Flow semi-continuous mechanochemistry as a versatile and efficient tool for the synthesis of hydrocalumite and the isomerization of glucose to fructose

Antonio M. Pérez-Merchán[a], Ramón Moreno-Tost[a], Irene Malpartida[b], Cristina García-Sancho[a], Juan Antonio Cecilia[a], Josefa M. Mérida-Robles[a], Pedro Maireles-Torres[a,]*

[a] Universidad de Málaga, Departamento de Química Inorgánica, Cristalografía y Mineralogía, Facultad de Ciencias, Campus de Teatinos, 29071, Málaga, Spain

[b] Deasyl S.A., Plan-les-Ouates, Geneva, 1228, Switzerland

Corresponding author: maireles@uma.es

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Abstract

In this work, hydrocalumite, a layered double hydroxide with formula $Ca_2Al(OH)_6Cl{\cdot}2H_2O$, has been prepared for the first time using flow semi-continuous mechanochemistry with a DYNO®-MILL RESEARCH LAB (Willy A. Bachofen AG, Switzerland), with stoichiometric amount of reactants in water, after only 5 minutes at 25ºC. Hydrocalumite, before and after thermal treatment, was characterized by X-ray diffraction (XRD), X-ray photoelectron spectroscopy (XPS), thermogravimetric analysis (TG-DTA) and N_2 sorption at -196 ºC. Moreover, calcined hydrocalumite has been evaluated as catalyst for the isomerization of glucose to fructose, a catalytic process which has also been performed in the same flow semi-continuous mechanochemical reactor. This mechanochemical system, unlike conventional ball milling, allows working in semi-continuous and/or continuous mode, using solvents and allowing heating control up to temperatures of 80ºC. The isomerization of glucose to fructose was successfully carried out in this reactor, demonstrating that hydrocalumite prepared by mechanochemistry is more active than that prepared by co-precipitation. The optimization of several experimental variables (reaction temperature and time, glucose/catalyst weight ratio and concentration of glucose in water) has resulted in a 23.5 % fructose yield, with a glucose conversion of 38.1 %, after 1 h of reaction, at 50 ºC, with a 17 wt% glucose and a glucose/catalyst weight ratio of 6. However, the highest fructose productivity was reached under similar experimental conditions, but after only 5 minutes, with a value of 0.50 $kg_{fructose}\ L_{H_2O}^{-1}\ h^{-1}$ (equivalent to 15 $kg_{fructosa}\ Kg_{cat}^{-1}\ h^{-1}$), which is susceptible to be improved by implementing a continuous mode, assisted with a liquid pump, in the mechanochemical reactor. Therefore, this work has evidenced the versatility and potential

of this new flow semi-continuous mechanochemical reactor for the synthesis of crystalline layered double hydroxides, under sustainable experimental conditions, and to perform catalytic processes with high performance, using water as solvent and atmospheric conditions.

1. Introduction

Lignocellulosic biomass is an attractive and sustainable resource for obtaining biofuels and high value-added chemicals, reducing our dependence on fossil-based feedstocks and moderating greenhouse gas emissions [1]. Recent advances in biomass valorization have enabled the efficient transformation of carbohydrates to a platform of chemicals with potential applications in many industrial sectors. Monosaccharides, present in most inedible biomass derived from waste cellulosic materials, have received special attention, especially glucose, because of its versatility and the possibility of obtaining fructose through its isomerization. Fructose, beyond being widely used as sweetener in food industry, is becoming the main reagent to produce numerous chemicals, that could be a sustainable alternative to many of those synthesized from fossil fuels, such as 5-hydroxymethylfurfural and levulinic acid. These two platform molecules are considered valuable chemicals derived from biomass. In this context, the development of fast, inexpensive and sustainable processes capable of performing selective glucose isomerization is essential to advance in biomass conversion [2, 3].

This process of isomerization of glucose to fructose is carried out, at industrial level, with glucose syrups which are transformed into high fructose syrups to be used as feedstock to other industrial processes, or for the food industry [4, 5]. These fructose syrups are produced by enzymatic catalysis using glucose isomerase, or mannose isomerase, and the necessary conditions are strict due to the different pH ranges required to an efficient work of enzymes. In addition, the subsequent steps for the removal of these enzymes, such as separation and purification, are costly processes. The reaction equilibrium limits the production of fructose to 42%, although higher values can be achieved by chromatographic separation or nanofiltration [6].Therefore, numerous studies aim at the development of acid and basic catalysts for the isomerization of glucose to fructose, many of them focusing on the search of heterogeneous catalysts, which exhibit low cost and high stability compared to enzymes [7, 8].

Among heterogeneous catalysts, several works have reported the use of zeolites, as a source of Lewis acid centers to catalyze the isomerization process. In particular, zeolites with low Sn content are selective to fructose and mannose at low temperatures, since otherwise they would favor the formation of secondary products derived from glucose [9–12].

