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PLACKETT-BURMAN DESIGN AND RESPONSE SURFACE OPTIMIZATION OF CONDITIONS FOR CULTURING *SACCHAROMYCES CEREVISIAE* IN *AGARICUS BISPORUS* INDUSTRIAL WASTEWATER

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ABSTRACT

Background. The *Agaricus bisporus* industrial wastewater that contains a variety of nutrients which could be used as culture for some beneficial microbiology will be one threat to our environment if the wastewater doesn't be comprehensively utilized. Plackett-Burman is the rapid and concise ways of screening the main effective factors. Box-Behnken response surface method is used to optimize interactions between the three main factors and predict optimal fermentation conditions. This study is aimed to select the main influence factors and optimize the conditions for culturing *Saccharomyces cerevisiae* in *A. bisporus* industrial wastewater by Plackett-Burman design and Box-Behnken response surface method.

Material and methods. We analyzed the total number of living *S. cerevisiae* in the fermentation broth using multispectral imaging flow cytometry. Plackett-Burman design was used to screen out three factors from the original six factors of processing wastewater concentration, initial pH, inoculum size, liquid volume, culture temperature, and rotation speed that affected the total number of viable *S. cerevisiae*. Factors significantly affecting the total number of viable *S. cerevisiae*, including culturing temperature, processing wastewater concentration, and initial pH were investigated.

Result. The results indicated that culture temperature ($p = 0.0007$) and pH ($p = 0.0344$) as negative factor and concentration ($p = 0.0080$) as positive effect were the significant factors affecting the total number of *S. cerevisiae*, inoculum ($p = 0.1237$) and shaking speed ($p = 0.2112$) as positive effect and loaded liquid ($p = 0.4811$) as negative factor were important factors. The optimum conditions for *S. cerevisiae* fermentation in *A. bisporus* wastewater were a rotational speed of 150 rpm, a culture temperature of 25°C, an initial pH of 6.0, a concentration of 8.4%, a inoculation volume of 8%, and a 100 mL liquid volume in a 250 mL flask, a culture time of 48 h. Under these conditions, the concentration of total viable yeast reached $1.04 \pm 0.02 \times 10^8$ Obj/mL which was at the 95% confidence interval of predicted model ($0.89–1.14 \times 10^8$ Obj/mL).

Conclusion. The experimental model is reliable and the experimental results are of good stability. Variance analysis is performed to determine the adequacy and significance of the linear model. Thus, Plackett-Burman

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and Box-Behnken response surface method improved the veracity of optimization of conditions for culturing *S. cerevisiae* in *A. bisporus* industrial wastewater.

Keywords: *Agaricus bisporus* industrial wastewater, *Saccharomyces cerevisiae*, multispectral imaging flow cytometry, Plackett-Burman, Box-Behnken response surface

INTRODUCTION

Agaricus bisporus (Lange) Sing, also known as mushrooms, is the most widely cultivated and most consumed edible mushroom with the highest yield in the world, accounts for about 25% of the total world edible fungus production (China…, 2008). In China, about 80% of mushroom is precooked and then made in canned food (Lin et al., 2016). In the canning production process, the fresh mushrooms are precooked firstly, in which the weight is reduced by 35% ~40%, in other words, at least about 30% of *A. bisporus* production will be lost to industrial wastewater each year (Huang et al., 2016). However, the mushroom industrial wastewater has high BOD and COD content, of which the content of COD is 540.29 g/L, which is 13.07 times higher than the national three level emission standard (Huang et al., 2018a). The discharge of the wastewater into the surrounding areas is a cause of environmental pollution. Therefore, the comprehensive utilization of this industrial wastewater is of practical significance for protecting the ecological system of origin and enhancing the comprehensive utilization of agricultural resources.

S. cerevisiae contains many nutritional compositions and active substances, such as protein, amino acid, vitamin, edible fiber and micronutrient (Branco et al., 2017; Lew et al., 2017), and is widely used in brewing, food, medicine and health care, feed, energy and chemical industry, environmental protection and life science research (Kwak and Jin, 2017; Turner et al., 2018; Wang et al., 2017; Wilson, 2017; You et al., 2017). *S. cerevisiae* has a simple nutrient type and is easy to culture, and more, there are 0.65% protein, 0.17% total sugar, 0.08% reducing sugar, and 0.04% amino acid nitrogen in the industrial wastewater (Chen et al., 2018; Duan et al., 2015), which could provide sufficient carbon and nitrogen source for microbiology (Huang et al., 2018b) or plants (Zhan et al., 2017), therefore, if the industrial wastewater could be used as a natural medium for *S. cerevisiae*, which would provide theoretical support for the fermentation of *S. cerevisiae* and the development of the downstream industry of *A. bisporus*, which is also the aim of this paper.

