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doi.org/10.1002/slct.202401794

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Optimisation of Catalytic Oxidation Conditions for the 2-Keto-L-Gulonic Acid Production Using Response Surface Methodology

Ceren Mutlu,[b] Cihadiye Candal-Uslu,*[a] and Mustafa Erbaş[c]

L-Ascorbic acid, also known as vitamin C, is a very important antioxidant ingredient situated many usage areas in different industries. 2-keto-L-gulonic acid (2-KLG) is the main precursor component of L-ascorbic acid production and it can be produced from L-sorbose via microbial fermentation or chemical (catalytic) oxidation. While some special strains are used in microbial fermentation, it is benefitted from some catalysts in chemical oxidation. Herein, it was aimed to determine the optimum reaction temperature, pH, and time conditions to produce maximum 2-KLG compound with the catalytic oxidation of L-sorbose in the presence of Pt/Al$_2$O$_3$ catalyst with response surface methodology approach. For this aim, the reaction temperature, pH, and time used as variable factors. The limit values of variable factors were applied as 40–60 °C for the temperature, 7.00–9.00 for the pH value, and 3–9 h for the time. The analyses results demonstrated that the increasing temperature and time negatively effected the conversion of L-sorbose into the 2-KLG. The optimum conditions of variable factors were determined as 41.30 °C for the temperature, 8.23 for the pH, and 3.25 h for the reaction time by the central composite design. Under these optimum conditions, L-sorbose was converted into 2-KLG with an average yield of 43.70 %.

1. Introduction

L-ascorbic acid, known as vitamin C, is a very important antioxidant ingredient for many industries such as pharmaceutical, cosmetic, animal feed, and food.[1–8] L-ascorbic acid has wide range of application areas in the food industry. It is added to oils, meat and dairy products, canned and frozen foods, and beverages as an antioxidant substance. In the beverage industry, it is considered as an important additive because it also provides antiseptic protection. In addition, L-ascorbic acid added to flour act as a structure regulator in doughs. The oxidation and browning reactions in foods can also be prevented, and unwanted changes in flavour and colour can be reduced with the addition of L-ascorbic acid.[9,10]

The main precursor component of L-ascorbic acid production is 2-keto-L-gulonic acid (2-KLG).[1,4–6,11–15] Although, L-ascorbic acid and 2-KLG are in the same oxidation level, they differ from each other regarding ring bondability. L-ascorbic acid is chemically identified as the enolized 1,4-lactone of 2-KLG compound.[16] This chemical difference also changes the properties of the product and consequently its usage areas. Although

2-KLG is not used directly in foods, it is very important for being the precursor component to the production of L-ascorbic acid and also L-xylose, which are frequently used in foods.[17]

The 2-KLG can be produced from L-sorbose by two different methods as the microbial fermentation or chemical oxidation.[16] Microbial 2-KLG production is generally carried out both by mono-culture fermentation of recombinant *Gluconobacter oxydans*[1,5] and by mixed co-culture fermentation of *Ketogulonicigenium vulgare*, the main producer strain of 2-KLG, and *Bacillus megaterium*, the subsidiary strain supported the necessary nutritional components for the *K. vulgare* growth.[2,5,7,8,12,13,15,18] However, procuring of these microorganisms is generally difficult. Even if these bacteria are procured, the optimization of process and the keeping under control of the fermentation are needed in co-culture systems. In addition, it requires to more energy and expensive fermentation equipment.[5,7] The production of 2-KLG via chemical oxidation is conducted by using catalysts such as Pt/Al$_2$O$_3$, Pt/C, Pd/Al$_2$O$_3$, Pd/C, Pt/Pd/Bi/C.[19–21] While the 2-KLG is produced in this method, L-sorbose is prepared in a certain concentration and subjected to direct oxidation in the presence of catalyst in neutral pH.[20] Additionally, this chemical oxidation reaction is generally carried out at the temperature of 20–80 °C and under the atmospheric pressure.[22]