However, most of works deal with the base-catalyzed isomerization of glucose, which was recently reviewed [13]. In this sense, hydrotalcites (mainly in calcined form), zeolites

with alkali and alkaline-earth metals, alkaline-earth metal oxides, transition metal oxides, soluble amines and nitrogen-containing materials have been reported as catalysts for this process. Regarding the experimental conditions, mostly water was used as solvent, at reaction temperatures ranging between 70 and 200 ºC (preferably at 80-100ºC) On the other hand, metal oxides, such as MgO, Al_2O_3, SiO_2, TiO_2, ZrO_2 and Nb_2O_5, treated with ammonia, have achieved fructose yields of 34-54 with conversions of 45 %, in water at 80 ºC, being the selectivity of the reactions relatively high [14]. Other inorganic solids that have been widely studied in the field of glucose isomerization to fructose are hydrotalcites. Hydrotalcite is layered double hydroxide (LDH) of general formula $Mg_6Al_2CO_3(OH)_{16}{\cdot}4H_2O$, where anions like CO_3^{2-} compensate the positive charge created by the isomorphic substitution of Mg^{2+} by Al^{3+} in a $Mg(OH)_2$ structure. After calcination, a mixture of MgO and Al_2O_3 is formed. Using calcined hydrotalcites, fructose yields up to 56 % with glucose conversions of 70 % can be achieved [15–18].

When Ca^{2+} and Al^{3+} ions exist in the hydroxide structure, and the interlaminar anion is Cl^-, hydrocalumite is formed, although other anions such as CO_3^{2-} or NO_3^- can be hosted in the interlayer region [12, 19, 20]. Therefore, hydrocalumite is another family of layered double hydroxides, where the total charge is also compensated by anions A^{m-}, with a general formula of $[M_{1-x}^{2+}M_x^{3+}(OH)_2]^{x+}A_{x/m}^{m-}\cdot nH_2O$. However, other divalent and trivalent cations can be incorporated into LDH structures besides Ca^{2+} and Mg^{2+}, such as Co^{2+}, Ni^{2+}, Zn^{2+}, Mn^{2+}, Cd^{2+} and the trivalent cation can also be Fe^{3+}, Cr^{3+}, Ga^{3+} [7, 20–22].

The syntheses of hydrotalcites and hydrocalumites are generally performed by co-precipitation and ageing of the corresponding metal hydroxides, but these processes are time-demanding and, depending on the solubility constant, a fraction of reactants remains in solution in equilibrium with the solid. Thus, new synthesis methodologies have been developed for the manufacture of these families of metal hydroxides, meeting the principles of Green Chemistry [23] . In this context, mechanochemistry, a part of chemistry that uses mechanical energy to carry out chemical processes, such as solid-state reactions, preparation of materials and treatment of biomass, among many others, arises as a sustainable alternative to conventional processes [23–26]. In addition to being a mostly green method due to the absence of harmful solvents, it stands out for the high loading of reagents that can be introduced in order to increase productivity.

Mechanochemistry processes are mainly based on ball milling, and they have already been applied for the synthesis of layered Mg-Al double hydroxides. Thus, for instance, Fahami et al. prepared at high purity $Mg_{0.8}Al_{0.2}(OH)_2Cl_{0.2}$ by mixing $Mg(OH)_2$, $AlCl_3$, NaOH and Na_2CO_3 in a high energy ball mill, with a milling time of 5 h [27]. However, a lower crystallinity was observed compared to a hydrothermal method [28]. Even manually grinding in a mortar of Mg and Al nitrates, an NaOH pellets was employed for the synthesis of a Mg-Al-NO_3 LDH [29]. Manually grinding is far away for any industrial purpose, so new technologies using mechanochemistry are envisaged. The intercalation of species, like salicylate, in a Mg:Al LDH was successfully carried out during the solvent-free deposition of this LDH on halloysite nanotubes, being a sustainable alternative to conventional methods based on solution chemistry [30].

In the present work, a mechanochemical equipment, allowing to work in a continuous or semi-continuous flow mode (depending if using a loop connection in the outlet to the inlet to increase residence times) has been used for both the preparation of catalyst precursors (hydrocalumite) and the isomerization of glucose to fructose, with the aim of improving productivity of the catalytic process, and facilitating the industrial scale-up.

2. Materials and methods

2.1. Reactants

$Ca(OH)_2$, $Al(OH)_3$ and $AlCl_3 \cdot 6H_2O$ (> 99 %) were supplied by VWR, Sigma-Aldrich and Alfa Aesar, respectively. Glucose, fructose and mannose were also obtained from Sigma-Aldrich (>99%).

2.2. Material preparation

The synthesis of hydrocalumite was carried out according to the Reaction 1:

$$2Ca(OH)_2 + \frac{1}{3}AlCl_3 \cdot 6H_2O + \frac{2}{3}Al(OH)_3 \rightarrow Ca_2Al(OH)_6Cl \cdot 2H_2O + H_2O \quad (1)$$

The stoichiometric amounts of reactants to prepare 20 g of hydrocalumite were dispersed in 200 ml of deionized water.

