entering and material exiting price to conduct the analysis. The price of material entering and material exiting was obtained from online website and some of them is decided by author self-based on fairness and the average prize in online market.

Cost analysis

A full economic analysis of the entire plant process considering the operating cost was estimated and summarized in Table 5. The construction year was assumed to be 2019 and the material cost was obtained from chemical market reporter (www.icis.com). Thus, basic labour cost was set based on the labour regulation in Taiwan to be around 5 US$/hr. The facility-dependent cost in this estimation accounted for roughly 1/15 of the overall operating cost. This is reasonable for medium value biopharmaceuticals which addressed for pets. Table 6 displays the various items related to the fixed capital estimate including TPDC, TPIC, TPC, CFC, and DFC. Thus, its clearly reveal that the DFC for a plant of this capacity is around US$ 3,6 million, or approximately 6 times the total equipment cost.

Table 5. Operating cost summary (Year 2019 price in US$).

ANNUAL OPERATING COST			
	Cost Item	$	%
1	Raw Materials	3,470,000	33.95
2	Labour-Dependent	1,330,000	12.01
3	Facility-Dependent	678,000	6.64
4	Consumables	483,000	4.73
5	Waste Treatment	31,000	0.30
6	Utilities	4,229,000	41.38
	TOTAL	10,222,000	100

Table 6. Fixed capital estimate summary (Year 2019 price in US$).

FIXED CAPITAL ESTIMATION		
Total Plant Direct Cost (TPDC) (physical cost)		
1	Equipment Purchase Cost	588,000
2	Installation	267,000
3	Process Piping	206,000
4	Instrumentation	235,000
5	Insulation	18,000
6	Electrical	59,000
7	Buildings	265,000
8	Yard Improvement	88,000
9	Auxiliary Facilities	235,000
	TPDC	1,961,000
Total Plant Indirect Cost (TPIC)		
10	Engineering	490,000
11	Construction	686,000
	TPIC	1,176,000
Total Plant Cost (TPC = TPDC+TPIC)		3,137,000
	Contractor's Fee & Contingency (CFC)	
12	Contractor's fee	157,000
13	Contingency	314,000
	CFC	471,000
Direct Fixed Capital Cost (DFC = TPC+CFC)		3,608,000

Table 7. Profitability analysis summary (Year 2019 price in US$).

PROFITABILITY ANALYSIS			
		Amount	unit
1	Direct Fixed Capital	3,608,000	$
2	Working Capital	911,000	$
3	Startup Cost	180,000	$
4	Revenue Rates	1,866,610	kg/yr
5	Revenue Price	6.50	$
6	Annual Operating Cost	10,222,000	$/yr
7	Gross Margin	15.78	%
8	Return on Investment	31.75	%
9	Payback Time	3.15	years

Sensitivity Analysis

SuperPro Designer can be used to perform sensitivity analysis with respect to key design variables after a model of a process has been develop. Moreover, changing the value of the variable to understand the effect toward the whole economic aspect is important to analyse the fluctuation or discover an opportunity to develop a project (de Aguiar et al., 2018).

The ROI (return of investment) is defined as the annual profit generated by a unit of invested capital. Thus, ROI value give us information that higher the ROI make the project more desirable. Typically, minimum ROI value ranged from 10-15% is accepted (Petrides et al., 2014; Bajić et al., 2017). From Table 7, the ROI vale for this project was 31.75% indicating that this procedure is acceptable. Thus, vary on BSFL purchase price fluctuations in 20% seems not change the ROI value evidently (Figure 3a). Its mean that the net profit will remain stable even the market price of BSFL might increase. In contrary, the change in main product price which is antifungal lotion was impactful to the ROI value. This condition suggest