MATERIALS AND METHODS

Strains, media and growth conditions

S. cerevisiae (ATCC9763) was purchased from the Guangdong Culture Collection Center. Seed medium consisted of yeast extract 3.0 g, malt extract 3.0 g, glucose 10.0 g, peptone 5.0 g, and 1000 mL distilled water (pH 6.0–6.2) that had been sterilized at 121°C for 15 min.

A. bisporus processing wastewater was collected from the processing enterprises (Fujian KEREN Biological Co., Ltd.), filtered (38 μm) to remove the impurities, concentrated in a rotary evaporator to increase the concentration of nutrients, and sterilized (121°C, 15 min) according to different experimental requirements.

Preparation of seed suspension

Activated *S. cerevisiae* was picked with a vaccination loop and transferred to 100 mL sterilized seed liquid medium. This yeast suspension was placed in a 28°C incubator with shaking at 150 rpm for 48 h.

Plackett-Burman design

In this study, the experimental design included 6 factors and the experimental number selected was $N = 12$. A, B, C, D, E, and F respectively represented the industrial wastewater concentration that means the soluble solid content in the industrial wastewater, initial pH, inoculum size, culture temperature, shaking speed, and liquid volume, which affect the biomass of *S. cerevisiae* (Huang et al., 2018a). The Plackett-Burman

Table 1. Plackett-Burman experimental design and result

Run	*A* concentration %	*B* pH	*C* inoculum %	*D* loaded liquid mL/250 mL	*E* shaking speed rpm	*F* culture temperature °C	Total viable *S. cerevisiae* 10^6 Obj/mL
1	0.5	6.5	10	100	200	36	1.42 ±0.02
2	0.5	8.0	10	100	200	36	0.88 ±0.02
3	1.0	8	10	100	150	28	8.51 ±0.01
4	1.0	6.5	8	100	200	28	10.73 ±0.01
5	1.0	6.5	10	125	150	36	4.19 ±0.02
6	1.0	8.0	8	100	150	36	0.34 ±0.01
7	0.5	8.0	8	125	200	28	4.34 ±0.01
8	0.5	6.5	8	100	150	28	4.12 ±0.03
9	0.5	6.5	8	125	150	36	0.38 ±0.01
10	1.0	6.5	10	125	200	28	9.96 ±0.03
11	1.0	8.0	8	125	200	36	0.19 ±0.03
12	0.5	8.0	10	125	150	28	3.50 ±0.02

experiments design was formulated for the six factors using the Design-Expert version 8.0.6 software (Stat-Ease, Inc., Minneapolis, MN, USA). The factors and levels of Plackett-Burman design were shown in Table 1.

Steepest ascent design

Based on the effect of each factor, the steepest ascent design is used to quickly and economically approximate the optimal value area. Therefore, according to the size of the key factor effect value in the Plackett-Burman experiment, the change distance and direction of climbing can be determined, which can be used to determine the best level range (Chen et al., 2015). And the design of the steepest ascent experiment is shown in Table 2.

Table 2. Experimental design of steepest ascent and corresponding results

Run	*F* culture temperature °C	*A* concentration %	*B* pH	Total viable *S. cerevisiae* 10^8 Obj/mL
1	40	0.5	8.0	0.44 ±0.01
2	36	1	7.5	0.36 ±0.02
3	32	2	7.0	0.64 ±0.03
4	28	4	6.5	0.86 ±0.01
5	24	8	6.0	1.01 ±0.02
6	20	16	5.5	0.79 ±0.03

Box-Behnken design

To evaluate the impact of various factors on the total number of viable yeast and identify the optimal fermentation conditions, three-factor three-level experimental design was utilized. In this design, the total number of viable yeast was considered as the response value, the key three variables were considered as the independent variables (Huang et al., 2018b). According to the results of the Plackett-Burman design and steepest ascent experiments, the factors and levels for the Box-Behnken design experiments were determined in Table 3.