Two different methods were used for the synthesis of hydrocalumite:

1) Conventional: co-precipitation carried out at 25 °C for 1 hour, where the reagents were mixed in water, maintaining a magnetic stirring of 500 rpm. Next, centrifugation at 7500 rpm for 10 minutes allowed to separate the solid, which

was washed with deionized water and dried at 70 ºC for 24 h. The sample was labelled as HC_conv

2) By mechanochemistry in a semi-continuous flow reactor (loop mode by leaving the machine at the outlet and feeding again to the inlet of the machine), DYNO®-MILL RESEARCH LAB (Willy A. Bachofen AG, Switzerland), with a tip speed of 8.5 m/s, using 1 mm beads (ZrO_2 doped with Y_2O_3) at 25º C (measured in the outlet of the machine) for 5, 15 and 60 min. After synthesis, the suspension was centrifuged at 7500 rpm for 10 minutes, and the solid was washed with deionized water and dried, being labelled as HC_*x*min_RL, where *x* is the time that suspension was passing through the mechanochemical reactor.

The final solids were calcined in a furnace with a heating rate of 5 ºC/min up to 650 ºC and then a cooling down to 200 ºC at 5 ºC/min in ramp-down. The labels of samples were: c_HC_conv and c_HC_*x*min_RL.

2.3. Physico-chemical characterization

N_2 adsorption-desorption isotherms were obtained using an automatic ASAP 2420 from Micrometrics at -196 ºC. Prior analysis, the samples were evacuated at 200 ºC and 10^{-4} bar. The specific surface area was calculated using the Brunauer-Emmett-Teller (BET) method, and Barrer-Joyner-Halenda (BET) method was employed to determine average pore diameter. N_2 cross-section was considered 16.2 $Å^2$.

X-ray photoelectron spectra (XPS) were recorded in a Physical Electronics PHI 5700, with a multichannel detector and non-monochromatic Mg K_α radiation (300 W, 15 kV, 1253.6 eV). Spectra were taken in pass-energy mode at 29.35 eV and a diameter area of 720 µm and calibrated using adventitious carbon at 284.8 eV. PHI ACCESS ESCA-V6.0 F software package was employed to record and treat XPS data. Peaks were fitted using a Gaussian-Lorentzian curve, and a Shirley type background was subtracted from the signals.

Powder X-ray diffraction patterns (XRD) were enregistered on a Philips EMPYREAN automated diffractometer using Cu $K_{\alpha1,2}$ (1,5406 Å) and a PIXcel detector. Divergence and anti-divergence slits were fixed at 1/4º and 1/2º Soller slits, respectively, for incident and refracted rays were employed at 0.04 rads. Measures were taken from 5 to 80º (2θ) for approximately 30 minutes with a step size of 0.0167º. The X-ray tube voltage

employed was 45 kV and current of 40 mA. The sample was rotated continuously to increase particle statistics.

Thermal analysis was carried out with a TA instruments (SDT-Q600 analyzer), employing open platinum crucibles under a N_2 flow in the range of 25–1000 °C and a heating rate of 10 °C·min^{-1}.

2.4. Catalytic tests

The isomerization process was also performed in the DYNO®-MILL RESEARCH LAB (Willy A. Bachofen AG, Switzerland), taking advantage of semi-continuous flow, which allows recirculating the reaction medium, and the control of temperature of the reaction chamber (until 80ºC) [31]. In all cases, the reactor filling volume occupied by 1 mm size beads was 60%. Experimental variables such as the glucose/catalyst weight ratio, reaction temperature and concentration of glucose in water (wt%) were optimized. In addition, the catalysts synthesized by mechanochemistry and by conventional method were compared to observe the effect of the synthesis method on the catalytic performance.

The resulting aqueous solutions were diluted with deionized water for the analysis of the products obtained. A JASCO high performance liquid chromatography (HPLC) system was used for this purpose. An autoinjector (AS-2055) introduces 6 μL of sample from a previously prepared vial. For the aqueous mobile phase, the HPLC has a quaternary gradient pump (PU-2089) that drives the mobile phase, which is microfiltered and degassed deionized water at a flow rate of 0.40 ml/min, to a Phenomenex Rezex ROA Organic Acid (8%) column (300 mm × 7.8 mm, 5 μm). This column is placed inside an oven (co-2065) at 70 °C during the analysis. Once the analytes have separated on the chromatographic column, they reach two detectors. A UV-visible detector (MD-2015) that analyses the aromatic compounds and a universal refractive index detector (RI-2031 PLUS) with which the analytes are identified and quantified.

3. Results and Discussion

3.1. Material characterization

The crystalline structure of hydrocalumite prepared by conventional and mechanochemical methods, by using the stoichiometric amount of $Ca(OH)_2$, $AlCl_3 \cdot 6H_2O$ and $Al(OH)_3$, was confirmed by X-ray diffraction (Figure 1). After only 5 minutes of mechanochemical treatment, the characteristic diffraction peaks of the hexagonal