The studies related to the catalytic oxidation of L-sorbose are so limited and reaction conditions were variable. In a patent research conducted by Dalmer and Heyns,[23] it was used Pt/C catalyst including 10 % of Pt and the direct oxidation of L-sorbose to 2-KLG was realized by applying the oxygen or air. In this study, it was reported that the obtained 2-KLG yield was about 50 % in the neutral or slightly alkaline pH value between 6 to 11, 70–80 h reaction time, and at the room temperature. In another research, it was expressed that the oxidation of L-

[a] C. Candal-Uslu
Department of Nutrition and Dietetics, Kütahya Health Sciences University, 43100 Kütahya, Turkey
E-mail: cihadiye.candaluslu@ksbu.edu.tr

[b] C. Mutlu
Department of Food Engineering, Balıkesir University, 10145 Balıkesir, Turkey
and
Centro de Investigação de Montanha (CIMO), Instituto Politécnico de Bragança, Campus de Santa Apolónia, 5300-253 Bragança, Portugal

[c] M. Erbaş
Department of Food Engineering, Akdeniz University, 07058 Antalya, Turkey

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doi.org/10.1002/slct.202401794

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sorbose was performed by using Pt/C catalyst including 5% Pt and adjusting the catalyst:L-sorbose ratio as 1.11. Under these circumstances, it was stated that the 2-KLG compound could be obtained with the yield of 62% by applying the air during the 54 h of oxidation time.[24] In a study conducted by Kim, et al.[25], the Pt/C catalyst containing 10% of Pt was used and the catalyst:L-sorbose ratio was adjusted to 0.2 for the oxidation of L-sorbose. In this study, when the oxidation was performed at the 50°C of reaction temperature, between 7.00 to 9.00 of pH value, and during the 6 h of reaction time, it was reported that the highest 2-KLG yield of about 50% was obtained. Bronnimann, et al.[21] obtained a higher yield of 2-KLG by using Pt/Al$_2$O$_3$ catalyst compared to the Pt/C catalyst. The maximum 2-KLG yield of 39% was obtained with the L-sorbose oxidation performed by using Pt/Al$_2$O$_3$ catalyst including 5% Pt and the optimum conditions of the L-sorbose oxidation with the oxygen was determined as 50°C for the reaction temperature, 7.3 for the pH value, 0.2 for the catalyst:L-sorbose ratio, and 1800 rpm/min for the mixing rate.

It has been reported quite different results and optimum values in the previous studies determining the optimum oxidation conditions of L-sorbose to produce 2-KLG. This research aimed to determine the optimum conditions with response surface methodology approach by using the reaction temperature, pH value, and time as the variable factors to produce 2-KLG at high yield with the catalytic oxidation of L-sorbose in the presence of Pt/Al$_2$O$_3$ catalyst. Therefore, in this research, a new experimental design was created by utilizing literature data. This new experimental design was constituted in the Design-Expert® program (Version 10.0.0, Stat-Ease Inc., Minneapolis, USA) by using central composite design (CCD) method.

Material and Methods

Material

The L-sorbose, NaOH, HCl, and catalyst (5% Pt/Al$_2$O$_3$) were purchased in the suitable purity considering the quality of production and analyses, from Acros Organics (New Jersey, USA), Merck (Darmstadt, Germany), and Sigma-Aldrich (Darmstadt, Germany) firms. Some characterization data such as the average Pt particle size, BET surface area, actual Pt loading, STEM micrograms, XPS (Cl% - metal free basis), and infrared spectroscopy results were given for 5% Pt/Al$_2$O$_3$ catalyst (Sigma-Aldrich Product Number #205974) in the literature.[26] Hare, et al.[26] reported that the average Pt particle size is 4.6 nm, BET surface area is 70 m^2/g, and actual Pt loading (by wt.) is 3.62% for this catalyst.

