Microwave-assisted conversion of D-glucose into lactic acid under solvent-free conditions

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The microwave-assisted alkaline degradation of D-glucose with alumina supported potassium hydroxide towards its conversion into lactic acid is reported. An experimental design approach was used to optimize the variables involved in this transformation. The reaction succeeded in yielding 75C-% of lactic acid starting from D-glucose using 1.5 equiv of KOH at 180 °C. The optimal conditions were applied to D-fructose, D-mannose and D-sucrose.

Introduction

Lactic acid (2-hydroxypropanoic acid) is a feedstock with a growing market. It is used in food and pharmaceutical industries and has the potential to be used for the production of biodegradable polymers, such as poly(lactic acid).[1]

Currently, lactic acid is produced by a fermentative route starting from different sources of sugar, such as starch, sucrose, lactose, sugarcane bagass or apple pomace.[2] However, the biotechnology process presents some disadvantages, such as limited space–time yield and requires control and regulation of the microorganism pool.

Alternative chemical processes exist starting from monosaccharides treated in aqueous alkaline solution.[3] These processes are less constraining than the fermentative route. However, their limits are the release of a broad excess of by-products and the high concentration of alkaline used.

Recently, Onda *et all* studied the conversion of D-glucose into lactic acid using noble metal supported catalyst with an alkaline in aqueous solution. This method allowed the reduction of the amount of complex by-products and lactic acid was obtained with 57%-C yield. Nevertheless, the reaction requires a broad alkali excess compared to the starting sugar (20 equiv compared to sugar).[4] In the last decades, microwave power has taken an undeniable place in chemical laboratory practice as a very effective and environmentally friendly process, particularly when it is carried out in solvent-less conditions. Microwave heating makes it convenient to perform reactions very efficiently in dry media conditions, and thus within the frame of the green chemistry concept. The advantages of using dry media conditions provide reaction rate enhancements with different selectivity compared to conventional conditions.[5]

In this study, we present the microwave-assisted conversion of D-glucose into lactic acid in dry media conditions using alumina supported potassium hydroxide. The effect of experimental conditions such as power, time and concentration of alkali on the reaction of monosaccharide were investigated. An experimental design was used to obtain optimal conditions for conversion of D-glucose into lactic acid.

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Results and discussion

The CEM Discover MW allows for irradiation either by assigning the power with continuous measurement of the resulting temperature by an optic fiber captor or by assigning the temperature with continuous adjustment of irradiation power. In this study, we decided to employ the first mode of irradiation, in solventless media with assigned power in order to obtain a temperature profile. First, we investigated a microwave-assisted protocol in solvent-free conditions with an experiment field starting from the identification of the boundary values (*i.e.*, minima and maxima) for three variables, specific power applied SP (W g^{-1} of product), alkali concentration (equiv) and time (min). We used the Box–Benkhen design to determine the reaction conditions with the three factors which could have a significant effect on the outcome of the reaction. The D-glucose mixed with previously crushed alumina supported potassium hydroxide was loaded in a glass tube and irradiated.

Optimization of reaction conditions

The execution of the experimental design yielded approximately 50% of lactic acid. The experimental matrix of the executed Box–Benkhen design with the coded values (–1, 0, +1) is given in Table 1. The corresponding real values are given in the Table 2.

We employed a full three-level quadratic design giving 15 experiments, which lead to the formation of up to 50% of lactic acid according to reaction conditions. Experiment 5 represents the alkaline degradation of glucose supported on alumina at level-0 of potassium hydroxide level-0 of specific power and level-0 for the contact time. This reaction provided approximately 50% of lactic acid.