Table 3. The design and results of Box-Behnken experiments

Run	X_1 culture temperature °C	X_2 concentration %	X_3 pH	Total viable *S. cerevisiae* 10^8 Obj/mL
1	24	8	6.0	1.09 ±0.02
2	20	4	6.0	0.45 ±0.02
3	28	8	5.5	0.72 ±0.01
4	24	4	6.5	0.58 ±0.02
5	20	8	6.5	0.28 ±0.01
6	28	8	6.5	0.68 ±0.01
7	28	4	6.0	0.79 ±0.03
8	24	8	6.0	1.05 ±0.01
9	20	16	6.0	0.25 ±0.01
10	24	16	5.5	0.29 ±0.02
11	24	16	6.5	0.17 ±0.01
12	28	16	6.0	0.30 ±0.02
13	24	8	6.0	1.01 ±0.01
14	24	8	6.0	1.01 ±0.01
15	24	8	6.0	1.02 ±0.02
16	24	4	5.5	0.59 ±0.02
17	20	8	5.5	0.62 ±0.01

Verification

To verify the reliability of the experimental model, three parallel experiments were performed according to the optimal fermentation conditions identified through Box-Behnken design experiments. The resulting values were averaged to obtain the final results.

Data analysis

Each experiment was set to be repeated three times, and the experimental data were expressed as mean ±standard deviation ($X \pm S$).

Quantification of the total number of living yeast

As described by Calvert et al. (2008), the fermentation broth was diluted 10-fold with PBS and 1 mL of the diluted solution was mixed and incubated with 3 μL LIVE/DEAD Baclight™ (L7012, Thermo) staining reagent in the dark for 30 min. The number of viable yeast was then quantified by multispectral imaging flow cytometer (FlowSight, Millipore, USA). The Objects per mL (Obj/mL) feature returns the object concentration with respect to local volume. PBS was used as a flow sheath and a 488 nm laser was used to collect fluorescence signals and images from the 20,000 bright field, channel 2 green fluorescence representing SYTO 9, and channel 5 red fluorescence representing propidium iodide (PI). The SYTO 9 signal was set as the X axis and the PI signal as the Y axis and a scatter plot was generated to distinguish between the dead and living yeast.

RESULTS AND DISCUSSION

The part results of the total number of living *S. cerevisiae* in the fermentation liquid analyzed by multispectral imaging flow cytometry

As shown in Figure 1, three segregated regions were identified and gated (Fig. 1A) by multispectral imaging flow cytometry. SYTO 9 stain generally labels all yeast, including both those with intact and damaged membranes. By contrast, PI penetrates only yeast with damaged membranes. Under the 488nm laser, SYTO 9 was green, PI was red. Therefore, when using a combination of SYTO 9 and PI stains, yeast with intact cell membranes stained SYTO 9, whereas yeast with damaged membranes stained SYTO 9 and PI. Dead yeast had red fluorescent signals or both green and red signals (Fig. 1B). Yeast with only the green fluorescent signal was considered living (Fig. 1C). Granules and fragments were circled in bright-field images (Fig. 1D).

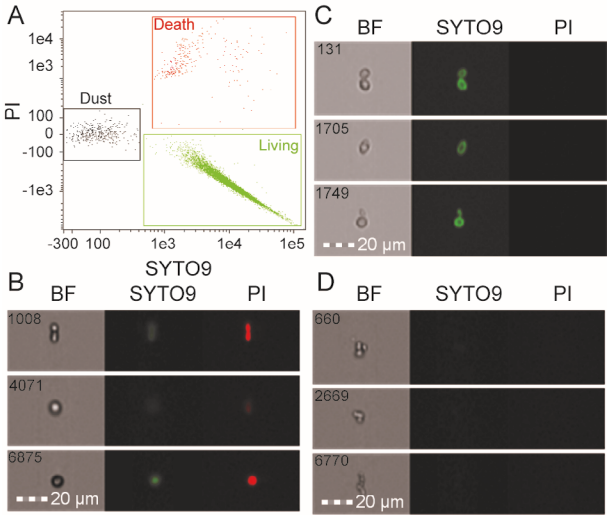

Fig. 1. Live and dead *S. cerevisiae* based on multispectral imaging flow: A – from the collected images, live and dead *S. cerevisiae* and dust were visually identified (as indicated by colored crosses) and the tagged populations were gated on the original plot, B – images of dust and cellular debris in the fermented liquid, C – images of live *S. cerevisiae* in the fermented liquid, D – images of dead *S. cerevisiae* in the fermented liquid. Images from within each region were chosen at random. From left to right, bright-field, SYTO 9, and propidium iodide channel images are displayed