Methods

Research Design, Optimization of 2-KLG Production and Statistical Methods

The temperature (°C), pH value, and time (hour) were selected as the independent variable factors for the optimization of oxidation conditions. The limit values of variable factors were applied as 40–60°C for the temperature, 7.00–9.00 for the pH value, and 3–9 h for

the time. The limit values used for optimization were organized based on the literature and these limit values were also confirmed with preliminary tests. The central composite design method (CCD) of Design-Expert® program (Version 10.0.0, Stat-Ease Inc., Minneapolis, USA) was used for the optimization of determined experimental parameters, and the experimental design was constructed with a total of 15 runs formed by repeating the mid-point 3 times. The applied experimental design is given in the Table 1. The analysis results of 2-KLG were evaluated as response, and it was used to determine the optimum oxidation temperature, pH, and time values by using Design-Expert® 10.0.0. The optimization conditions were confirmed with the re-production of 2-KLG by applying these conditions.

Determination of Catalyst Type and Ratio Used in the Optimization of 2-KLG Production

The catalyst of Pt/Al$_2$O$_3$ and its ratio were selected based on literature findings to use in the 2-KLG production with catalytic oxidation of L-sorbose.[20,21,27] The ratio of L-sorbose:Pt/Al$_2$O$_3$ was applied as 1.00:1.50 in the reaction solution.

The L-sorbose concentration was kept stable as 0.1 M in these experiments[27] and all productions were carried out with 100 mL of 0.1 M L-sorbose solution.

Oxidation of L-sorbose

For the conversion of L-sorbose to the 2-KLG with the oxidation, 100 mL of 0.1 M (18 g/L) L-sorbose solution was prepared with ddH$_2$O. This solution was transferred to the 250 mL graduated cylinder, and this graduated cylinder was placed in a beaker including water. The temperature was adjusted the value (40, 50 or 60°C) indicated in the related experimental design run (Table 1). After equilibrating the temperature of L-sorbose and the water found outside of the graduated cylinder, the L-sorbose solution was stirred on the magnetic stirrer at 1000 rpm by giving N$_2$ gas into it with a plastic tube to remove of dissolved gases in the solution.

Table 1. The applied experimental design to produce the 2-KLG from L-sorbose by catalytic oxidation.

Run	Temperature (°C)	pH	Time (h)
1	50	9	9
2	40	8	3
3	50	7	3
4	40	9	6
5	50	8	6
6	60	8	3
7	40	7	6
8	60	9	6
9	50	8	6
10	50	7	9
11	60	8	9
12	50	8	6
13	50	9	3
14	40	8	9
15	60	7	6

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The process of giving the N_2 gas was continued for 10 min. At the end of this period, the N_2 gas tube was taken out and 2.70 g of Pt/Al_2O_3 catalyst was added to the graduated cylinder by transferring O_2 gas into this system at the rate of 0.2513 g/min. After that the pH value of the mixture was adjusted to the value indicated in the experimental design by using NaOH or HCl solutions, and it was kept stable during the reaction time. The L-sorbose and 2-KLG contents of the sample were analysed each hour during the reaction time.

The Analyses of L-sorbose and 2-KLG

The contents of L-sorbose and 2-KLG were determined by using HPLC system (Agilent, 1260 Infinity II) equipped with refractive index detector (RID) (Agilent, 1260 Infinity II), and Hi-Plex Ca column (Agilent, 300x7.7 mm) according to modified method reported by Mutlu and Erbas.[28] For this purpose, the sample was centrifuged at 7100*xg* for 10 min and the obtained supernatant was filtered by the 0.45 μm membrane filter to inject HPLC system as 10 μL. The ddH_2O was used as the mobile phase at the isocratic flow with the flow rate of 0.6 mL/min. The temperature of the column and detector were adjusted at 75 °C and 30 °C, respectively. The identification and quantification of L-sorbose and 2-KLG were performed by the curves formed with standard solutions of each compound.