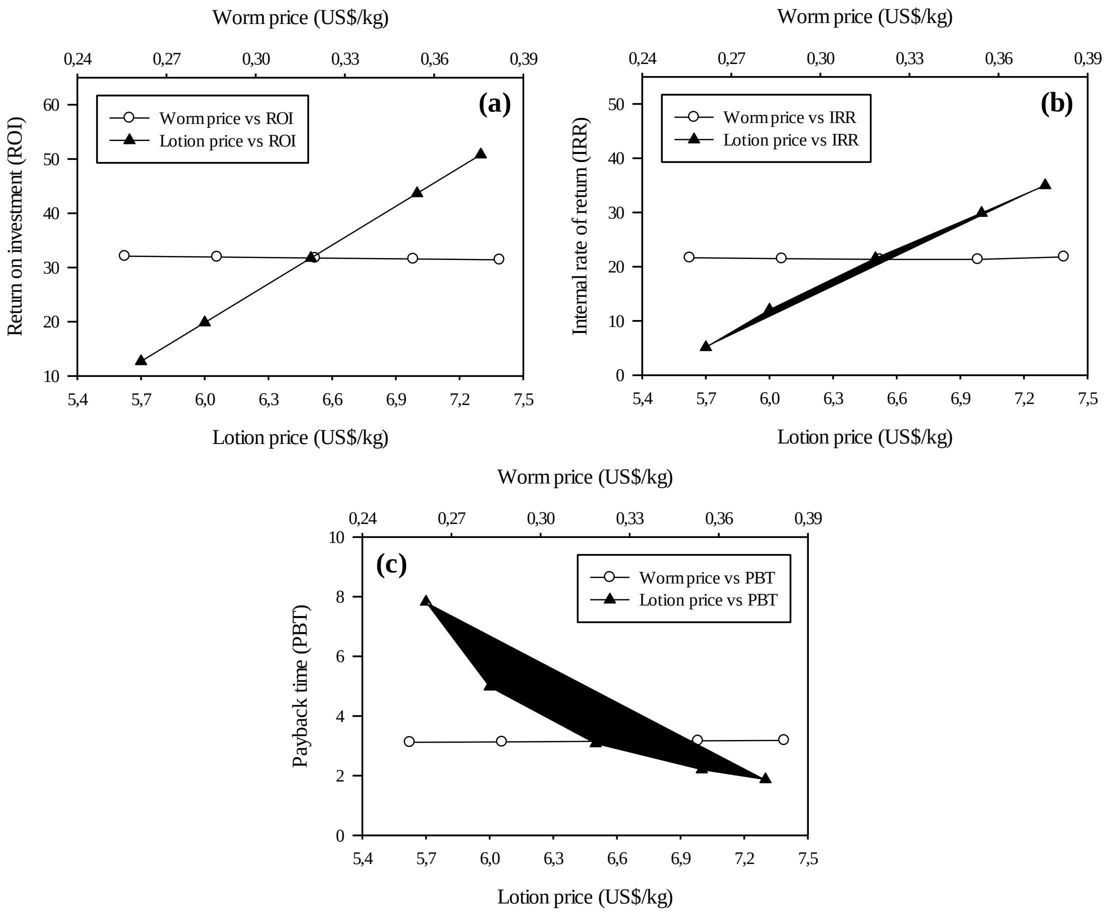

Figure 3. Worm purchase price and lotion selling price in arrange of 20% fluctuation toward (a) Return on investment (ROI), (b) Internal rate of return (IRR) and, (c) Payback Time (PBT).

that maintain the product price in proper range is important to control the safe revenue.

The internal rate of return (IRR) defined as the rate of return at which the projects present NPV equal to zero. In other word, IRR represents the average intrinsic profitability of a project. Desirable IRR value gain as high as the project can reach by considering the following aspect like minimum ROI value and product acceptability in market. For the process evaluated in this study, IRR increased with the product selling price increase, but IRR remain constant with fluctuating of BSFL purchasing price. This finding suggest us to consider the feasibility of the proposed process, with product price higher than US$ 6.26/kg is acceptable (Figure 3b).

The payback time (PBT) is the time required to recover the cost of an investment. This approach is very useful to determine the appropriateness of a project. In general, the PBT value is around 2 years, but this condition can be varied depend on the project favourability (Petrides et al., 2014). In this project, PBT value was gain at 3.15 years. Thus, sensitivity analysis suggests that the PBT value trend is similar with ROI variance. Where, when the lotion selling price is lower than US$ 6/kg make the PBT not feasible (Figure 3c). In overall, to get the save profitability, the result suggest that the product price need to be necessary not lower than 5.7 USD to maintain the revenue is higher than the total operating cost.

The performed economic analysis gives a result which provides information to make the decision whether the project is feasible or not. Thus, further studies should also consider the packaging, distribution and improving product quality to meet market requirements in order to obtain more accurate results and high-quality biopharmaceutical product.

CONCLUSION

Biomass processing is a promising outcome that can be facilitated by the use of simulation tools. SuperPro Designer (SPD) software is a comprehensive simulator due to its large database of unit operations and chemical compounds to accomplish project development simulation. The study showed the net profitability will remain stable even the market price of BSFL might fluctuate in the range of 20% but in contrary with the lotion market price. The result suggest that the product price need to be necessary not lower than 5.7 USD to maintain the revenue is higher than the total operating cost. The overall result suggests that this project worthy to being built by emphasizing the economic parameters and readiness of the materials. Thus, improving this study is necessary to obtain more accurate results and high-quality biopharmaceutical product.

Conflict of Interest

The authors declare that they have no conflict of interest.

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