Plackett-Burman design

The Plackett-Burman experimental design and result showed in the Table 1 and analysis of variance results was presented in Table 4. The model had a $p = 0.0048 < 0.01$, indicating this model is extremely significant. Based on the p values of the 6 factors assessed, the factors affecting the total number of *S. cerevisiae* in order of influence were $F > A > B > C > E > D$. The factors that had a significant impact ($p < 0.05$) were F, A, and B, i.e., temperature, concentration and pH, respectively. Therefore, culture temperature, concentration and pH were assessed as key factors in the next experiment.

Steepest ascent design

According to the positive and negative effects of the coefficient estimate of F, A, and B three factors depicted in Table 4, culture temperature and the initial pH exhibited negative effects; concentration exhibited positive effect. The results of the steepest ascent design are shown in Table 2. As the culture temperature and pH gradually decreased, concentration was found to gradually increased, the total number of *S. cerevisiae* first increased and then decreased. The maximum total number of viable *S. cerevisiae* was reached when the concentration was 8%, temperature was 24°C, and pH was 6.0. Accordingly, these levels of the three factors in the fifth set were considered the center point of Box-Behnken design.

Optimization of fermentation parameters by response surface methodology

To describe the nature of the response surface in the experimental region and to identify the optimum conditions for culturing *S. cerevisiae* in *A. bisporus* industrial wastewater, a Box-Behnken design was applied. The design matrix consisted of 17 trials was used to study the most significant variables affecting the total number of living *S. cerevisiae* in the fermentation broth as shown in Table 3. To predict the optimal point, a second order polynomial function was fitted to correlate the relationship between the independent variables and the response. Therefore, the total number of viable *S. cerevisiae* was considered as the predicted response value (Y), and the three factors (X_1 (culture temperation), X_2 (concetration), X_3 (pH)) were considered as the independent variables. The two

Table 4. Analysis of variance in Plackett-Burman

Source	Sum of squares	df	Mean squares	*F*-value	*p*-value Prob > *F*	Coefficient estimate	Importance
Model	150.43	6	25.07	14.72	0.0048		
A	30.98	1	30.98	18.18	0.0080	1.61	2
B	14.17	1	14.17	8.32	0.0344	–1.09	3
C	5.82	1	5.82	3.42	0.1237	0.70	4
D	0.99	1	0.99	0.58	0.4811	–0.29	6
E	3.50	1	3.50	2.05	0.2112	0.54	5
F	94.98	1	94.98	55.76	0.0007	–2.81	1
Residual	8.52	5	1.70				
Cor Total	158.95	11					

regression model of the total number of *S. cerevisiae* and each factor influencing *S. cerevisiae* growth were as follows:

$$Y = 1.02 + 0.099X_1 - 0.17X_2 - 0.066X_3 - 0.073X_1X_2 + 0.075X_1X_3 - 0.016X_2X_3 - 0.21X_1^2 - 0.36X_2^2 - 0.25X_3^2$$

The results of variance analysis of the regression model are shown in Table 5. The regression model had a $p < 0.0001$, revealing the regression equation used to describe the relationship between every factor and response value yielded a very significant linear relationship between the dependent variable and each independent variable. Overall, the experimental method was reliable. The "lack of fit *F*-value" of 2.77 implies the lack of fit is not significant relative to the pure error. There is a 17.51% chance that a "lack of fit *F*--value" this large could occur due to noise. The model displayed no loss of imitation phenomenon, indicating no abnormalities in the data, more items did not have to be introduced, and the model was appropriate. The parameters X_1, X_2, X_3, X_1X_2, X_1X_3, X_1^2, X_2^2, and X_3^2 were also significant ($p < 0.05$), revealing the three factors of temperature, concentration and pH significantly influenced the model. The predicted $R^2 = 0.9003$ can also reasonably explain the change in the positive determination coefficient $R^2_{adj} = 0.9793$ as there was a good fit between the measured and predicted total number of viable *S. cerevisiae* and it can be used for the theoretical prediction of *S. cerevisiae* fermentation.

An analysis chart was generated based on the regression equation to investigate the shape of the response surface. The response surface contour maps for each factor are shown in Figure 2.