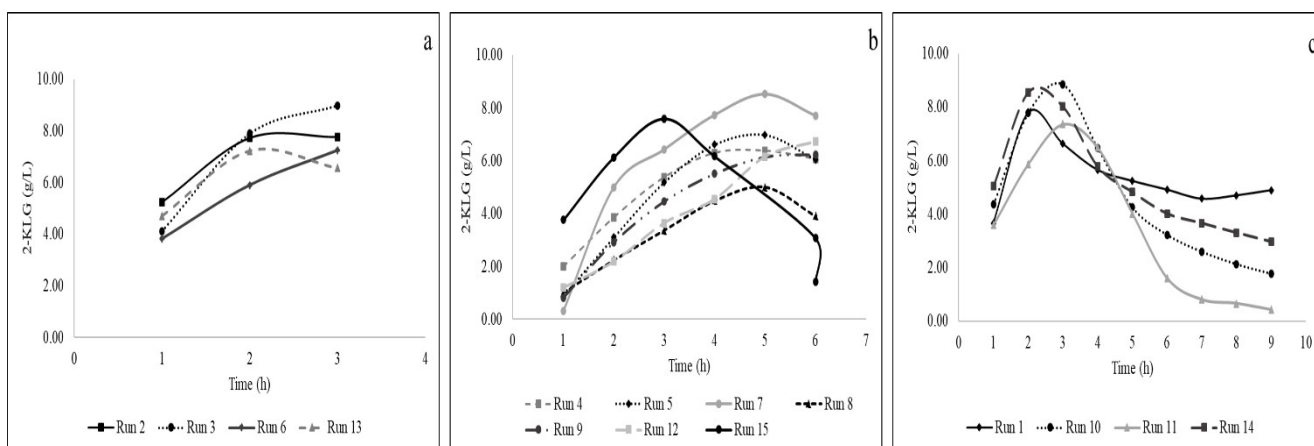## 2. Results and Discussion

2.1. 2-KLG Production Results

The analysis results obtained from 15 oxidation runs are given in Table 2. It was determined that the 2-KLG production amount varied between 0.43 and 8.99 g/L, and the highest 2-KLG production rate was achieved with 49.95% at 50 °C, pH 7.00, and 3 h reaction time conditions with the run 3.

It was reported that 0.1 M L-sorbose was converted to approximately 0.04 M (7.2 g/L) 2-KLG compound at 70 °C, pH 7.7 about 2 h with Pt/Al_2O_3 catalyst.[27] In another study, the Pt catalyst on Al_2O_3 support material was used to convert 0.3 M L-sorbose at 50 °C, and pH 7.5 conditions and while the L-sorbose conversion rate was found to be 37%, the 2-KLG production was between 36–38% at the end of 8 h reaction time.[29]

The residual L-sorbose amounts were between 0.22–3.37 g/L. It was evaluated that, the used all L-sorbose amount was not converted to the 2-KLG compound, and there were by-products formed during oxidation reaction. In a study, it was reported that during the oxidation of L-sorbose to the 2-KLG compound, various short-chain aldehydes and dicarboxylic acids were formed because of breaking the C—C bond by side reactions. Besides, the addition of NaOH, especially at high pH, promoted aldol dimerization and polymerization reactions.[20,21] It was stated that C—C bond cleavage might be sourced from formed H_2O_2 by the reduction of O_2 with metal hydride.[29–31] Additionally, samples were taken every hour during the reaction, and obtained L-sorbose and 2-KLG findings are given in Figure 1. When the obtained findings were examined, it was evaluated that the amount of the 2-KLG compound decreased with the prolongation of the reaction time. The decomposition of the 2-KLG was higher at 50 °C and pH 9.00 applications (run 1 and 13) and after two hours produced 2-KLG amount decreased. It was evaluated that the 2-KLG compound was decomposed into advanced oxidation products. It was reported that approximately 50% of the produced 2-KLG decomposed in an hour of the reaction with Pt/Al_2O_3 catalyst at 60 °C and pH 9.00 conditions. Moreover, when pH was above 11.00, there was no 2-KLG formation.[20] However, the decomposition of 2-KLG was at the lowest amount at the mid-points of experimental design as 50 °C and pH 8.00. Therefore, it was concluded that this compound was more stable under these conditions.

Table 2. Central composite design applied to produce 2-KLG by oxidation from L-sorbose and the results of 2-KLG production.

