
Original paper

Kinetics for the Subcritical Treatment of Glucose Solution at Various Concentrations

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Kinetic analysis was performed for the isomerization of glucose and side reactions (decomposition) in subcritical water with low-to-high saccharide concentrations (0.001–0.40 kg/kg-water). An aqueous solution of glucose was treated under subcritical conditions at 200 °C for 30–400 s using a tubular reactor. Isomerization of glucose to fructose predominantly occurred when the glucose concentration was low, while isomerization to mannose scarcely occurred. Decomposition of glucose to byproducts was promoted with increasing glucose concentration, while the isomerization was suppressed. Selectivity of fructose and mannose for the isomerization became lower at higher glucose concentrations and with longer reaction times. Kinetic analysis of the reaction indicated that the decomposition step of fructose most greatly affected the selectivity of fructose during the subcritical water treatment of glucose.

Keywords: decomposition, glucose, isomerization, kinetics, subcritical water

Introduction

Subcritical water is water in its liquid state under pressurized conditions and has the characteristics of a high ion product. This property means that there are hydronium and hydroxide ions at high concentrations in subcritical water. Further, because of this property, subcritical water exhibits catalytic activity for many reactions. Many kinds of reactions occur in subcritical water, such as hydrolysis of polysaccharides and peptides, and reverse hydrolysis (Sasaki *et al.*, 1998; Oomori *et al.*, 2004; Sato *et al.*, 2004; Faisal *et al.*, 2005; Haghghat Khajavi *et al.*, 2005; Haghghat Khajavi *et al.*, 2006; Wang *et al.*, 2010; Kobayashi *et al.*, 2012; Gao *et al.*, 2014; Shimanouchi *et al.*, 2019). In addition, saccharides can isomerize to form other types of saccharides; for example, glucose isomerizes to fructose and mannose in subcritical fluids (Usuki *et al.*, 2007; Daorattanachai *et al.*, 2012; Lü *et al.*, 2012; Gao *et al.*, 2015a). Although kinetic analysis of the isomerization has also been performed (Usuki *et al.*, 2007; Gao *et al.*, 2015a; Gao *et al.*, 2015b; Gao *et al.*, 2015d; Soisangwan *et al.*, 2016), these studies were performed only in

dilute saccharide solutions. The reaction behavior of the saccharide at high concentrations remains unclear.

This isomerization process is also applicable to other saccharides such as galactose, xylose, and maltose to form corresponding rare sugars (tagatose, xylulose, and maltulose, respectively) (Gao *et al.*, 2015c; Soisangwan *et al.*, 2016; Soisangwan *et al.*, 2017). Rare sugars have low calories and show biological functions (Lu *et al.*, 2008; Beerens *et al.*, 2012). To efficiently produce these rare sugars, it is necessary to optimize the saccharide concentration and to clarify the isomerization behaviors of saccharides at high concentrations.

Glucose is the most common saccharide and can be a model saccharide for many reactions. Kinetic analysis of the reactions related to glucose would be therefore applicable to many other saccharides. In this study, the effects of glucose concentration on its reaction behaviors were kinetically analyzed under subcritical conditions. Formation of the isomerization products, i.e., fructose and mannose, and the side reactions (decomposition) were quantitatively evaluated.

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Materials and Methods

Materials Glucose, fructose, mannose, and other reagents were purchased from FUJIFILM Wako Pure Chemical (Osaka, Japan) or from Kanto Chemical (Tokyo, Japan).

Subcritical water treatment Glucose was dissolved in distilled water at concentrations of 0.001–0.40 kg/kg-water. The solution was sonically degassed under reduced pressure to remove dissolved oxygen. Subcritical water treatment of the solution was performed using a tubular reactor made of an SUS 316 tube at 200 °C, as previously described (Gao *et al.*, 2015b). The solution reservoir was connected to a helium gasbag to prevent redissolution of oxygen and avoid oxygen-related side reactions. The solution was delivered into a coiled SUS 316 tubular reactor (0.8 mm I.D. × 1.0 m length) with a residence time (reaction time) of 30–400 s using an LC-10ADVP high-performance liquid chromatography (HPLC) pump (Shimadzu, Kyoto, Japan). The reactor was heated by immersing the tube in a silicone oil bath. The effluent side of the tube was immersed in an ice bath to rapidly terminate the reaction. The pressure inside the reactor was maintained at ca. 10 MPa using a back-pressure regulator (P-880; Upchurch Scientific, Oak Harbor, WA, USA). Effluent from the reactor was collected and analyzed by HPLC.