The identified quadratic model giving the lactic acid yield according to the experimental conditions is given in eqn (1)

$$Y = 31.25 + 8.875x_1 - 1.375x_2 + 6.5x_3 - 3.5x_1x_2 - 7.25x_1x_3 - 4.75x_2x_3 - 13.624x_1^2 - 6.125x_2^2 + 8.625x_3^2 \quad (1)$$

Table 1 Full Experimental values of the Box-Benkhen design

Exp.	x_1	x_2	x_3	Lactic acid C-% yield	Total mass/g	Power/W	Final T/°C
1	−1	−1	0	0	8	16	52
2	+1	−1	0	24	8	32	199
3	−1	+1	0	6	12	24	68
4	+1	+1	0	16	12	49	280
5	0	0	0	49	10	31	230
6	−1	0	−1	0	10	20	62
7	+1	0	−1	33	10	41	220
8	−1	0	+1	34	10	20	174
9	+1	0	+1	38	10	41	244
10	0	0	0	39	10	30	214
11	0	−1	−1	28	8	24	117
12	0	+1	−1	33	12	37	280
13	0	−1	+1	44	8	24	165
14	0	+1	+1	30	12	37	280
15	0	0	0	37	10	31	218

x_1: microwave specific power SP (W g^{-1}). x_2: potassium hydroxide (equiv/initial glucose). x_3: contact time (min).

Table 2 Lactic acid yields starting from glucose at 3.1 W g^{-1} with 1.5 equiv of alkali at different reaction times in comparison to predicted experiment

Coded values of time	Real values of time/min	Predicted C-% yield in lactic acid	Observed C-% yield in Lactic acid	% Conversion of glucose
+1	30	48	49	99
+1.5	35	63	59	99
+2	40	82	75	99

Different response surfaces were calculated from eqn (1) by setting alternatively one factor at a time at different levels (0, −1, +1). Only level-0 of both the specific power (*i.e.* 3 W g^{-1}) and the concentration of KOH (*i.e.* 2 equiv/initial glucose) are shown in Fig. 1 and 2, respectively.

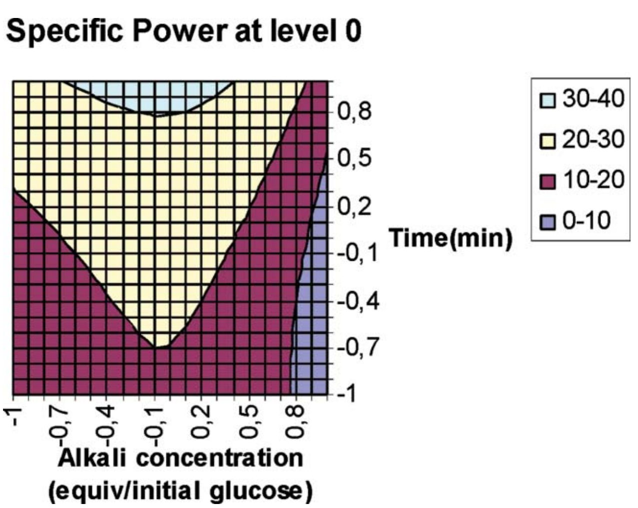

Fig. 1 Contour plot of lactic acid yield from regression analysis of experimental data at level-0 of the specific power.

As indicated by these plots, when the specific power was fixed at level-0 (*i.e.* 3 W g^{-1}), it was possible to produce 30% of lactic acid at level-0 of KOH (*i.e.* 2 equiv/initial glucose) and level-1 for the time (*i.e.* 30 min). When the alkali concentration was

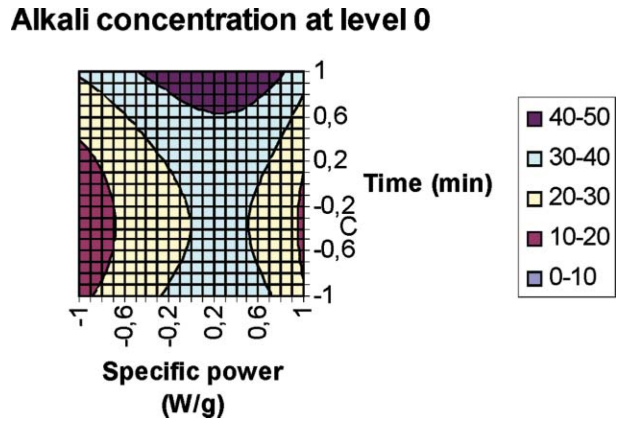

Fig. 2 Contour plot of lactic acid yield from regression analysis of experimental data at level-0 of alkali (equiv/initial glucose).

