Chemical Methodologies

Original Research Article

Increasing in the Selectivity of Formose Reaction for Glyceraldehyde Production in the Presence of Fumed Silica and Montmorillonite Catalysts

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ABSTRACT

In the present paper, the Formose reaction is investigated to produce polyols in the presence of two different catalysts at different pHs. The Formose reaction mechanism is the same as aldol condensation, which occurs in alkaline media and is accelerated by the presence of a heterogeneous catalysis. The products observed in the reaction medium are ethylene glycol, and glyceraldehyde. The present study shows that in the presence of fumed silica catalyst, increasing the pH from 7.6 to 9.3 reduces the production of ethylene glycol; however, it increases the conversion of ethylene glycol to glyceraldehyde. As a result, the amount of ethylene glycol in the reaction mixture decreases compared with neutral pHs. Nevertheless, the selectivity of the reaction to the production of glyceraldehyde increases. The same result can be observed when using montmorillonite as another heterogeneous catalyst. The difference is that the montmorillonite catalyst has less ability to accelerate the reaction than fumed silica. Also, at pH around 9 and above, practically no product is observed in the reaction medium.

GRAPHICAL ABSTRACT
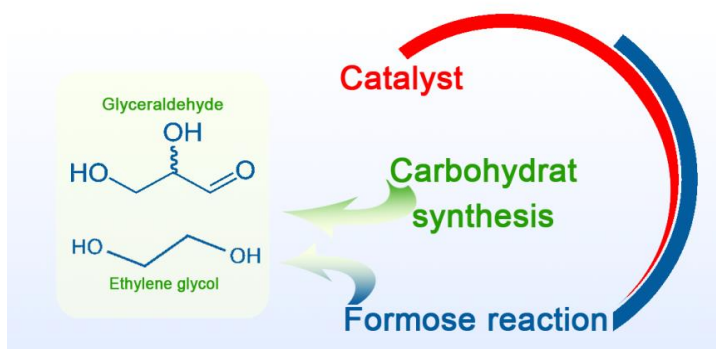
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Introduction

Life on Earth initiated from abiotic beginnings, some period of time after our solar system was formed about 4.6 billion years ago [1]. Scientists believe that life on Earth is as the result of numerous natural experiments in which different kinds of organic molecules combine to form complex active systems. Basic molecules for the formation of life, such as heterocycles, amino acids, and polysaccharide sugars, are thought to exist before life begins [2-5]. Essential nutrients for life, including monosaccharide or carbohydrates along with proteins and fats, are necessary [6-7]. Also, carbohydrates are essential and very important in the origin of life [8, 9].