The treatment for the glucose concentration of 0.01 kg/kg-water was performed in triplicate. Under this condition, coefficients of variation for the remaining glucose ranged between 2.2–6.8 % and were not very large. Therefore, the other treatments were performed at $n=1$.

HPLC analysis Glucose, fructose, and mannose were quantified by an HPLC system equipped with an RI-101 refractive index detector (Showa Denko, Tokyo, Japan) and LC-10ADVP HPLC pump (Shimadzu) connected to a COSMOSIL Sugar-D column (3 mm I.D. × 250 mm; Nacalai Tesque, Kyoto, Japan). The eluent was 80 % (v/v) acetonitrile with a flow rate of 0.4 mL/min.

Results and Discussion

Isomerization of glucose Figure 1A shows the time courses for the decrease of glucose in subcritical water with various initial glucose concentrations on a semilogarithmic scale. The remaining fraction of glucose greatly depended on the initial glucose concentration, referred to as $C_{\text{Glc}0}$, as described later in detail. Dashed lines in Fig. 1A are the calculated results assuming first-order reaction kinetics in the early-stage of the reaction (0–50 s). In all cases, the time courses did not match the dashed lines, and the reaction tended to become slower with time. The reaction, therefore, did not follow simple first-order kinetics.

The effects of reaction time and $C_{\text{Glc}0}$ on the fructose yield are shown in Fig. 1B. The fructose yield was defined as the amount of formed fructose against the initial amount of glucose. The fructose yield increased with time during the initial period for all $C_{\text{Glc}0}$ values. When $C_{\text{Glc}0}$ was less than