structure of the hydrocalumite ($Ca_2Al(OH)_6Cl{\cdot}2H_2O$, with R3 rhombohedral symmetry, with Cl^- and CO_3^{2-} anions located between [$Ca(OH)_6$ H_2O] and [$Al(OH)_6$] double sheets, were observed [32].Thus, the diffraction signals associated to the basal spacing appear at a 2θ (º) of 11.30 (003) and 22.67 (006). However, the presence of small fraction of $CaCO_3$ (JCPDS 05-0586) was confirmed in all cases, resulting from the reaction of $Ca(OH)_2$ with atmospheric CO_2, but its amount decreases when hydrocalumite was prepared under mechanochemical conditions at longer reaction times. Compared to the conventional method using the same reaction time, the presence of $CaCO_3$ is higher when this last one is employed. Therefore, another advantage of this mechanochemical reactor, allowing to work in semi-continuous mode and in the presence of solvent, is the shortening of reaction times. For example, the formation of a MgAl hydrotalcite with classical ball milling, besides the formation of NaCl due to the use of NaOH, brucite ($Mg(OH)_2$) was detected until 5 h of milling [27]. Therefore, as observed for hydrotalcites, the synthesis of hydrocalumite can be successfully achieved in this new mechanochemical reactor, using stoichiometric amounts of reactants, without the formation of by-products, thus opening the way to the easy scale-up of the synthesis of hydrocalumite, inasmuch the capacity of the mechanochemical reactor used in the present work can be largely increased. In order to compare with previously reported syntheses, it should be mentioned that most of methods are based on co-precipitation from a aqueous solution of precursors (mainly, Ca and Al nitrates or chlorides) by addition of a basic solution (Na_2CO_3, NaOH), requiring a very long reaction time (12 h at 80ºC) [33], or crystallization time (in water: 17 h at 80ºC [34], in water/ethanol: 18 h at 65ºC [35]). On other cases, the synthesis was assisted by microwaves, operating with a power of 1250 W and a frequency of 2450 MHz, during 2.5 min [36]. Even ball milling has been used, using a mixture of $AlCl_3$, $CaCl_2$ and NaOH, which was treated for 30 h [37]. Therefore, the advantages of the novel methodology proposed in the present work is clear, since it uses stoichiometric amounts of $AlCl_3$, $Ca(OH)_2$ and $Al(OH)_3$, water as solvent, and, after only 5 minutes, this semi-continuous mechanochemical method is able to provide crystalline hydrocalumite, in addition to offering the opportunity to scale-up this sustainable process.

The calcination of hydrocalumite leads to the formation of mayenite ($Ca_{12}Al_{14}O_{33}$, JCPDS 9-413) and calcium oxide, because the excess of Ca in hydrocalumite (Ca:Al= 2:1) respect to mayenite (Ca:Al= 6:7) (Figure 2). Nevertheless, the presence of CaO (JCPDS 37-1497) could be beneficial for the isomerization of glucose to fructose, since basic sites catalyze

this process. In addition, diffraction peaks associated to calcium hydroxychloride were observed at 2θ (º) of 28.12, 38.22 and 47.03.

On the other hand, textural properties of hydrocalumite, before and after calcination, were determined from N_2 sorption at -196 ºC. The main textural data of HC_conv and HC_5min_RL, before and after calcination, are gathered in Table 1, whereas the adsorption-desorption isotherms are shown in Figure 3. In both cases, the textural properties worsen with the thermal treatment, with an important reduction of BET surface area and pore volume, although the sample prepared by co-precipitation (c_HC_conv) becomes more microporous that that obtained by mechanochemistry (c_HC_5min_RL). The average pore diameters varied between 7.9 and 12.0 nm, large enough to facilitate the access of glucose molecules to the active sites and the exist of fructose and mannose. Nevertheless, there are no important differences between both synthesis methods in terms of textural properties.

Thus, both calcined hydrocalumite prepared in the present work (c_HC_conv and c_HC_5min_RL) exhibited similar BET surface areas to those reported by Ventura et al. (6 m^2/g *versus* 7.70/6.45 m^2/g in the present work) [38]. It is noteworthy that HC_5min_RL was synthesized in just 5 minutes using the mechanochemical reactor, while the HC_conv required 60 min and, and usually hydrotalcites require over 18 h, under an inert atmosphere, as described Ventura et al. [38]. This highlights the positive effect of mechanical energy associated to the continuous impact of beads for the synthesis of crystalline hydrocalumite.

Considering that the thermal analysis of hydrocalumite prepared with conventional methods, even from different sources of aluminum, has been previously reported [39], thermogravimetric and differential thermal analysis (TG-DTA) was only performed of the sample prepared in the mechanochemical reactor (HC_5min_RL), and results are displayed in Figure 4. The TG curve shows four weight losses: room temperature – 100ºC, 200-400ºC, 550-700ºC and above 900ºC. The first mass loss (12.01 %), below 100ºC, is associated to the removal of hydration water, since, assuming the formation of hydrocalumite (Reaction 2), the two water molecules per formula could correspond to a 12.8 wt%.

$$Ca_2Al(OH)_6Cl \cdot 2H_2O \rightarrow Ca_2Al(OH)_6Cl + 2H_2O \quad (2)$$

The second weight loss involves structural dehydroxylation of the CaAl layers, where hydroxyl groups seem to be bonded to Ca^{2+} weaker than to Al^{3+}, as evidenced by the FT-IR spectroscopy data with stretching vibrations at 3478 cm^{-1} (Ca-OH bonds) and 3643 cm^{-1} (AlO-H bonds) [39]. Thus, the dehydroxylation of hydrocalumite corresponds to a theoretical weight loss of 19.25%, where the sum of the second and the third weight loss in the TG curve supposes a 20.55%. This slight divergence could be explained by considering the intercalation of some carbonate ions in the interlayer region, whose interaction with calcium species gives rise to CaO, which requires high temperatures to decompose. Therefore, at 700ºC, a mixture of mayenite ($Ca_{12}Al_{14}O_{33}$), CaO and Ca(OH)Cl is formed. At temperatures higher than 850ºC, hydrogen chloride could evolved from Ca(OH)Cl, although, even at 1000ºC, the weight loss still continues.