Run	Temperature (°C)	pH	Time (h)	Residual L-sorbose amount (g/L)	2-KLG amount (g/L)	Conversion (%)
1	50	9	9	2.09	4.89	27.19
2	40	8	3	2.20	7.77	43.18
3	50	7	3	2.07	8.99	49.95
4	40	9	6	3.02	6.07	33.72
5	50	8	6	1.43	6.05	33.61
6	60	8	3	3.37	7.24	40.21
7	40	7	6	1.27	7.70	42.77
8	60	9	6	3.17	3.90	21.67
9	50	8	6	3.03	6.24	34.65
10	50	7	9	0.33	1.78	9.88
11	60	8	9	0.22	0.43	2.37
12	50	8	6	2.09	6.73	37.37
13	50	9	3	1.22	6.56	36.46
14	40	8	9	0.76	2.97	16.50
15	60	7	6	0.57	1.43	7.95

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Figure 1. Composition and decomposition of the 2-KLG depending on time (a: run with 3 h reaction time, b: run with 6 h reaction time, c: run with 9 h reaction time).

The 2-KLG results as a response were analysed by linear, quadratic and cubic models, and the most suitable model was chosen depending on the p-value, lack of fit test, and regression coefficient. It was determined that the model that best expresses the production of the 2-KLG compound by catalytic oxidation method under experimental conditions was the linear model with a 74% ($R^2 = 0.742$) confidence level. The ANOVA results for the 2-KLG production are presented in Table 3. The model F-value of 10.52 referred that the model was significant and there was only a 0.15% chance that an F-value this large could indicate by the reason of noise. According to the ANOVA results, while the temperature and time were significant, the pH was insignificant model terms. The lack of fit F-value of 21.76 showed that the lack of fit was significant. There was 4.47% chance that a large lack of fit F-value could be revealed by the reason of noise. Additionally, the pred-R^2 of 0.4868 was in line with the adj-R^2 of 0.6711 because of the difference between them was less than 0.2. Adequate precision value expresses the ratio of signal to noise, and it should be greater than 4 value. The obtained ratio of 10.45 value stated a sufficient signal, and the selected model could be used to navigate the design space.
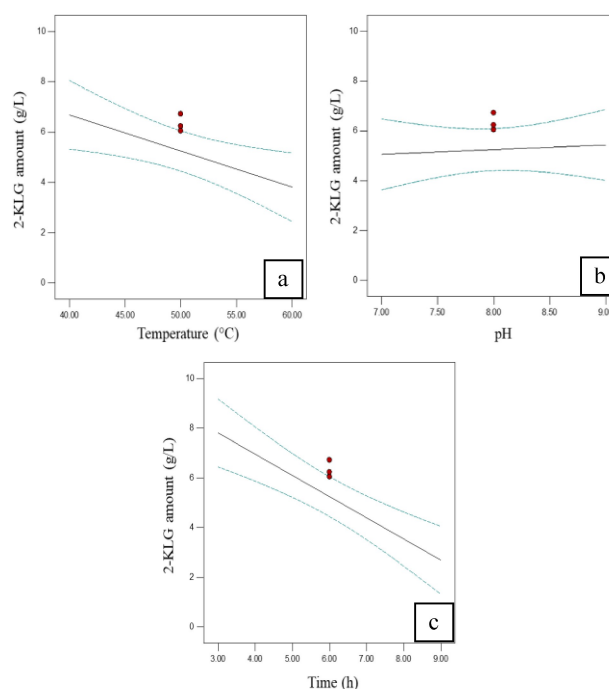
Table 3. ANOVA results of the linear model for the 2-KLG production.

Variation	Mean square	F-value
Model (Linear)	23.12	10.52**
Temperature	16.57	7.54*
pH	0.29	0.13
Time	52.50	23.89**
Lack of fit		21.76*
R^2	0.742	
Adj-R^2	0.671	
Predicted-R^2	0.487	
Adequate precision	10.45	
*: $0.01 < p < 0.05$, **: $p < 0.01$.		