fixed at level-0 (*i.e.* 2 equiv/initial glucose) it is necessary to work around level-0.5 of the specific power (*i.e.* 2.5 W g^{-1}) and level-1 for the time (*i.e.* 30 min) to produce 50% of lactic acid. Plots at other levels of alkali and power are qualitatively similar but the yields are lower. Analysis of variance indicates that the response models are suitable for lactic acid yields. Indeed the correlation coefficient ($R^2 = 0.85$) indicated that the yield of lactic acid depended on the factors studied.

In the experimental design, the maximum product yield was obtained for a specific power of 3 W g^{-1}, 2 equiv of potassium hydroxide and 30 min reaction time conditions. Using these conditions, lactic acid yielded 49%. However, However, this result was obtained or accomplished along the boundary of the time parameter (*i.e.* after 30 min of reaction) in the design.

Experimental predictions were investigated using the quadratic model at different levels of specific power, concentration of potassium hydroxide and time. It appears that by working under 3.1 W g^{-1} and 1.5 equiv of alkali for 40 min, it can be possible to produce 82% of lactic acid. For this reason, additional experiments were carried out at different times while specific power and alkali concentration were set at 3.1 W g^{-1} and 1.5 equiv, respectively, to determine if mathematical simulations matched authentic experiments. The predicted values of the response under these experimental conditions and the values obtained experimentally are given in Table 2.

We observed that optimal conditions for the production of lactic acid based on these additional experiments occurred when glucose was irradiated at 3.1 W g^{-1} in the presence of 1.5 equiv of alkali for 40 min. Moreover, between 30 min and 40 min, the predictions fit the experiments. But working beyond 40 min proved to be harmful for the production of lactic acid.

Impact of alkali concentration and the temperature on reaction conditions

Investigation of the experiments enabled us to study the effects of the temperature and the quantity of alkali on the output of the formed products. Fig. 3 demonstrated that lactic acid formation was enhanced by temperatures ranging between 180 and 190 °C for 1.5 equiv of alkali compared to glucose. Under these conditions, it was then possible to achieve more than 50% of lactic acid.

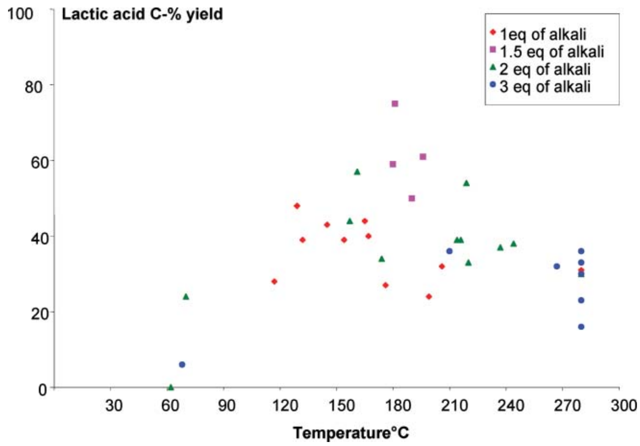

Fig. 3 Effect of alkali concentration and the temperature on the lactic acid yield.

Using the optimal conditions, we realized a reaction without solid support. In comparison with the reaction including solid support, the yield of lactic acid was four times less, as shown in Table 3. Solid support is thus an important component in the reaction.

In order to elucidate the importance of microwaves on these reactions, similar experiments were realized using conventional heating (Table 4).

As shown in Table 4, the use of microwave irradiation at fixed power is the best method for the production of lactic acid under dry media conditions, the yield reached 75 C-%. Indeed, when the reaction was accomplished in an oil bath, only 36% of lactic acid was obtained. Proceeding with fixed temperature with microwaves induced a lower yield in lactic acid, probably caused by a reduction of the power during the reaction. In contrast, executing the reaction at fixed power managed to stabilize the temperature during the reaction (Fig. 4).