Sugars are considered as essential metabolites. They are primary products of glycolysis and photosynthesis, and are of great importance in the synthesis of nucleotides and many amino acids. These can prove that sugars are the basic building blocks in life creation on Earth [10, 11]. The Formose reaction is believed to be related to the synthesis of prebiotic sugar [10-14]. In other words, it can be argued that prebiotic synthesis of sugars in aqueous solution is related to one of the acceptable pathways of the sequence step of Formose reaction [15, 16]. So, chemists believe that sugar formation relies on Formose synthesis [17-20]. Formose reaction was first discovered by Butlerow in the 19th century, involving the polymerization of formaldehyde (HCHO) in the presence of simple mineral catalysts to form a mixture of sugars [21-26]. Since the first Butlerow reports which were published in 1861 on the spontaneous compression of HCHO to the production of a complex mixture of carbohydrates with the alkaline catalyst of calcium hydroxide, Formose reaction has received much attention [19, 25]. These attentions consists of Butlerow reaction and other so-called close reactions related to important research topics such as photosynthesis, the origin of the formation of monosaccharides, and industrial production of edible carbohydrates [27-33]. It was clear from survey on the literature that some of the mineral and organic compounds act as catalysts. However, the most effective catalyst was calcium hydroxide which was first discovered by Butlerow [34, 35, 17], and a neutral or slightly alkaline pH is required for the reaction. A wide range of compounds are used to catalyze the reactions. All alkaline earth oxides and hydroxides such as calcium hydroxide are widely used as the common catalysts. Reports confirm that copper, zinc, lead and iron oxides can be used as catalysts, too. The Formose reaction is of great importance considering the question of the origin of life [30, 36-42], and is a possible process by which sugars are abiotic created [31, 26]. It has long been considered as a simple way for the synthesis of important biologically complex monosaccharides and other sugar molecules from the simplest organic materials such as HCHO [43-47]. The importance of the Formose reaction is somehow related to the identification of acceptable chemical evolution scenarios that may have happened in origin of life to create the earliest carbohydrates molecules, amino and nucleic acids and other important substances. An important scientific study on this reaction is the discussion of catalytic methods for the synthesis of monosaccharaides and abnormally rare polyols [44, 48-51]. Despite being useful, the Formose model has limitations in self-catalytic reactions, the most important of which is the high production of unstable sugars in the reaction [10, 30]. Reports have shown that the toxic mixture induced by the Formose reaction is dangerous to animals [52]. Formose sugars have also examined to suppress the growth of cancerous tumors, but no effect has been observed. The use of silicate has also been reported to remove one of the first possible barriers to the synthesis of prebiotic sugars in the Formose reaction. Lambert et al., found that formation and stabilization of four- and six-carbon sugars are being catalyzed by silicate ions and suggest a possible procedure for the synthesis of important biological sugars [10, 46, 53]. They also indicated that hydroxyapatite, which is composed of calcium ions and phosphate, increases the formation of ribose from HCHO and glycol aldehyde in hot water (80 °C) [18, 54]. Castells et al., found that the catalyzed HCHO condensation by conjugate bases of thiazolium ions led to the production of a

complex mixture (Formion mixture) of aldoses with branched chain and ketosis [28].

Indeed, the Formose reaction is a catalyzed reaction [55] and is considered as a possible pathway for different sugar's formation in prebiotic conditions [47]. In the present work, our focus is on the Formose reaction and the ability to increase the selectivity of this reaction. For example, how much of the sample volume involved in this reaction is converted to sugars using the fumed silica catalyst [56] and the montmorillonite catalyst [57]. Also, how to make carbohydrates in prebiotic conditions will be examined. This goal is according to the assumptions of changing simple organic substances into complex ones at the origin of life, which happened after cooling and calming the earth's surface [58].

Material and methods

Methanol (GC grade), hydrochloric acid 37% (analytical purity grade), Acetone (pure grade), fumed silica (with CAS number of 112945-52-5) from Sigma-Aldrich, Sodium sulfate (dehydrated) from Merck Company, and montmorillonite (with CAS number of 1318-93-0) from Sigma-Aldrich were prepared. Aqueous solution of formaldehyde37% (pure grade), and sodium hydroxide (guaranteed grade), which was used as a strong base, were purchased from Shimi Delta Company and deionized water was purchased from Morvarid Pars Dastjerd Company.

Instrumentation

Polyol analysis of samples was performed using a GC-MS device, model 5975C, Agilent Company. Effective and mild separation of liquid phases of the samples by evaporation method was done by a rotary evaporator, model RE200, Bibby Company. Moreover, a WTW inoLab 720 pH meter was used to adjust the pH of the solutions. Heater Stirrer, model HO502 Bibby Company was used to control the temperature. An electronic analytical balance (Scaltel, SPB55-Germany, read ability of 0.0001 g) was used for weighting solid materials. A centrifuge model 155 from Zag Chemie Company was used to separate solid particles of samples before injection of samples into the GC-MS device.