2.2. Effects of Independent Variables on 2-KLG Production

2.2.1. Temperature

It was determined that temperature had a statistically significant ($0.01 < p < 0.05$) effect on the 2-KLG production amount. This effect is shown in Figure 2a. It was determined that the amount of the 2-KLG production decreased with the temperature increased from 40°C to 60°C. The mean 2-KLG production amounts were 6.13 g/L at 40°C, 5.89 g/L at 50°C, and 3.25 g/L at 60°C. In addition, there was a 50% decrease in mean 2-KLG production yield from 34.04% to 18.05% with the increase in temperature. It was evaluated that although it changes

Figure 2. Effects of reaction temperature (a), pH (b), and time (c) on the 2-KLG production.

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according to the effects of other independent variables in the reaction, a temperature above 50 °C decreases the amount of 2-KLG production.

It was reported that even though the increasing temperature increased the reaction rate and the suitable reaction temperature was stated as 60–70 °C, the higher 2-KLG yield can also be achieved at 28–35 °C.[32] Moreover, it has been reported in a study that the 2-KLG compound rapidly degrades in aqueous solutions above 55 °C.[20] In another study, it has been stated that if the reaction temperature is below 50 °C, the degradation amount of the 2-KLG compound is quite low, and therefore its decomposition is insignificant.[21] It was also noted that the oxidation reaction rate increases with the increase in temperature from 40 to 75 °C, but it decreases the reaction selectivity for 2-KLG formation.[21]

2.2.2. pH

It was determined that pH value did not have a statistically significant ($p > 0.05$) effect on the 2-KLG production amount. The graph showing the effect of pH value on the amount of 2-KLG is given in Figure 2b. The amount of 2-KLG production did not significantly change by increasing the pH level from 7.00 to 9.00. The mean 2-KLG production amounts were found to be 4.98 g/L at pH 7.00, 5.35 g/L at pH 8.00, and 5.36 g/L at pH 9.00. Additionally, the 2-KLG production yields were between 27.64–29.76%.

It was reported that L-sorbose oxidation reaction occurs at a lower rate under acidic conditions, and therefore it should be performed at neutral or slightly basic pH values. Although basic pH values accelerate the reaction rate, they can cause sugar decomposition, especially above the pH 11.00 value. Therefore, the reaction pH range is suggested to be between 8.00 and 10.00 for the 2-KLG production.[32]

The oxidation of L-sorbose to the 2-KLG compound was carried out at a pH of 7.70 by Sulman, et al.[33] Similarly, Bronstein, et al.[34] converted L-sorbose at pH 7.70 to the 2-KLG compound by catalytic oxidation method. Additionally, the 2-KLG was produced at pH 7.30[21] and 8.00[27] in some previous studies.

2.2.3. Time

The reaction time has a statistically significant ($p < 0.01$) effect on the 2-KLG production amount. The effect of time on the 2-KLG amount is shown in Figure 2c. It was determined that the amount of the 2-KLG production decreased by increasing the reaction time from 3 to 9 hours. The mean 2-KLG production amounts were 7.64 g/L at 3 h, 5.45 g/L at 6 h, and 2.52 g/L at 9 h. When the production efficiency was evaluated, there was a 70% decrease in the average 2-KLG production yield from 42.45% to 13.99% with the increase in reaction time. Considering all data, it was evaluated that the reaction time longer than 4 hours had a generally negative effect on the 2-KLG production.

The oxidation reaction times were applied between 3.00–9.17 h in previous studies.[27,33,34] It was highlighted that reaction time was directly affected by reaction conditions, and even if the conditions were similar, there might be considerable differences between the reaction times that produce approximately the same rate of the 2-KLG.[27] Besides, it is not recommended to extend the reaction time, since conversion of L-sorbose to the 2-KLG is not possible with the poisoning of catalyst by the reaction by-products.[32]