X-ray photoelectron spectroscopy (XPS) has proven to be a reliable tool for the analysis of solid surfaces, giving information about the chemical composition and environment of chemical elements. In this work, the sample c_HC_5min_RL was studied by XPS, because calcined hydrocalumite prepared by conventional method was reported in a previous work [40]. The O 1s core level spectrum exhibits an asymmetric band, which can be deconvoluted in in two components, at 531. eV and 529.7 eV (shoulder), which can be assigned to oxygen in metal oxides (CaO and $Ca_{12}Al_{14}O_{33}$) and hydroxyl groups of Ca(OH)Cl, respectively. Regarding the Ca 2p, a doublet is observed at 347.2 and 350.7 eV, assigned to Ca $2p_{3/2}$ and Ca 2p1/2, with a typical spectral separation of 3.5 eV, characteristic values of Ca^{2+} ions in calcium oxide and hydroxide. The binding energy of Al 2p appears at 73.8 eV, while the Cl 2p core level spectrum also shows an asymmetric band, whose deconvolution gives rise to values of 198.6 and 200.2 eV, attributed to the Cl $2p_{3/2}$ and Cl $2p_{1/2}$, with a separation of 1.6 eV. These last values are characteristics of Al^{3+} in oxides, and Cl^{-} in metal chlorides.

The surface Ca/Al and Al/Cl atomic ratios were 1.94 and 0.99, respectively, very close to those corresponding to hydrocalumite (2 and 1, respectively), confirming that its thermal treatment gives rise to a mixture of CaO, Ca(OH)Cl and $Ca_{12}Al_{14}O_{33}$.

3.2.Catalytic tests

The first catalytic study was carried out using the mechanochemical reactor, since it has been demonstrated that chemical processes can be assisted by mechanical energy [41]. The objective was to demonstrate the versatility of this mechanochemistry approach, not

only for the preparation of catalysts (as evidenced in the synthesis of hydrocalumite in the present work), but also to perform chemical processes. In this sense, the catalytic behavior of calcined hydrocalumite obtained by mechanochemistry (c_HC_5min_RL, c_HC_15min_RL, c_HC_60min_RL) was compared using % (Figure 5). Very similar fructose yields (15 - 16 %) were obtained for the three catalysts after 60, 90 and 120 minutes of reaction, while glucose conversion was between 35 and 55 %, giving a fructose selectivity around 30 %.

There is approximately 20-30% conversion not shown in the graphs. In these cases, no products are detected by HPLC analysis. The products resulting from this conversion are derivatives of glucose and fructose degradation. These products, such as formic acid and levulinic acid, are formed under certain conditions, often leading to high conversions and low selectivities for fructose.

The maximum activity in the isomerization of glucose to fructose is attained at a reaction time of 60 min, in all cases, so the catalyst c_HC_5min_RL, prepared at the shortest reaction time in the mechanochemical reactor was chosen to optimize different experimental variables influencing on the isomerization of glucose using the mechanochemical reactor, such as glucose/catalyst weight ratio, concentration of glucose in water and reaction temperature. In all cases, the filling volume with beads (made of Y-doped zirconia with a size of 1 mm) was 60%, so the available volume into the reactor was 40 mL, and a tip speed of 8.5 m/s was used.

On the other hand, it is worth noting the determination of the productivity of this process in the mechanochemical reactor at different reaction times. Table 2 shows the catalytic results together with the productivity at each reaction time obtained with c_HC_5min_RL at 50 ºC, using a 17 wt% glucose in water, with a glucose/catalyst weight ratio of 12. The fructose yield increases from 5.0 to 16.5% when the reaction is extended from 5 to 120 min, with glucose conversion ranging between 40 and 50%, but, in all cases, the selectivity toward fructose was lower than 33 %. Regarding productivity, an industrially important parameter in catalysis, it decreases from 0.12 until 0.02 $kg_{fructose}\ L_{H_2O}^{-1}\ h^{-1}$, from 5 to 90 minutes. However, the yield is similar to that obtained by Ventura et al., but they achieve a productivity of 0.108 $kg_{fructosa}\ L^{-1}\ h^{-1}$, after 4 h [38]. Even with high fructose yields and selectivity values, as those obtained by Zhang et al., with 40.7 and 99.9%, respectively, a productivity of only 0.004 $kg_{fructosa}\ L^{-1}\ h^{-1}$ was attained [42].