Formose procedure for the synthesis of Polyol

Experiments were performed to produce carbohydrates through the Formose reaction [30]. First, 23 mL of aqueous formaldehyde solution (formalin) with 200 mL of deionized water was transferred to a 250 mL three-necked flask and brought to a temperature of 60 °C. Then, sodium hydroxide solution (2M) was added to it to reach the desired pH, and finally 0.17 g of the desired catalyst was added to the flask to start the reaction. Also, from the beginning to the end of reaction, a condenser was connected to a three-necked flask, and its end was blocked by a piece of cotton along with sodium sulfate (dehydrated) and a balloon. Nitrogen gas was continuously flowed into the flask and the temperature was controlled between 55 and 65 °C. Then, at the desired intervals, 5 mL of the mixture was taken from mixture and immediately acidified with a solution of hydrochloric acid (HCl; 6M) to stop the reaction. In the next step, these liquid samples were slowly dried in a rotary evaporator to a white solid sample, and after dissolving these solid samples in 5 mL of methanol, they were centrifuged and ready for analysis.

Result and Dissection

Fumed silica catalyst at different pHs

Figures 1 and 2 show changes in EG concentration over time through Formose reaction at pH of 7.6. The two main products of the Formose reaction under the conditions applied during this project are 1,2-ethanediol (ethylene glycol) and 2,3-dihydroxypropanal (glyceraldehyde). Comparing Figure 1 with Figure 2 shows that the amount of ethylene glycol (EG) synthesized at this pH is about fifty times greater than the amount of glyceraldehyde (GA).

As depicted in Figure 1, the amount of EG in the mixture increases from the beginning of the reaction and reaches to a maximum of 9 mmol/dL in 450 minutes. Continuation of the reaction up to 630 minutes indicates a slight decrease in the amount of EG in the mixture, so that the amount of this substance reaches a stable state at a concentration of 8.6 mmol/dL.
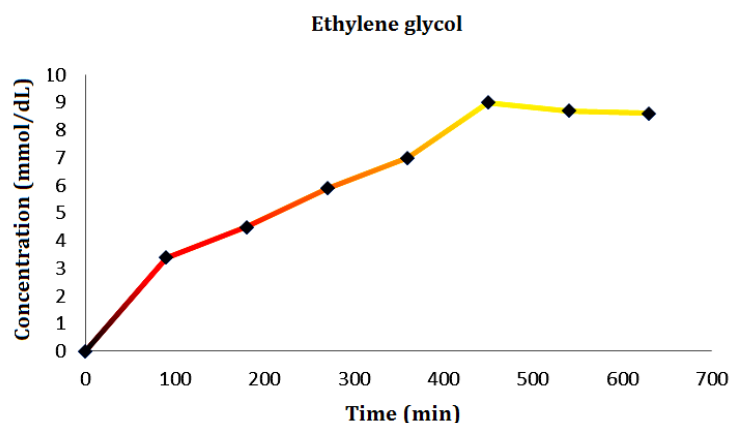
Ethylene glycol

Figure 1: Changes in ethylene glycol (EG) concentration over time through the Formose reaction in the presence of fumed silica catalyst at pH = 7.6
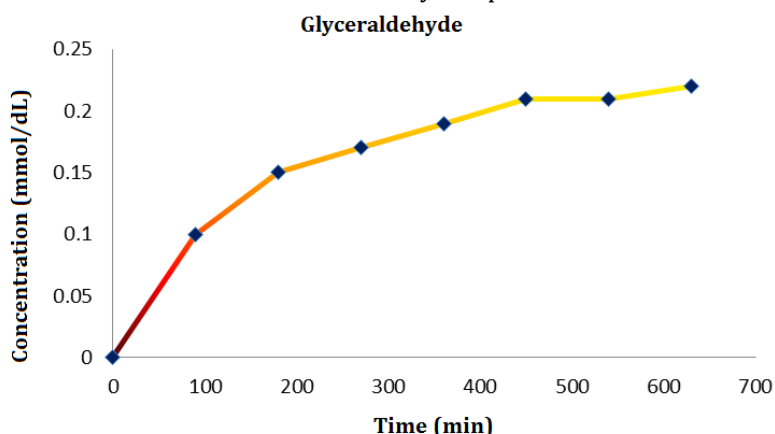
Glyceraldehyde

Figure 2: Changes in glyceraldehyde (GA) concentration over time through the Formose reaction in the presence of fumed silica catalyst at pH = 7.6

Due to the reaction mechanism of Formose and the fact that high-carbon polyols are made from low-carbon polyols, the reason for this small reduction and steady state at high times can be attributed to the equilibrium in EG synthesis rate and its conversion rate to GA.