Table 3 Effect of solid support on the degradation of glucose using optimal conditions[a]

	Time/min	Final T/°C	C-% Lactic acid yield	% Conversion of glucose
Without solid support	40	180	19	99
With solid support	40	180	75	99

[a] Reactions were carried out with 11.1 mmol of D-glucose, 16.65 mmol of KOH and 200% w/w of alumina at 3.1 W g^{-1} as specific power.

Table 4 Comparison between microwave and conventional heating[a]

	Time/min	Final T/°C	C-% Lactic acid yield	% Conversion of glucose
Oil bath	40	180	36	99
MW[b]	40	180	75	99
MW[c]	40	180	21	99

[a] Reactions were carried out with 11.1 mmol of D-glucose, 16.65 mmol of KOH and 200% w/w of alumina at 3.1 W g^{-1} as specific power. [b] With assigned power (specific power: 3 W g^{-1}). [c] With assigned temperature: 180 °C.

Table 5 Lactic acid yields obtained from different carbohydrates with optimized reaction conditions determined with D-glucose

Carbohydrates	% Conversion of glucose	%-C Lactic acid yield
D-Glucose	99	75
D-Mannose	99	41
D-Fructose	99	36
D-ribose	99	43
D-arabinose	99	35
D-Sucrose	99	23

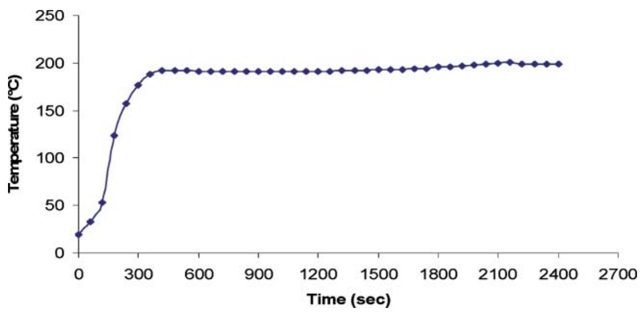

Fig. 4 Temperature profile of glucose irradiation at continuous power (28 W) during 40 min.

Similar studies have been conducted in the presence of hydrotalcite-type catalysts to initiate the formation of lactic acid from glucose. These catalysts have Brønsted-base sites and are able to catalyze aldolization reaction.[6] The reaction mechanism of alkaline degradation of glucose into lactate has been described as a reverse aldol condensation and studied using ^{13}C-labeled glucose.[7]

The optimized conditions were applied to other sugars such D-mannose, D-fructose, D-ribose, D-arabinose and D-sucrose to compare the production of lactic acid (Table 5).

The yields obtained are lower for other sugars under the optimal conditions found for producing lactic acid from D-glucose. This means that it is necessary to perform another experimental designs for each type of sugar in order to maximize the lactic acid yield.

Conclusion

Solvent-free organic syntheses combined with supported reagent and microwave irradiation is an effective process to obtain lactic acid starting from sugar source. Ideal temperature for the production of lactic acid is between 180 and 190 °C with a specific power of 3.1 W g^{-1}. Compared to classical heating, MW accelerates the conversion rate of glucose and consequently enhance the yield of lactic acid, when the optimal temperature for this conversion is assigned, a lower yield in lactic acid is obtained.

These results suggest that beneficial rate enhancements are probably due to microwave effects, by comparing conventional and microwave heating. Pilot scales for industrial applications are being studied.

Experimental

Material

D-Glucose anhydrous and KOH (90%) were purchased from Verfilco and used without further purification.

Neutral alumina (150 mesh, 58 Å) was purchased from Sigma–Aldrich. Microwave irradiation was performed in a CEM Discover® System. This system operates at a frequency of 2.45 GHz with continuous MW irradiation power up to 300 W.