As shown in Figure 2, the profiles of the response surfaces between temperature and concentration, temperature and pH, and concentration and pH are all convex with an open downward direction, indicating a high total number of viable *S. cerevisiae*. The contour centers of the three response surfaces are located within the set range, indicating optimal design conditions exist within the designed level of factors.

Analysis of variance revealed the interaction between different concentration and culture temperature was significant ($p < 0.05$). As seen in Figure 2A, the response surface is steep, indicating the obvious influence of culture temperature and different concentration on the total number of viable yeast. In addition, the contour line in Figure 2B is oval and the interaction between temperature and concentration was significant. When the pH was 6.0 (pH test level is 0), the total number of living yeast first gradually increased and then decreased as the culture temperature and concentration increased. When the pH was 6.0, concentration was 8%, culture temperature was 24°C, the total number of living yeast reached the actual maximum closing to the design points.

The response surface in Figure 2C is steep, indicating the obvious influence of culture temperature and

Table 5. Analysis regression and variance results

Source	Sum of squares	df	Mean squares	*F*-value	*p*-value Prob > *F*	Significance
Model	1.59	9	0.18	85.05	<0.0001	**
X_1	0.075	1	0.075	35.96	0.0005	**
X_2	0.24	1	0.24	118.09	<0.0001	**
X_3	0.034	1	0.034	16.17	0.0050	
X_1X_2	0.023	1	0.023	10.85	0.0132	**
X_1X_3	0.023	1	0.023	10.85	0.0132	**
X_2X_3	1.106E-0.03	1	1.106E-0.03	0.53	0.4890	
X_1^2	0.19	1	0.19	89.93	<0.0001	**
X_2^2	0.41	1	0.41	195.93	<0.0001	**
X_3^2	0.26	1	0.26	127.35	<0.0001	**
Residual	0.015	7	2.075E-0.03			
Lack of fit	9.803E-0.03	3	3.268E-0.03	2.77	0.1751	
Pure error	4.720E-0.03	4	1.180E-0.03			
Cor total	1.60	16				

$R^2 = 0.9909$, $R^2_{adj} = 0.9793$, $R^2_{pred} = 0.9003$.
* Significant, ** Very significant.

pH on the total number of living yeast. In addition, the contour line in Figure 2D is oval and the interaction between temperature and pH was significant. Under a constant concentration, the total number of living yeast first increased and then decreased as the temperature and pH increased and the vertex of the surface is the maximum amount of total living yeast.

The response surface in Figure 2E is steep, indicating the notable influence of concentration and pH on the total number of living yeast. In addition, the contour line in Figure 2F is oval and the interaction between different concentration and pH was significant. Under a constant culture temperature (the level is 0), the total number of living yeast first increased and then decreased as the concentration and pH increased and the vertex of the surface indicates the maximum amount of total living yeast.

Verification test

Based on the above analysis using Design-Expert 8.0.6 software to optimize the fermentation conditions, the optimal fermentation conditions were a culture temperature of 25.06°C, concentration of 8.39, and pH of 5.96, which was predicted to yield a total of 1.01×10^8 Obj/mL viable *S. cerevisiae*. After these values were rounded, each experiment was performed 3 times. The fermentation conditions used for *S. cerevisiae* were a shaking speed of 150 rpm, a culture temperature of 25°C, a pH of 6.0, a 100 mL liquid volume in 250 mL, an inoculums dose of 8%, and an industrial wastewater concentration of 8.4%. After 48 h, the total number of viable *S. cerevisiae* was $1.04 \pm 0.02 \times 10^8$ Obj/mL that was at the 95% of confidence interval of predicted model from 0.89×10^8 Obj/mL to 1.14×10^8 Obj/mL, which showed the experimental results were in good agreement with the model.