Figure 2 shows the amount of GA synthesized in the process. The importance of this substance is its presence in the biological processes of modern living organisms. According to Figure 2, it is clear that the amount of GA slowly increases during the process and increases to 0.22 mmol per deciliter, and a steady state is created at this concentration. The reason for this behavior is to balance the rate of EG production and its rate of conversion to GA. The concentration ratio of GA to EG at pH of 7.6 are about 39 at the steady state. This means that at this pH, EG is obtained 39 times more than the GA. This process in the mentioned conditions can be considered as a process for industrial production of EG.
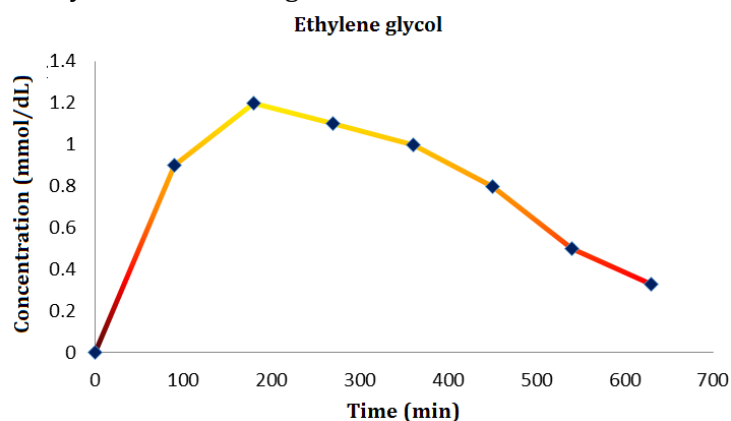
Ethylene glycol

Figure 3: Changes in EG concentration over time through the Formose reaction in the presence of fumed silica catalyst at pH = 8.6
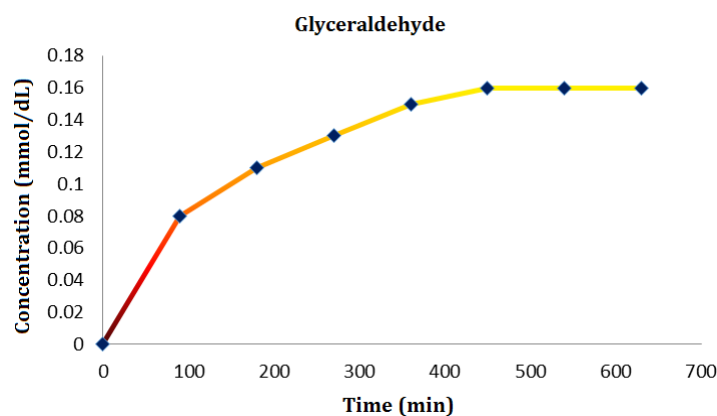
Figure 4: Changes in GA concentration over time through the Formose reaction in the presence of fumed silica catalyst at pH = 8

Figure 3 shows the amount of EG produced during the Formose process at pH of 8.6. Figures 1 and 3 clearly reveal two things. The first case is a significant decrease in the amount of EG produced at pH = 8.6 compared to pH = 7.6, and the maximum amount of EG produced at pH of 8.6 are about 7.5 times lower than the maximum amount of EG produced at pH of 7.6. This finding clearly shows that increasing the pH reduces the production of EG in solution.

Another difference between Figures 1 and 3 are the significant reduction in EG production considering Figure 3. At pH of 7.6, after the maximum EG concentration was observed in 450 minutes, the amount of this substance slightly increased and reached constant value of 8.6 mmol/dL. At pH of 8.6, a different behavior was observed. The maximum production of EG was observed in 180 minutes, and the amount of this substance slightly decreased and reached a constant value of 0.33 mmol/dL.