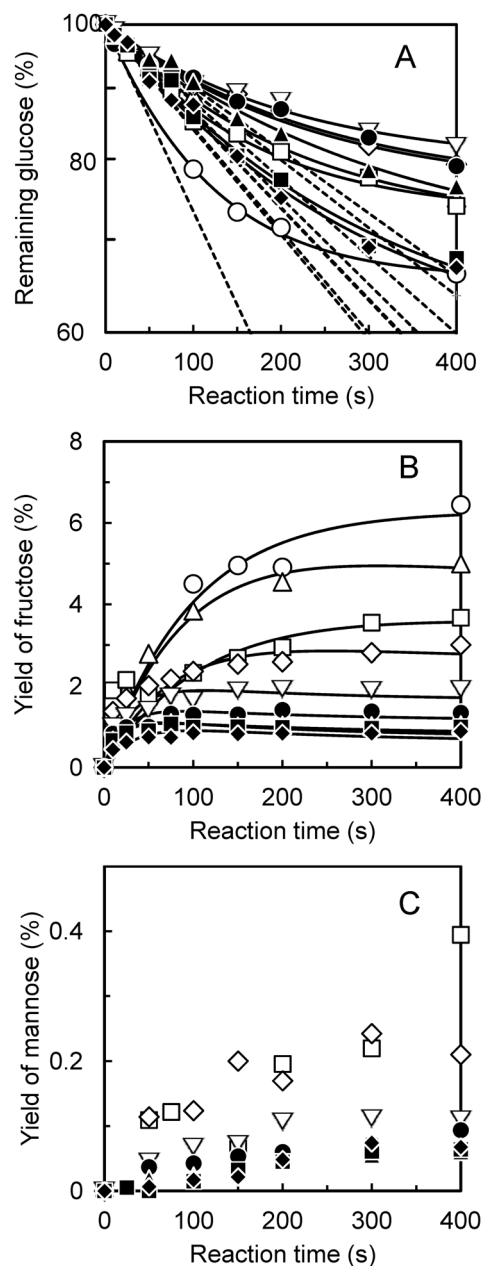


Fig. 1. Time courses for (A) the decrease of glucose and formation of (B) fructose and (C) mannose in subcritical water at various initial glucose concentrations. Symbols represent the initial glucose concentration: (○) 0.001 kg/kg-water glucose, (△) 0.005 kg/kg-water, (□) 0.01 kg/kg-water, (◇) 0.02 kg/kg-water, (▽) 0.05 kg/kg-water, (●) 0.10 kg/kg-water, (▲) 0.20 kg/kg-water, (■) 0.30 kg/kg-water, (◆) 0.40 kg/kg-water. Solid curves in A and B are the calculated results. Dashed lines are the calculated results assuming first-order reaction kinetics.

0.05 kg/kg-water, the yield of fructose increased with time within 200 s. When $C_{\text{Glc}0}$ was in the range of 0.10–0.40 kg/kg-water, the yield of fructose increased only within the reaction time of 75 s and then leveled off. Although the glucose concentration continued to decrease even after 200 s, as shown in Fig. 1A, the fructose yield scarcely changed, even if the

reaction time was extended, and remained at a lower level. These facts suggest decomposition of the formed fructose.

Figure 1C shows the formation of mannose during the subcritical water treatment. The yield of mannose was extremely low (less than 0.4 %) under all the treatment conditions. Isomerization of glucose at lower glucose concentrations afforded a low yield of mannose under subcritical conditions (Gao *et al.*, 2015b). The highly concentrated glucose (0.10–0.40 kg/kg-water) also showed a much lower yield of mannose (<0.1 %) in this study. The reason for the low mannose yield is described as follows. In subcritical water, isomerization progresses through a Lobry de Bruyn-Alberda van Ekenstein (LBAE) transformation (Kabyemela *et al.*, 1999; Mukherjee *et al.*, 2015). An LBAE transformation is a combination of reversible reactions through the enediol-structured compound, in which glucose, fructose, and mannose can mutually isomerize. However, we have earlier reported that the isomerization from fructose to glucose and to mannose scarcely occurred (Kobayashi *et al.*, 2016). This could be because of the reaction equilibrium between each isomer. The equilibrium constant of isomerization from glucose to fructose would be much greater than that from glucose to mannose, resulting in little formation of mannose.

Figure 2 shows the remaining fraction and yield of each saccharide at 400 s. When $C_{\text{Glc}0}$ was less than 0.05 kg/kg-water, the fraction of the remaining glucose rose with increasing $C_{\text{Glc}0}$ (82 % of glucose remained at $C_{\text{Glc}0} = 0.05$ kg/kg-water); it decreased with increasing $C_{\text{Glc}0}$ when $C_{\text{Glc}0}$ was over 0.05 kg/kg-water (67 % of glucose remained at $C_{\text{Glc}0} = 0.40$ kg/kg-water). Yields of fructose and mannose became lower with increasing $C_{\text{Glc}0}$ within its range of 0.001–0.20 kg/kg-water and were almost constant at much higher $C_{\text{Glc}0}$ (yield of fructose was ca. 1 % and that of mannose was ca. 0.2 %). Higher concentrations of glucose negatively affected the yields of fructose and mannose. This was due to the decomposition of fructose at lower pH, which is described later in detail.

The sum of the yields of fructose and mannose was much lower than the glucose conversion, indicating the occurrence of decomposition. The selectivity, defined as a ratio of the yield of fructose or mannose against the total glucose conversion, was therefore further investigated. The selectivity can be defined by the following expression:

$$\text{Selectivity} = \frac{\text{Yield of fructose or mannose}}{\text{Conversion of glucose}} \quad \text{.....Eq. 1}$$

Figure 3 shows the selectivity of fructose at 50–400 s plotted against $C_{\text{Glc}0}$. Except for the case of the 0.001 kg/kg-water glucose solution, fructose selectivity at each specific reaction time decreased with increasing $C_{\text{Glc}0}$. The selectivity also decreased with increasing reaction time. On the other hand, the mannose selectivity was extremely low and was less than 0.05 under every reaction condition (data not shown); and when using a highly-concentrated glucose solution, the