The influence of the glucose/catalyst weight ratio was studied by using values of 3, 6 and 12 (Figure 6)**.** The best catalytic results, as inferred from a fructose yield of 24.5%, after 60 minutes, and a carbon balance higher than 90%, were achieved with a ratio of 6. In all cases, mannose was detected, resulting from the epimerization of glucose, but its yield was always lower than 10%. With a glucose/catalyst weight ratio of 3, corresponding to the highest catalyst loading, fructose yield remained nearly constant from 15 to 60 minutes, with a carbon balance close to 60%. It is well-known that the isomerization of glucose to fructose tends to thermodynamic equilibrium, with a K_{eq}= 1.45 at 110 ºC, although some catalysts have reached up to 40% fructose yield in water. However, with most of inorganic solids, such as hydrotalcites or similar families, this yield does not exceed 35%, at reaction temperatures of 80-120 ºC, in water [13]. Ventura et al. obtained a fructose yield of 21% with a carbon balance of 85%, at 45 ºC, with a glucose/catalyst weight ratio of 1, after 4 h of reaction [38].

However, the productivity was much better for a glucose/catalyst weight ratio of 6, reaching a value of 0.50 $kg_{fructose}$ $L_{H_2O}^{-1}$ h^{-1} after 5 minutes (Table 3), equivalent to 15 $kg_{fructosa}$ Kg_{cat}^{-1} h^{-1}, but decreases for longer reaction times. This value holds considerable significance, as after just 5 minutes of reaction with a 17 wt% glucose concentration, the mentioned productivity values tripled compared to those previously reported, but working in a flow semi-continuous mode, in water, at 50 ºC.

Next, the effect of the reaction temperature was studied at temperatures of 50, 70 and 90 ºC (Figure 7), because most of studied carried out on the isomerization of glucose to fructose use higher temperatures. Fructose yield decreases with increasing temperature, as expected, which can be attributed to the degradation of glucose and fructose into other products, such as levulinic acid or other acids derived from sugars by cleavage of C-C bonds. The presence of these acids can catalyze other secondary processes leading to a decrease in the carbon balance, selectivity and yield. In addition, the use of basic heterogeneous catalysts does not require high temperatures to shift the equilibrium of this reaction to some extent either in water or other solvents such as ethanol [16, 18]. Therefore, an increase in temperature has no beneficial effect on the isomerization process under the experimental conditions used in the present work.

Finally, the concentration of glucose in the aqueous solution varied from 17 to 50 wt%, to evaluate the capacity of the catalyst to isomerize a higher amount of glucose (Figure 8). The catalytic data reveal that, even with a 50 wt% glucose, maintaining a

glucose/catalyst weight ratio of 6, a fructose yield of 12% can be obtained after 5 minutes at 50 ºC, with a 19% of glucose conversion, which raises until 42% after 60 minutes.

There is a decrease in the carbon balance but not to a large extent, reaching in most cases more than 80 %. In addition, the fructose yields decrease with increasing glucose concentration due to the kinetics of the glucose to fructose isomerization reactions, but eventually tending to equilibrium [43, 44]. The increase of glucose in solution increases the productivity values in large ranges. The highest fructose productivity obtained was 0.50 $kg_{fructose}$ $L_{H_2O}^{-1}$ h^{-1}. This productivity result indicates the great potential that this type of reactor has for working with high reagent concentration loadings and thus being able to obtain high productivity values.

When the optimum reaction conditions were determined in the mechanochemical reactor for the calcined hydrocalumite obtained by mechanochemistry, this catalytic performance was compared with the calcined hydrocalumite prepared by conventional synthesis (coprecipitation). The catalytic performance was compared at 50 ºC, 17 wt% glucose in water, a glucose/catalyst weight ratio of 6 and different times varying from 15 to 120 minutes. Figure 9 shows the kinetics of both catalysts inside the mechanochemical reactor.

The reaction carried out with c_ HC_conv is much faster, with glucose conversions close to 60%, but low fructose yields (less than 14%), providing a carbon balance lower than 60%. However, with c_HC_5min_RL, although the glucose conversion values are lower (25-38%), fructose yields rise until 23 wt%, with carbon balances higher than 95%. In addition, the maximum productivity reached with c_HC_5min_RL is 0.50 $kg_{fructose}$ $L_{H_2O}^{-1}$ h^{-1}, which is twice the value obtained with c_ HC_conv. This would demonstrate the advantage of this mechanochemical reactor for the fast and sustainable preparation of hydrocalumite.

Finally, Table 4 shows the experimental conditions and catalytic performance of a selection of basic catalysts reported in the literature, which are compared with c_HC_5min_RL prepared in the present work. Although the fructose yield is not the highest (21 versus 54%), it presents some important advantages, such as scalability and easy synthesis, working at low temperature (50ºC) and short reaction time (5 min), with a high percentage of glucose (17 wt%) and a high selectivity towards fructose (82%), in addition to achieving high productivity compared to other continuous methods (15 versus

0.216 $kg_{fructose}$ Kg_{cat}^{-1} h^{-1}). Furthermore, this novel glucose-fructose isomerization process is environmentally friendly, low-cost, and catalyst separation is feasible.