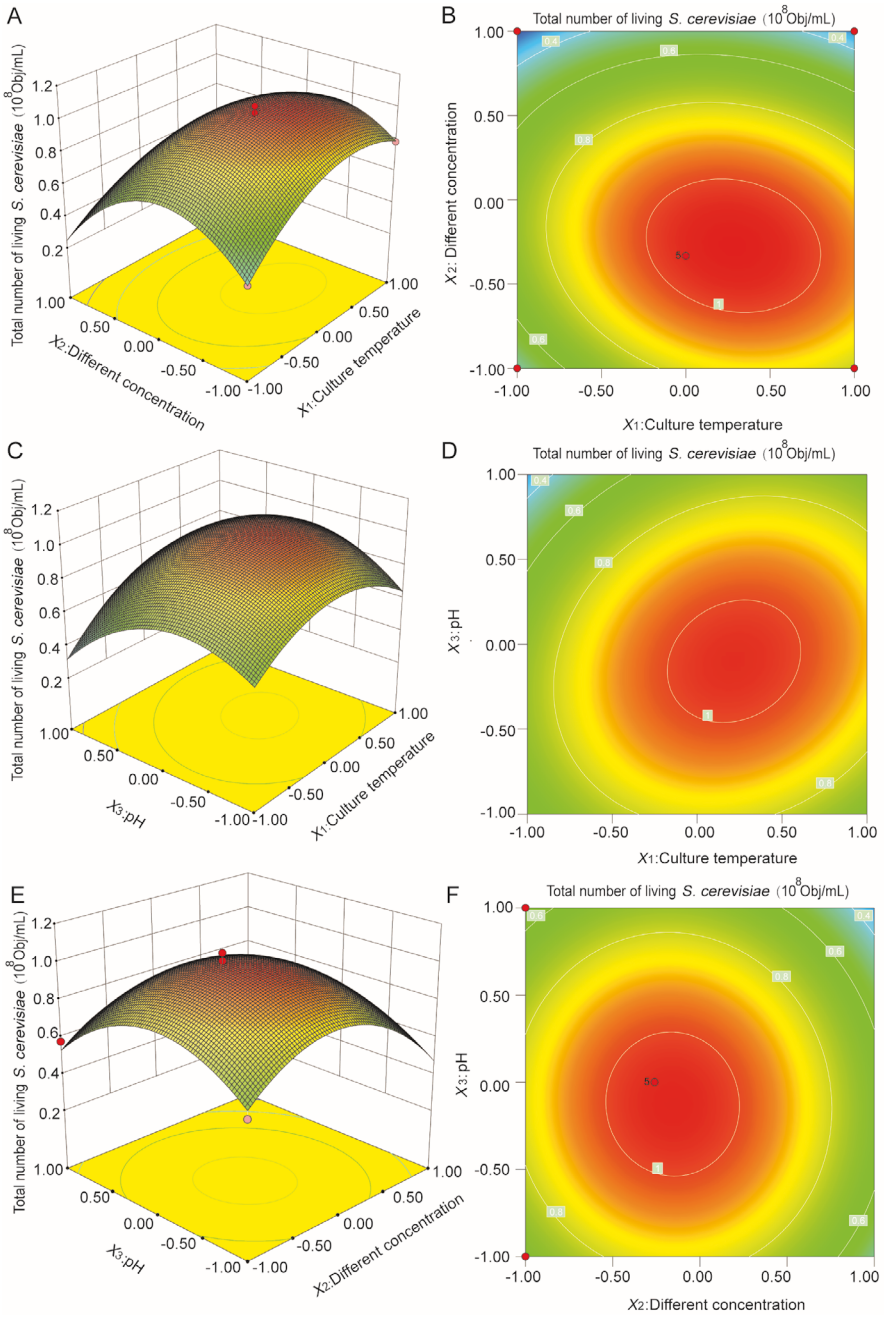

Fig. 2. The effect of cross-interaction among culture temperature, concentration and pH on total number of alive *S. cerevisiae*: A – response surface plot of effects of interaction between culture temperature and different concentration on total number of alive *S. cerevisiae*, B – contour line of effects of interaction between culture temperature and different concentration on total number of alive *S. cerevisiae*, C – response surface plot of effects of interaction between culture temperature and pH on total number of alive *S. cerevisiae*, D – contour line of effects of interaction between culture temperature and pH on total number of alive *S. cerevisiae*, E – response surface plot of effects of interaction between different concentration and pH on total number of alive *S. cerevisiae*, F – contour line of effects of interaction between different concentration and pH on total number of alive *S. cerevisiae*

Due to the short storage period of fresh *A. bisporus*, the main form of international trade of this product is canned processed products. Tank processing must be promptly used to precook fresh *A. bisporus*, therefore, the soluble components of *A. bisporus* were extracted in the processing (Chen et al., 2018; Duan et al., 2015; Huang et al., 2016; Lin et al., 2016). Even though the concentration of industrial wastewater was low, it was suit for microorganism growth. For example, 0.25% concentration of industrial wastewater was suitable to support *B. mucilaginous* growth (Huang et al., 2018b), and 1% concentration was suit for *B. megaterium* (Huang et al., 2018a). Comparing with *B. mucilaginous* and *B. megaterium*, the growth of *S. cerevisiae* needed more nutrition that higher concentration of industrial wastewater supported in the study.