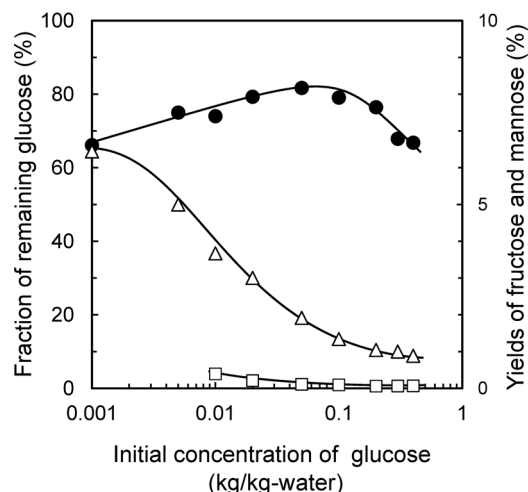


Fig. 2. Dependence of the remaining fraction of glucose and yields of fructose and mannose on the initial glucose concentration at 400 s. Symbols (\bullet , \triangle , and \square) respectively represent glucose, fructose, and mannose. Curves are empirically drawn.

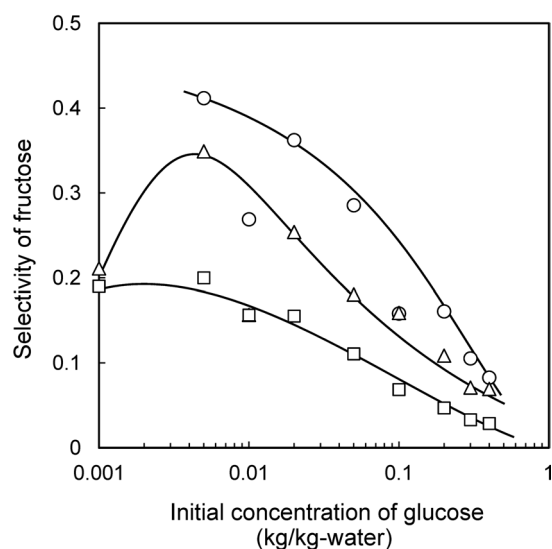


Fig. 3. Dependence of the selectivity of fructose on the initial glucose concentration. Symbols (\circ , \triangle , and \square) represent the selectivity at 50, 100, and 400 s of reaction time. Curves are empirically drawn.

selectivity was much lower.

The following reasons are proposed to elucidate this result. (1) Fructose is more prone to decomposition than glucose. (2) Any byproduct changes the reaction behavior; for example, organic acids, such as formic, levulinic, and acetic acids, were formed during the decomposition of saccharides (Mukherjee *et al.*, 2015). These compounds influenced the isomerization and decomposition behaviors. (3) In the highly concentrated glucose solution, glucose itself would act as a component of the solvent, and the activity coefficient of water would be

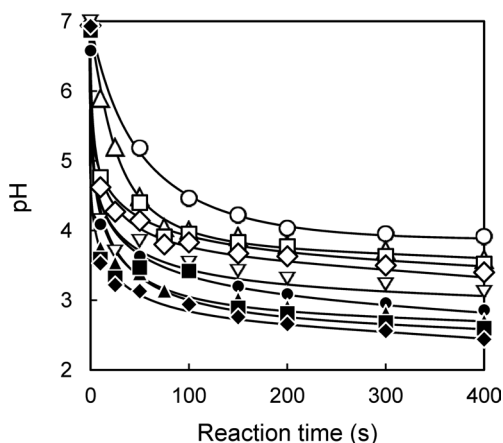


Fig. 4. Time courses for the pH during the subcritical water treatment of glucose at various initial glucose concentrations. Symbols are the same as in Fig. 1. Curves are empirically drawn.

lowered by glucose. Therefore, this solution could be assumed to be a different solvent from water. If the reaction solvent is different, it is natural that the reaction behavior should be different. In fact, it has been reported that the reaction behavior of saccharides in subcritical water was different from their behavior in subcritical aqueous alcohols or acetonitrile (Gao *et al.*, 2015b; Gao *et al.*, 2017). (4) When the glucose solution was employed for the reaction, a brown precipitate (humins and hydrochar) was formed after long reaction times (Rasrendra *et al.*, 2013). This would be caused by carbonization of saccharides (Jain *et al.*, 2016). The resulting carbide can exhibit catalytic activity as activated carbon, resulting in the acceleration of side reactions.