Figure 4 shows the amount of GA productions at pH of 8.6. The amount of produced GA in the process increases continuously over time and eventually reaches 0.16 mmol/dL. The comparison of Figures 2 and 4 show that the amount of produced GA at pH of 8.6 are slightly less than pH of 7.6. The comparison of the production ratio of EG to GA (maximum production of both substances) at pHs 7.6 and 8.6 reveals an interesting point. As mentioned earlier, the ratio of EG to GA at pH of 7.6 is 39; however, this ratio reaches about 7.5 at pH of 8.6. These findings show that increasing the pH has a negative effect on the production of EG and reduces the production of this substance by about 7.5 times; however, it has a positive effect on the conversion of EG to GA and increases the ratio by about 5.2 times comparing GA with EG in the mixture. In other words, increasing the pH reduces the conversion rate of the raw material (formaldehyde) and increases the selectivity of the final product (GA). The sharp decrease in the concentration of EG in Figure 3 can also be attributed to the increase in its conversion to GA.
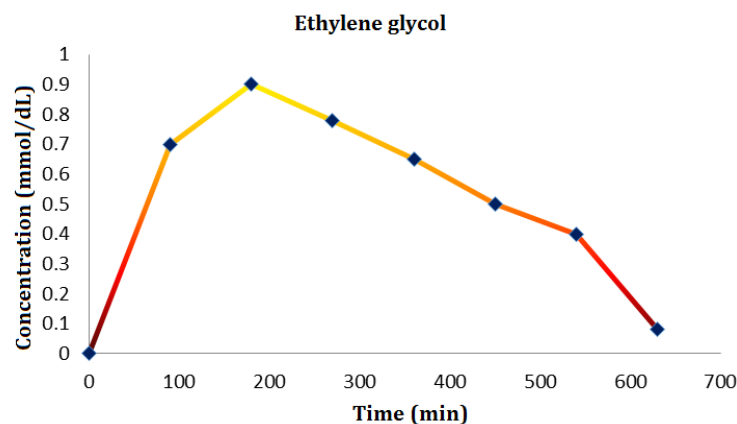

Figure 5: Changes in EG concentration over time through the Formose reaction in the presence of fumed silica catalyst at pH = 9.3
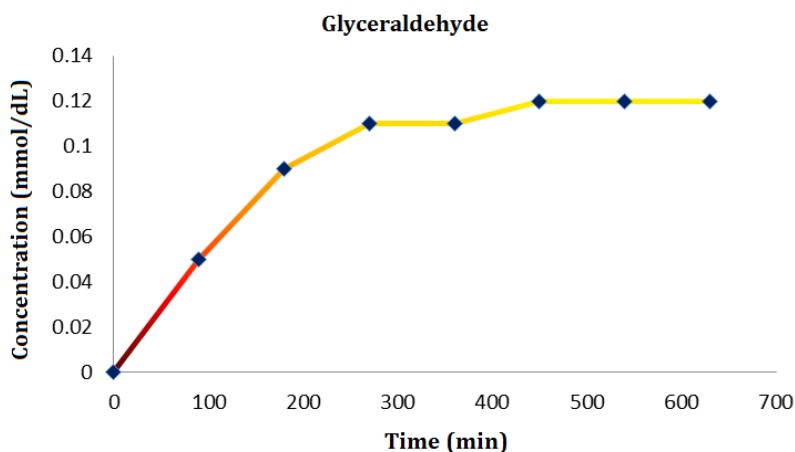
Figure 6: Changes in GA concentration over time through the Formose reaction in the presence of fumed silica catalyst at pH =9.