4. Conclusion

In this work, the effect of mechanochemistry on the preparation of hydrocalumite was studied. It was observed that the use of the mechanochemical reactor DYNO®-MILL RESEARCH LAB reduces the hydrocalumite preparation time to 5 minutes. Furthermore, the presence of calcium carbonate together hydrocalumite, as inferred from XRD, was minimized by using this new flow semi-continuous mechanochemical reactor. Physico-chemical characterization has demonstrated that sample prepared by mechanochemistry (c_HC_5min_RL) is more mesoporous than that obtained by co-precipitation (c_HC_conv), although specific surface area and pore volume are similar. The calcination of hydrocalumite ($Ca_2Al(OH)_6Cl{\cdot}2H_2O$) leads to a mixture of mayenite ($Ca_{12}Al_{14}O_{33}$), CaO and Ca(OH)Cl. The isomerization of glucose to fructose was successfully carried out in the mechanochemical reactors, and the optimization of reaction temperature and time, glucose/catalyst weight ratio and concentration of glucose in water, has resulted in a 23.5 % fructose yield, with a glucose conversion of 38.1 %, after 1 h of reaction, at 50 ºC, with a 17 wt% glucose in water and a glucose/catalyst weight ratio of 6. Nevertheless, the highest fructose productivity of 0.50 $kg_{fructose}$ $L_{H_2O}^{-1}$ h^{-1} (equivalent to 15 $kg_{fructosa}$ Kg_{cat}^{-1} h^{-1}) was achieved after only 5 minutes, under similar experimental conditions. Therefore, this work has evidenced the versatility and potential of this new flow semi-continuous mechanochemical reactor for the synthesis of crystalline layered double hydroxides, under sustainable experimental conditions (water), and to perform catalytic processes with high performance, using water as solvent and no control of the atmosphere.

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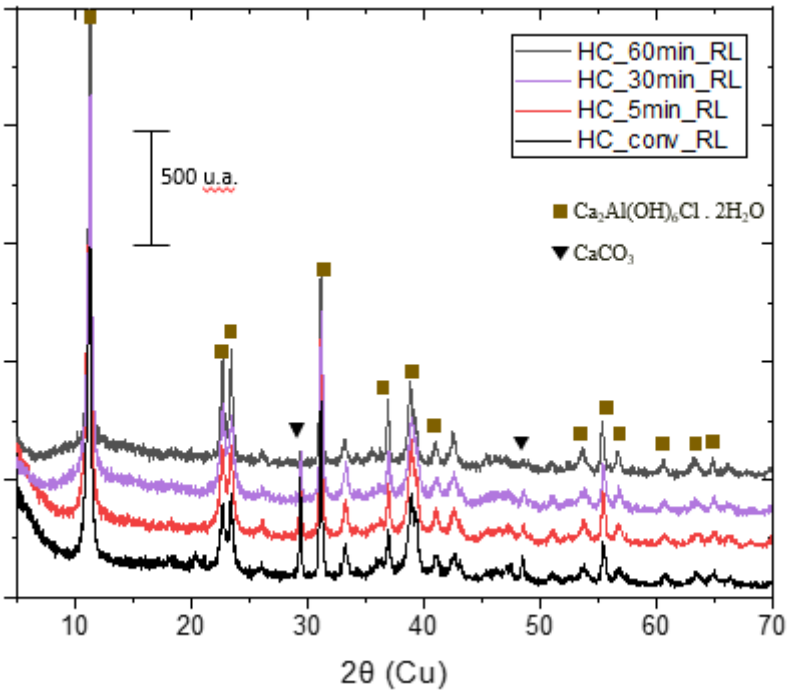

Figure 1. XRD patterns of hydrocalumites prepared under conventional and mechanochemical treatments.