2.2.4. Determination of Optimum 2-KLG Production Conditions and Verification

When the effects of temperature, pH, and reaction time used as independent variables to produce 2-KLG by oxidation from L-sorbose on the amount of 2-KLG produced were evaluated, the optimum oxidation conditions were suggested according to desirability function as 41.26 °C temperature, pH 8.23, and 3.25 h reaction time. The 2-KLG production was carried out with two replications under these conditions. The 2-KLG production at a concentration of 7.86 g/L with an average yield of 43.70% was achieved from these productions. The model verification was evaluated with the minimum mean absolute percentage error (E%). The E% value calculated with the model estimation (8.88 g/L), and the experimental data was determined to be below 13%. It was reported that being the E% value lower than 10% indicates the fitness of the model to represent the data.[35] The calculated E% value was higher than the acceptable limit value. This might have resulted from the lower R^2 (0.742) value of the model. That can cause some deviations in the inaccurate prediction of optimum conditions and the calculation of the theoretical expected 2-KLG results. The determined 2-KLG amount was lower than the predicted value. However, when the reaction time was extended for an hour, it was seen that the predicted result was achieved.

3. Conclusions

It was determined that the effects of reaction temperature and time were statistically significant, but the effect of pH value was insignificant on the amount of 2-KLG formed by the oxidation of L-sorbose. The increase in time and temperature had a negative effect on the conversion of L-sorbose into the 2-KLG compound. It was achieved the highest conversion yield of 49.95% with the run 3 reaction conditions that had the temperature of 50 °C, the pH of 7.00, and the reaction time of 3 h. The optimum reaction conditions obtained by evaluating the data belonging to the all runs formed by using the central composite design were determined as 41.30 °C for the temperature, 8.23 for the pH, and 3.25 h for the reaction time. Under these optimum conditions, L-sorbose could be converted into the 2-KLG with an average yield of 43.70%.

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Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