Figures 5 and 6 show the production of EG and GA at pH of 9.3, respectively. A comparison of Figure 5 with Figure 1 and 3 shows a similar pattern. Thus, increasing the pH reduces the maximum amount of EG production (to 0.9 mmol per deciliter) over the same time. The amount of EG reaches maximum after 180 minutes, then it continuously decreases by the passage of time. The main difference between Figure 5, 1, and 3 are that the decrease in EG production is about 7.5 times by changing pH of 7.6 to 8.6 and about 1.3 times by changing pH of 8.6 to 9.3. This indicates that the sensitivity of the Formose reaction to pH decreases at higher pHs.

Figure 6 shows that the amount of GA increases during the reaction and reaches a constant value of 0.12 mmol/dL. This is less than the final amount of GA produced at pHs of 7.6 and 8.6. The ratio of EG to GA (maximum values of both substances) is about 7.5 at pH of 9.3, which is similar to pH of 8.6.

Comparing the results obtained at pH of 9.3 with previous pHs, we can observe that increasing the pH from 7.6 to 8.6 reduces the conversion of formaldehyde to the product, and at the same time increases the selectivity of GA production. Further increase of pH from 8.6 to 9.6 only reduces the conversion rate of formaldehyde and has no significant effect on the selectivity of the process.

Montmorillonite catalyst at different pHs

Figure 7 shows the amount of produced EG over time on the montmorillonite catalyst at pH of 7.5. Comparing Figure 7 with Figure 1, which are in the same pH condition, shows the effect of the catalyst on the Formose reaction well. In Figure 7, the amount of EG produced in the process is almost three times less than that in Figure 1. Likewise, unlike Figure 1, where the amount of EG reached a maximum and then decreased, Figure 7 does not show this behavior, and the amount of EG increases continuously over time.
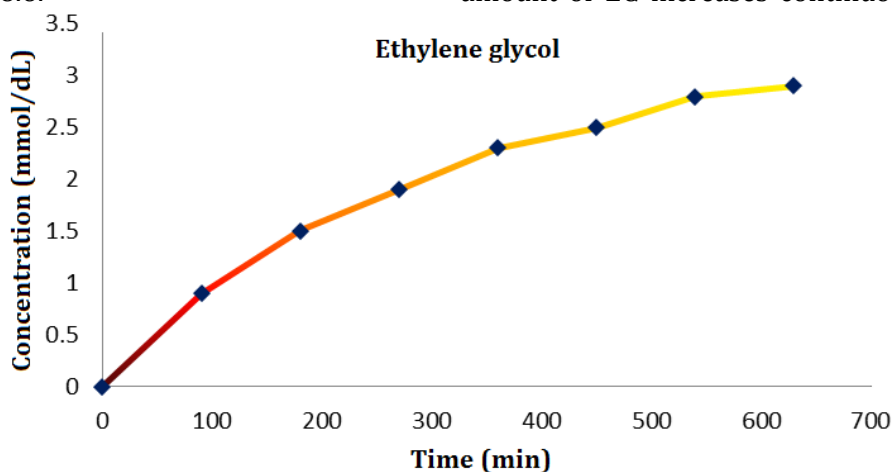

Figure 7: Changes EG concentration over time through the Formose reaction in the presence of montmorillonite catalyst at pH = 7.5

When using montmorillonite catalyst at pH of 7.5, GA is not observed during the Formose reaction. From all the laboratory data, it can be concluded that montmorillonite catalyst has less conversion power to produce EG compared with fumed silica and cannot catalyze GA at the pH of 7.5 in practice. For this reason, the concentration of EG in the medium is increasing and, unlike Figure 1, does not decrease after reaching the maximum value.

Figure 8 shows the changes in the concentration of EG over time in the Formose reaction at pH of 8.7 in the presence of a montmorillonite catalyst.