Effect of pH on the reaction behavior The pH of the reaction mixture was measured to investigate the effects of the formation of organic acids on the reaction behavior. Figure 4 shows the time courses for the change in pH values as the reaction progressed. The initial pH values ranged between 6.58 and 7.18 under every reaction condition. The pH value decreased with the progress of the reaction, and its decrease was remarkable, especially when the reaction time was shorter than 50 s. Subsequently, the pH change decreased and it approached a constant value. The initial glucose concentration affected both the decrease of pH during the initial period and the final pH values (pH = 3.91 at 400 s using the 0.001 kg/kg-water glucose solution; pH = 2.44 at 400 s using the 0.40 kg/kg-water solution). The change in the pH values became smaller near pH = 3–4 during the latter period, indicating that carboxylic acids were mainly formed during the reaction.

The relationship between the pH value and selectivity is shown in Fig. 5. The selectivity was relatively high in the higher pH range (3.5–5.9) at every initial glucose concentration and reached more than 0.4 in some cases. When pH decreased below 3.5, the selectivity tended to fall significantly; moreover, when pH was less than 3, the selectivity was extremely low

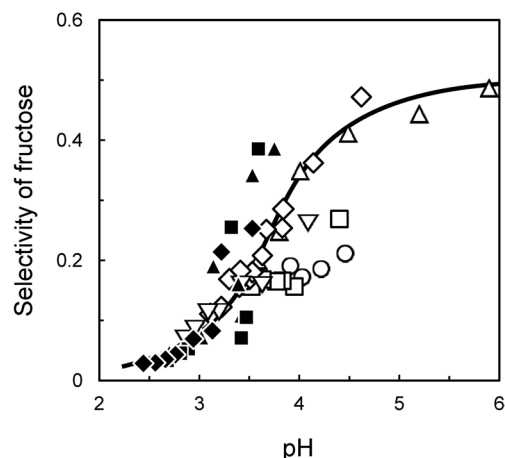


Fig. 5. Relationship between the selectivity of fructose and pH value. Symbols are the same as in Fig. 1. Curves are empirically drawn.

(0.03–0.07).

These differences could be due to the following reasons. LBAE transformation occurs under basic conditions, and the pH values were higher in the early period of the reaction. The isomerization would predominantly occur at a higher pH, resulting in higher selectivity. The pH decrease would suppress LBAE transformation. As a result, decomposition of saccharides was promoted, and further formation of organic acids, such as formic and levulinic acids, occurred. Acid-catalyzed decomposition of the saccharides became dominant at a lower pH. This would cause a low degree of isomerization and lower selectivities of fructose and mannose. If the initial glucose concentration was high, a higher amount of organic acids would form in the early period of the reaction. This greatly promoted lowering the pH and negatively affected the selectivity.

Kinetic analysis Based on these results, kinetic analysis was performed. It was reported that isomerization of glucose progresses through LBAE transformation (mutual isomerization between glucose and fructose), as shown in Fig. 6A. This model assumes the presence of reaction pathways through which each sugar directly decomposes parallel to the isomerization. In these pathways, LBAE transformation and decomposition of saccharides are supposed to be reversible and irreversible reactions, respectively. Mannose was scarcely formed in this study; thus, the reaction model can be simplified by ignoring mannose (Fig. 6B). Changes in the glucose and fructose concentrations with time can be expressed by the following equations:

$$dC_{\text{Glc}}/dt = k_4 C_{\text{Fru}} - (k_1 + k_3) C_{\text{Glc}} \quad \dots \text{Eq. 2}$$

$$dC_{\text{Fru}}/dt = k_1 C_{\text{Glc}} - (k_2 + k_4) C_{\text{Fru}} \quad \dots \text{Eq. 3}$$