[1] L. L. Gao, Y. F. Liu, X. Y. Zhang, H. S. Zhang, *J. Chem.* **2020**, *2020*, 1–8.
[2] W. Zou, L. M. Liu, J. Chen, *Crit. Rev. Microbiol.* **2013**, *39*, 247–255.
[3] W. Yang, L. Han, M. Mandlaa, H. Chen, M. Jiang, Z. Zhang, H. Xu, *Lett. Appl. Microbiol.* **2013**, *57*, 54–62.
[4] Z. Huang, W. Zou, J. Liu, L. M. Liu, *J. Biotechnol.* **2013**, *164*, 454–460.
[5] J. Fang, H. Wan, W. Z. Zeng, J. H. Li, J. Chen, J. W. Zhou, *Appl. Biochem. Biotechnol.* **2021**, *193*, 128–141.
[6] Mandlaa, W. C. Yang, C. B. Liu, H. Xu, *J. Ind. Microbiol. Biotechnol.* **2015**, *42*, 897–904.
[7] L. L. Gao, Y. D. Hu, J. Liu, G. C. Du, J. W. Zhou, J. Chen, *Metab. Eng.* **2014**, *24*, 30–37.
[8] S. C. Fan, Z. Y. Zhang, W. Zou, Z. Huang, J. Liu, L. M. Liu, *J. Biotechnol.* **2014**, *169*, 15–22.
[9] V. Delić, D. Šunić, D. Vlašić, Microbial reactions for the synthesis of vitamin C (L-ascorbic acid). In *Biotechnology of Vitamins, Pigments and Growth Factors*, (Eds.: E. J. Vandamme), Springer, Dordrecht, **1989**, pp. 299–334.
[10] C. Mutlu, M. Erbaş, *J. Food* **2020**, *45*, 92–102.
[11] Y. Chen, L. Liu, S. Q. Yu, J. H. Li, J. W. Zhou, J. Chen, *Front. Bioeng. Biotechnol.* **2021**, *9*, 673844, 1–9.
[12] W. C. Yang, H. Sun, D. Dong, S. Ma, Mandlaa, Z. X. Wang, H. Xu, *Braz. J. Microbiol.* **2021**, *52*, 257–265.
[13] Mandlaa, Z. Y. Sun, R. G. Wang, X. D. Han, H. Xu, W. C. Yang, *Amb Express* **2018**, *8*, 30, 1–7.
[14] V. Kaswurm, W. van Hecke, K. D. Kulbe, R. Ludwig, *Biochem. Eng. J.* **2013**, *79*, 104–111.
[15] C. Ye, W. Zou, N. Xu, L. M. Liu, *J. Biotechnol.* **2014**, *182*, 61–67.
[16] G. Pappenberger, H. P. Hohmann, Industrial production of L-ascorbic acid (Vitamin C) and D-isoascorbic acid. In *Biotechnology of Food and Feed Additives, Vol. 143* (Eds.: H. Zorn, P. Czermak), Springer, Berlin, Heidelberg, **2014**, pp. 143–188.
[17] Y. Chen, L. Liu, X. Shan, G. Du, J. Zhou, J. Chen, *Front. Bioeng. Biotechnol.* **2019**, *7*, 385.
[18] W. C. Yang, L. T. Han, M. Mandlaa, H. H. Zhang, Z. Z. Zhang, H. Xu, *Braz. J. Microbiol.* **2017**, *48*, 397–402.
[19] P. Gallezot, *Catal. Today* **2007**, *121*, 76–91.
[20] T. Mallat, C. Bronnimann, A. Baiker, *Appl. Catal. a-Gen.* **1997**, *149*, 103–112.
[21] C. Bronnimann, Z. Bodnar, P. Hug, T. Mallat, A. Baiker, *J. Catal.* **1994**, *150*, 199–211.
[22] M. Besson, P. Gallezot, *Catal. Today* **2000**, *57*, 127–141.
[23] O. Dalmer, K. Heyns, US2190377A, **1940**, *United States Patent Office*, USA, 1–3.
[24] K. Heyns, H. Paulsen, *Adv. Carbohydr. Chem.* **1963**, *17*, 169–221.
[25] V. Kim, E. Zakharova, I. Kozhevnikov, *React. Kinet. Catal. Lett.* **1991**, *45*, 271–276.
[26] B. J. Hare, R. A. G. Carcamo, T. Xie, P. J. Meza-Morales, R. B. Getman, C. Sievers, *J. Catal.* **2021**, *402*, 218–228.
[27] E. Grünewald, U. Prüße, K.-D. Vorlop, *Catal. Today* **2011**, *173*, 76–80.
[28] C. Mutlu, M. Erbas, *J. Apic. Res.* **2023**, *62*(2), 364–373.
[29] C. E. Chan-Thaw, L. E. Chinchilla, S. Campisi, G. A. Botton, L. Prati, N. Dimitratos, A. Villa, *ChemSusChem: Chem. Sustain. Energy. Mater.* **2015**, *8*, 4189–4194.
[30] M. Sankar, N. Dimitratos, D. W. Knight, A. F. Carley, R. Tiruvalam, C. J. Kiely, D. Thomas, G. J. Hutchings, *ChemSusChem: Chem. Sustain. Energy. Mater.* **2009**, *2*, 1145–1151.
[31] A. Villa, G. M. Veith, L. Prati, *Angew. Chem. Int. Ed.* **2010**, *49*, 4499–4502.
[32] G. Tojo, M. Fernández, Heyns oxidation. *Oxidation of Primary Alcohols to Carboxylic Acids: A Guide to Current Common Practice*, Springer, New York, NY, **2007**, pp. 43–60.
[33] E. Sulman, V. Matveeva, L. Bronstein, A. Sidorov, N. Lakina, S. Sidorov, P. Valetsky, *Green Chem.* **2003**, *5*, 205–208.
[34] L. M. Bronstein, G. Goerigk, M. Kostylev, M. Pink, I. A. Khotina, P. M. Valetsky, V. G. Matveeva, E. M. Sulman, M. G. Sulman, A. V. Bykov, *J. Phys. Chem. B* **2004**, *108*, 18234–18242.
[35] M. E. Sormoli, T. A. Langrish, *LWT-Food Sci. Technol.* **2015**, *62*, 875–882.