The general process of change is very similar to that of Figure 3, but unlike fumed silica catalyst, the amount of produced EG is small, almost ten times less. Also, the maximum amount of EG production is observed in 450 minutes, while in Figure 3, this is observed in 180 minutes. Comparing these two processes shows that in addition to the behavioral similarities of the two catalysts at slightly alkaline pHs, the reaction rate on the montmorillonite catalyst is slower than that of fumed Silica, which reduces the total amount of EG production and increases the production peak time.
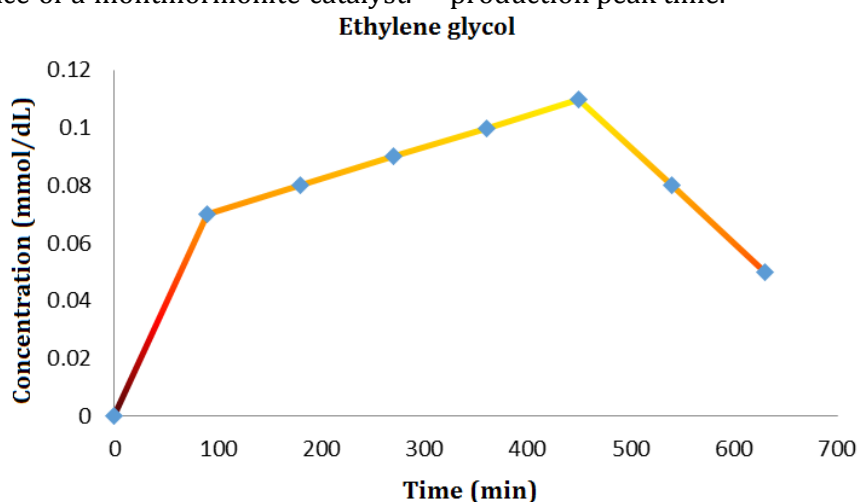
Ethylene glycol

Figure 8: Changes EG concentration over time through the Formose reaction in the presence of montmorillonite catalyst at pH= 8.7
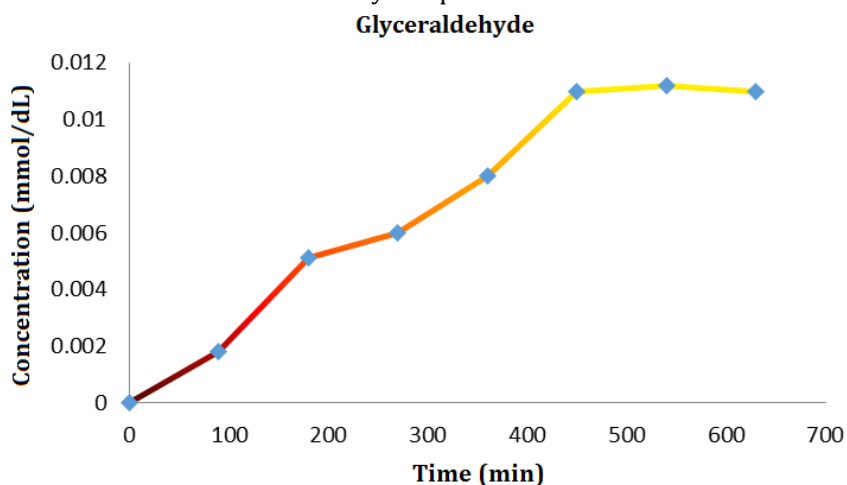
Glyceraldehyde

Figure 9: Changes GA concentration over time through the Formose reaction in the presence of montmorillonite catalyst at pH = 8.7

Figure 9 shows a graph of changes GA concentration over time by using of montmorillonite as a catalyst at pH of 8.7. As can be seen, the amount of produced GA is about sixteen times less than when a fumed silica catalyst is used at the same pH (Figure 4). Furthermore, the time to reach a maximum concentration of GA occurs later in the reaction medium. Examining Figure 9 and comparing it with Figures 8, 3, and 4 clearly showed that montmorillonite is a weaker catalyst than fumed silica.