where C_{Glc} , C_{Fru} , and t are the concentrations of glucose and

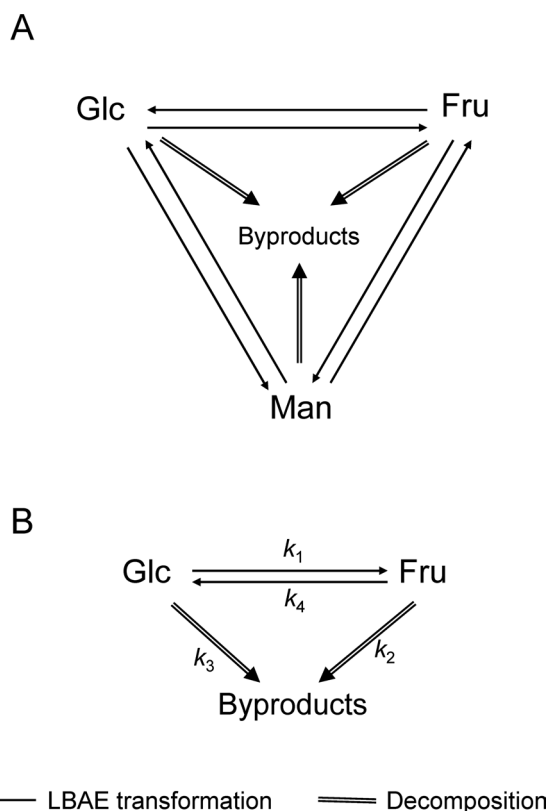


Fig. 6. Proposed models for the reaction of glucose in subcritical water. (A) Complete reaction model and (B) simplified reaction model.

fructose, and time, respectively. Based on these equations, the rate constants (k_1 , k_2 , k_3 , and k_4) were estimated. Initially, tentative rate constants (k_1 – k_4) were set, and the time course was calculated by Euler's method with a step size of 1 s. The residual sum of squares between the experimental and calculated results of each time course was calculated and was minimized using the Solver function of Microsoft® Excel 2016. Figure 7 shows the effects of the initial glucose concentration on the estimated rate constants. Based on these data, time courses were calculated (Fig. 1). The calculated results showed good agreement with the experimental ones, indicating that the kinetics were accurately described by the proposed reaction model and the rate constants.

If each reaction (LBAE transformation or decomposition) is supposed to be a first-order reaction, the rate constants must be independent of the initial glucose concentration. The values of k_1 , k_3 , and k_4 depended minimally on the initial glucose concentration and were on the same order of magnitude, although there were small differences ($k_1 = 5.69 \times 10^{-4} \pm 1.50 \times 10^{-4} \text{ s}^{-1}$, $k_3 = 4.78 \times 10^{-3} \pm 1.81 \times 10^{-3} \text{ s}^{-1}$, $k_4 = 3.74 \times 10^{-3} \pm 1.26 \times 10^{-3} \text{ s}^{-1}$). These reaction steps would be roughly first-order reactions. Meanwhile, the k_2 values became exponentially larger with increasing initial glucose concentration. In other words, it can be considered that the decomposition of fructose was not a first-order reaction. This would be one of the reasons

that the reaction of glucose in subcritical water cannot be expressed by simple first-order kinetics, as shown in Fig. 1. As described above, organic acids were formed at higher concentrations, especially in the early period of the reaction, when $C_{\text{Glc}0}$ was high. If these acids promoted the decomposition of fructose, the estimated k_2 values were the apparent ones including the concentration of hydrogen ions, and this decomposition would be an autocatalytic reaction (Jow *et al.*, 1987; Ma *et al.*, 2015). The values of k_1 , k_3 , and k_4 were in the order of 10^{-3} or 10^{-4} s^{-1} ; however, the apparent k_2 values were in the range of 10^{-3} – 10^{-1} s^{-1} and were the greatest among the estimated rate constants. This indicates that the decomposition of fructose was the dominant reaction and would greatly influence the selectivity for the isomerization.