Temperature is a factor that could directly affect the growth rate of yeasts and metabolic reactions. Suitable temperatures could increase the grown of yeast. In accordance with this, the biomass of *S. cerevisiae* first increased and then decreased as the temperature increased. The most suitable temperature range was 20–28°C with an optimal incubation temperature of 25°C, which was similar with that 25°C was selected as the best culture temperature for *S. cerevisiae* (Sun et al., 2016).

pH has some influence on microbiological nutrient absorption through changing the permeability of cytomembrane, the stability of membrane structures, and the solubility or ionization of substances, thereby, affects the growth rate of microorganisms. In this study, *S. cerevisiae* had a higher growth state in slightly acidic environments (pH = 6.0), which significantly affected the total number of viable bacteria in the fermentation broth. As reported by Kwun et al. (2016), the optimal conditions for ceramide production of *S. cerevisiae* were found to be pH 6.0 and 30°C, and more, the maximum growth of yeast cells was reached when the pH of solid yeast extract peptone dextrose was 6.0 (Anh et al., 2016).

The three factors that were screened out by Plackett-Burman design significantly affected the biomass of *S. cerevisiae* through a different course, and were grouped together into the optimum conditions for the fermentation of *S. cerevisiae* through response surface methodology.

CONCLUSION

The effect of the concentration of industrial wastewater, incubation temperature, and pH, and interactions between these factors all had a significant effect on the total number of viable *S. cerevisiae*. After optimization of the response surface, the optimum conditions for the fermentation of *S. cerevisiae* using *A. bisporus* wastewater were determined to be a rotational speed of 150 rpm, concentration of 8.4%, culture temperature of 25°C, initial pH of 6.0, inoculum of 8%, culture time of 48h, and amount of liquid loaded of 100 mL/250 mL. Under these conditions, the total number of living yeast can reach 1.04 $\pm 0.02 \times 10^8$ Obj/mL.

REFERENCES

Anh, D. T., Sakai, T., Kishida, M., Furuta, M. (2016). Isolation and characterization of a variant manganese resistant strain of *Saccharomyces cerevisiae*. Biocontrol Sci., 21(4), 253–260. http://dx.doi.org/10.4265/bio.21.253

Branco, P., Kemsawasd, V., Santos, L., Diniz, M., Caldeira, J., Almeida, M. G., …, Albergaria, H. (2017). *Saccharomyces cerevisiae* accumulates GAPDH-derived peptides on its cell surface that induce death of non-*Saccharomyces* yeasts by cell-to-cell contact. FEMS Microbiol. Ecol., 93(5). http://dx.doi.org/10.1093/femsec/fix055

Calvert Meredith, E. K., Lannigan, J. A., Pemberton L. F. (2008). Optimization of yeast cell cycle analysis and morphological characterization by multispectral imaging flow cytometry. Cytometry A, 73(9), 825–833. http://dx.doi.org/10.1002/cyto.a.20609

Chen, H., Niu, J., Qin, T., Ma, Q., Wang, L., Shu, G. (2015). Optimization of the medium for *Lactobacillus acidophilus* by Plackett-Burman and steepest ascent experiment. Acta Sci. Pol. Technol. Aliment., 14(3), 227–232. http://dx.doi.org/10.17306/J.AFS.2015.3.24

Chen, H., Zhang, Q., Hong, S., Wu, J., Nie, X., Lin, L., …, Cao, M. (2018). Analysis of the components of preboiled liquid of Agaricus bisporus and its effect on antihypertension. J. Jimei Univ. (Natural Sci.), 23(3), 171–177. http://dx.doi.org/10.19715/j.jmuzr.2018.03.002

China Chamber of Commer of Foodstuffs and Native Produce (2008). The present situation of edible fungus import and export trade and the countermeasures of industrial development in China. Zhejiang Shiyongjun, 16(5), 3–5.