The use of montmorillonite catalyst at pHs above 9 has no effect on the reactions, and no trace of EG or GA is observed in the reaction medium.
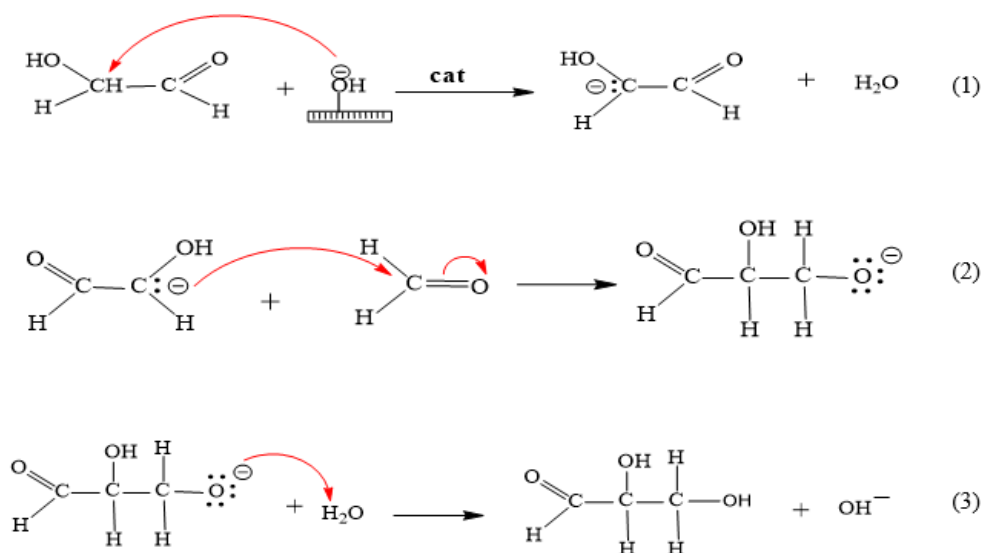
Mechanism of the reactions

In the first step of the mechanism, the glycol aldehyde molecule produced from the slow reaction step of the Formose receives an OH^- molecule from the catalyst bed (fumed silica or montmorillonite) and forms the carbanion according to the following reaction in Scheme 1 [30, 14].

In the second step of the mechanism, the unpaired electron of the carbanion breaks the aldehyde double bond by attacking to a formaldehyde molecule in the reaction medium according to the following reaction.

In the third step, the unpaired electron on the oxygen atom attacks a water molecule in the reaction medium, producing a by-product (a hydroxide anion) and a glyceraldehyde molecule (a triose sugar), according to the following reaction.

Of course, as the mechanism progresses, other sugars are produced with more carbon such as pentose and hexose [4, 6, 39, 59-60].

Scheme 1: Mechanism of glyceraldehyde production by Formose reaction in the presence of fumed silica or montmorillonite catalysts

Conclusion

Formose reaction is a chemical reaction based on the mechanism of aldol condensation, in which low-carbon aldehyde compounds are converted to polyol with more carbon. This process is known as the basis of non-biological chemical reactions to produce carbohydrates. This reaction is accelerated in an alkaline medium in the presence of a heterogeneous catalyst. Formose reaction can be performed in aqueous or non-aqueous media such as alcohols.

In the present work, the Formose reaction is performed in the presence of two catalysts, fumed silica and montmorillonite. The products observed in this reaction include EG and GA. The obtained results show that in the presence of fumed silica catalyst, the amount of EG in the medium decreases with increasing pH from 7.6 to 9.3; however, the conversion of EG to GA increases.

The same procedure is observed when using montmorillonite catalyst; however, the changes in the amount of product at different pHs are more severe than in fumed silica, so that at pHs around 9 and above, practically no product is seen in the reaction medium.

The results reveal that fumed silica catalyst is a better option for use as a catalyst in the Formose reaction. If the target of the reaction is the production of EG, pHs around 7 to 8 are the best

conditions, because at this pH range, the amount of EG production is high and the amount of conversion to GA is low. More alkaline pHs can be used if the reaction is intended to produce GA. At alkaline pHs, although the total conversion rate of the reaction is lower, the conversion rate of EG to GA is high, which significantly increases the selectivity of the reaction to GA.

Authors' contributions
All authors contributed toward data analysis, drafting and revising the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest
We have no conflicts of interest to disclose.

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