In conclusion, the isomerization and decomposition behaviors of glucose in subcritical water greatly depended on the initial glucose concentration. Isomerization of glucose in subcritical water predominantly occurred at low $C_{\text{Glc}0}$. Increasing $C_{\text{Glc}0}$ promoted the decomposition of saccharides into byproducts, such as organic acids, and suppressed isomerization. During the subcritical water treatment, mannose formation scarcely occurred. The selectivity of fructose and mannose for the isomerization became lower with increasing $C_{\text{Glc}0}$ and with longer reaction times. The main reasons for the side-reactions would be the low pH. To overcome this drawback and achieve high selectivity, it is necessary to develop a process for the removal of the formed organic acids.

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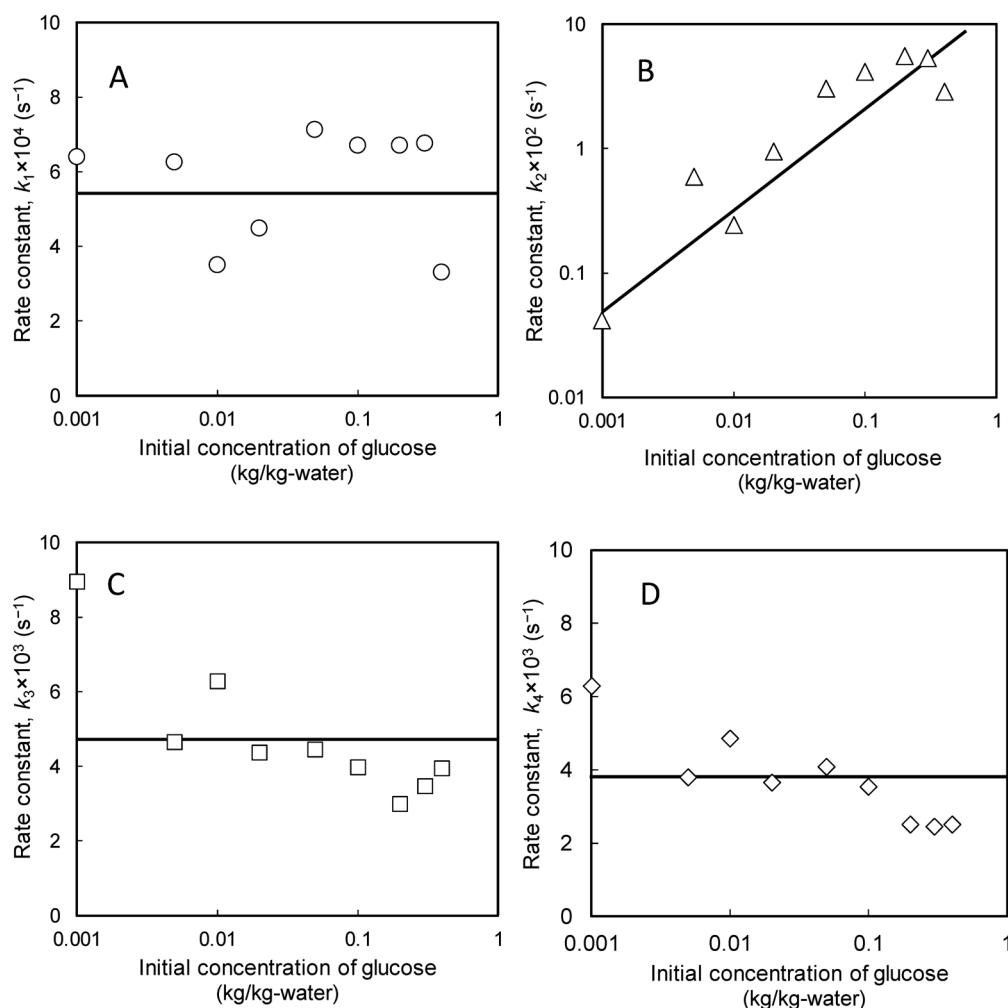


Fig. 7. Dependence of the rate constants on the initial glucose concentration. (A) k_1 , (B) k_2 , (C) k_3 , and (D) k_4 . Lines in A, C, and D indicate the averaged values of the rate constant.

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