Duan, X. H., Li, L., Xue, S. J., Huang, W., Gao, H., Yang, D., …, Cheng, W. (2015). Analysis of nutritional composition from blanching liquid of three edible fungus. Hubei Agric. Sci., 54(19), 4801–4804. http://dx.doi.org/10.14088/j.cnki.issn0439-8114.2015.19.037

Huang, J. F., Ou, Y. X., Yew, T. W., Liu, J. N., Leng, B., Lin, Z. C., …, Pan, Y. T. (2016). Hepatoprotective effects of polysaccharide isolated from *Agaricus bisporus* industrial wastewater against CCl_4-induced hepatic injury in mice. Int. J. Biol. Macromol., 82, 678–686. https://doi.org/10.1016/j.ijbiomac.2015.10.014

Huang, J. F., Zhang, D. F., Ou, Y. X., Zhang, G. G., Zheng, L. H., Lin, L. Z., …, Pan, Y. T. (2018a). Optimization of cultural conditions for *Bacillus megaterium* cultured in *Agaricus bisporus* industrial wastewater. BioMed Res Inter, 9. http://dx.doi.org/10.1155/2018/8106245

Huang, J. F., Ou, Y. X., Zhang, D. D., Zhang, G. G., Pan, Y. T. (2018b). Optimization of the culture condition of *Bacillus mucilaginous* using *Agaricus bisporus* industrial wastewater by Plackett-Burman combined with Box-Behnken response surface method. AMB Expr., 8(1), 141. http://dx.doi.org/10.1186/s13568-018-0671-7

Kwak, S., Jin, Y. S. (2017). Production of fuels and chemicals from xylose by engineered *Saccharomyces cerevisiae*: a review and perspective. Microb. Cell Fact., 16(1), 82. http://dx.doi.org/10.1186/s12934-017-0694-9

Kwun, K. H., Lee, J. H., Rho, K. H., Yun, H. S. (2006). Production of ceramide with *Saccharomyces cerevisiae*. Appl. Biochem. Biotechnol., 133, 203–210.

Lew, D. B., Michael, C. F., Overbeck, T., Robinson, W. S., Rohman, E. L., Lehman, …, Gaber, M. W. (2017). Beneficial effects of prebiotic *Saccharomyces cerevisiae* mannan on allergic asthma mouse models. J. Immunol. Res., 2017, ID 3432701. http://dx.doi.org/10.1155/2017/3432701

Lin, J. M., Huang, J. F., Chen, J. Y., Lin, Z. C., Ou, Y. X., Yao, L. Y., …, Pan, Y. T. (2016). Low cytotoxic d-mannitol isolated from the industrial wastewater of *Agaricus bisporus*. J. Food Nutr. Res., 4(9), 610–614. http://dx.doi.org/10.12691/jfnr-4-9-8

Sun, S. Y., Gong, H. S., Zhao, Y. P., Liu, W. L., Jin, C. W. (2016). Sequential culture with *Torulaspora delbrueckii* and *Saccharomyces cerevisiae* and management of fermentation temperature to improve cherry wine quality. J. Sci. Food Agric., 96(6), 1880–1887. http://dx.doi.org/10.1002/jsfa.7293

Turner, T. L., Kim, H., Kong, I. I., Liu, J. J., Zhang, G. C., Jin, Y. S. (2018). Engineering and evolution of *Saccharomyces cerevisiae* to produce biofuels and chemicals. Adv. Biochem. Eng. Biotechnol., 162, 175–215. http://dx.doi.org/10.1007/10_2016_22

Wang, G., Huang, M., Nielsen, J. (2017). Exploring the potential of *Saccharomyces cerevisiae* for biopharmaceutical protein production. Curr. Opin. Biotechnol., 48, 77–84. http://dx.doi.org/10.1016/j.copbio.2017.03.017

Wilson, D. (2017). A tale of two yeasts: *Saccharomyces cerevisiae* as a therapeutic against candidiasis. Virulence, 8(1), 15–17. http://dx.doi.org/10.1080/21505594.2016.1230580

You, S. K., Joo, Y. C., Kang, D. H., Shin, S. K., Hyeon, J. E., Woo, H. M., …, Han, S. O. (2017). Enhancing fatty acid production of *Saccharomyces cerevisiae* as an animal feed supplement. J. Agric. Food Chem., 65(50), 11029–11035. http://dx.doi.org/10.1021/acs.jafc.7b04485

Zhan, X. R., Huang, J. F., Chen, J. M., Pan, Y. T. (2017). Optimization of tissue culture medium of *Anoectochilus roxburghii* using liquid of the mushroom precooking process (LMPP). J. Minnan Norm. Univ., 2, 57–64. http://dx.doi.org/10.16007/j.cnki.issn2095-7122.2017.02.009