The reactions are carried out in round bottom pyrex tubes with a diameter of 38 mm and a height of 200 mm. Mechanical agitation is used.

Reaction procedure

Glucose (11.1 mmol) and potassium hydroxide (16.65 mmol) were introduced into the reactor with alumina (200% w/w compared to initial glucose and alkali). The mixture (total mass of 9 g) was stirred for a minute then was irradiated by MW at the desired power and time. A mechanical system of agitation was used to homogenize the powder. After reaction, a solution of H_2SO_4 0.2 M was added so as to obtain a pH of approximately 2–3. The aqueous solution was separated from alumina by filtration for analysis.

Product analysis

The filtrate was analyzed by HPLC (Surveyor photodiode array detector from ThermoFinnigan) with a UV detector (wavelength 220 nm). A Prevail Organic Acid column from Alltech (250 × 4.6 mm, 5 μm) was used with an aqueous solution of formic acid 0.15% as eluant at 0.5 mL min^{-1} flow rate for 40 min.[8] The remaining sugar was quantified by HPLC analysis (Surveyor LC pump from ThermoFinnigan) coupled with an evaporative light scattering detector. A Prevail carbohydrates ES column, also from Alltech (250 × 4.6 mm, 5 μm), was used with a solution of 75% acetonitrile in water as eluant at 1 mL min^{-1} flow rate for 30 min. In addition, a guard column of the same packing material was also used for both sugar and acid analysis.

Output in lactic acid and conversion of glucose were estimated on a carbon percentage basis (C-%) from eqn (2) and (3) in the following way:

$$\text{C-\% yield of lactic acid} = \frac{(\text{molar concentration of lactate formed} \times 3) \times 100}{(\text{molar concentration of introduced sugar} \times 6)} \quad (2)$$

$$\text{\% glucose conversion} = \frac{\{1 - (\text{molar concentration of remained sugar})\} \times 100}{(\text{molar concentration of introduced sugar})} \quad (3)$$

Optimization method

A response surface methodology (RSM) was used to find optimum operating conditions for the formation of lactic acid. Thus, a Box–Benkhen design, with three factors was chosen. The execution of such a design is a rapid and effective technique for finding the optimal operating conditions in order to improve the results.[9,10] The implementation of the design includes the setting of the minima and maxima levels for all the retained factors of the experimental design (Table 5). That makes it possible to carry out the experiments under the conditions stipulated and to correlate the answers of the design (here the yield in lactic acid) to the experimental conditions (the factors of the experimental design) thanks to the quadratic model presented below (eqn (4)).The linear regression function on Excel® software was used in order to identify the coefficients a_i, a_{ij} and a_{ii} of this quadratic model.

$$Y = a_0 + a_1x_1 + a_2x_2 + a_3x_3 + a_{12}x_1x_2 + a_{13}x_1x_3 + a_{23}x_2x_3 + a_{11}x_1^2 + a_{22}x_2^2 + a_{33}x_3^2 \quad (4)$$

Where:

Y is the response (lactic acid C-%),

a_0 is the value of the response at the center point response of the design,

a_i, a_{ii} and a_{ij} are the coefficients of linear, quadratic and interactive effects respectively.

In our study, three reaction conditions designated by x_1, x_2, and x_3 for specific power applied (W g^{-1} of product), alkali concentration (equiv/initial sugar) and time (min), respectively, were selected as being the experimental factors. For economic reasons, we have chosen to work between a specific power range of 2 W g^{-1} to 4 W g^{-1}. The coefficients (a_i, a_{ij}) in the model equation were determined using the linear regression function on Excel® software. The determination of optimum conditions and investigation of lactic acid output behaviour are illustrated by contour plots produced from eqn (1).

Table 6 presents the boundary values of reaction conditions in the experimental field.

Table 6 Box–Benkhen design reaction conditions

Parameter	Boundary values −1	0	1
x_1: Microwave specific power SP (W g^{-1})	2	3	4
x_2: Alkali concentration (equiv/initial glucose)	1	2	3
x_3: Time (min)	10	20	30

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