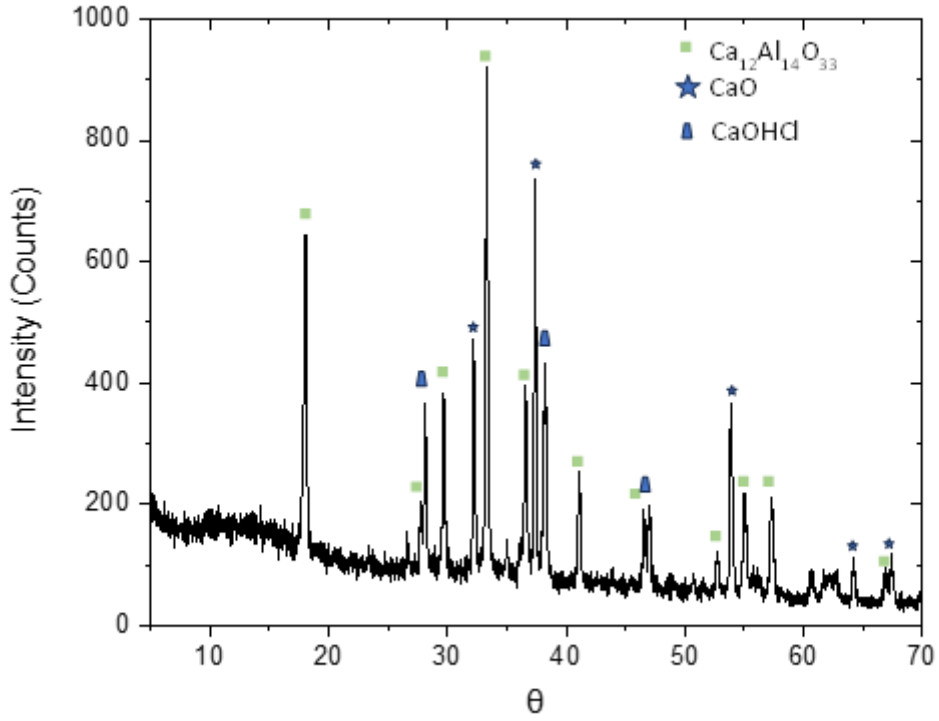

Figure 2. XRD pattern of calcined hydrocalumite prepared in the mechanochemical reactor during 5 minutes (c_HC_5min_RL)

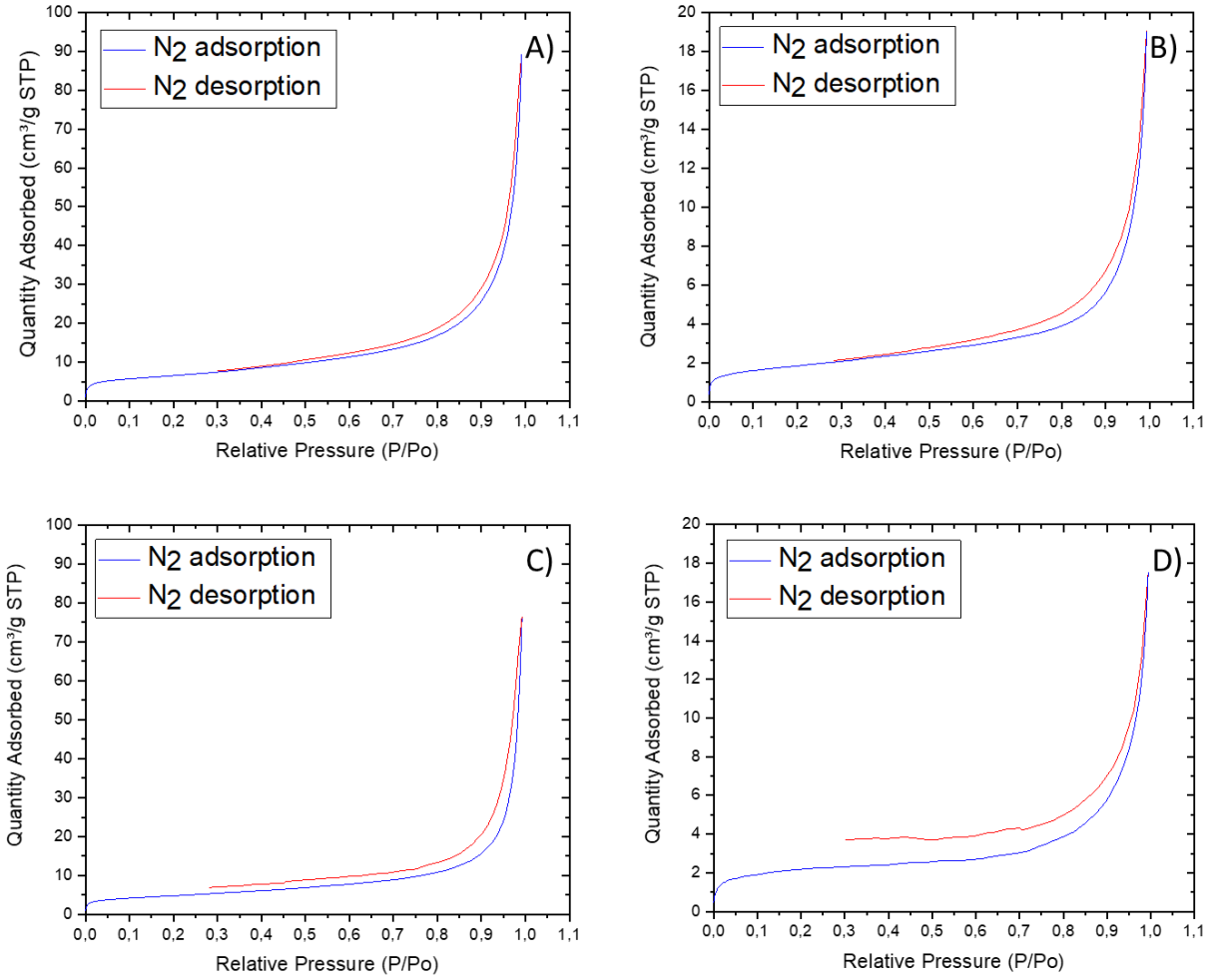

Figure 3. N_2 adsorption-desorption isotherms at-196ºC of fresh and calcined hydrocalumite. HC_5min_RL (A), c_HC_5min_RL (B), HC_conv (C) and c_HC_conv (D).

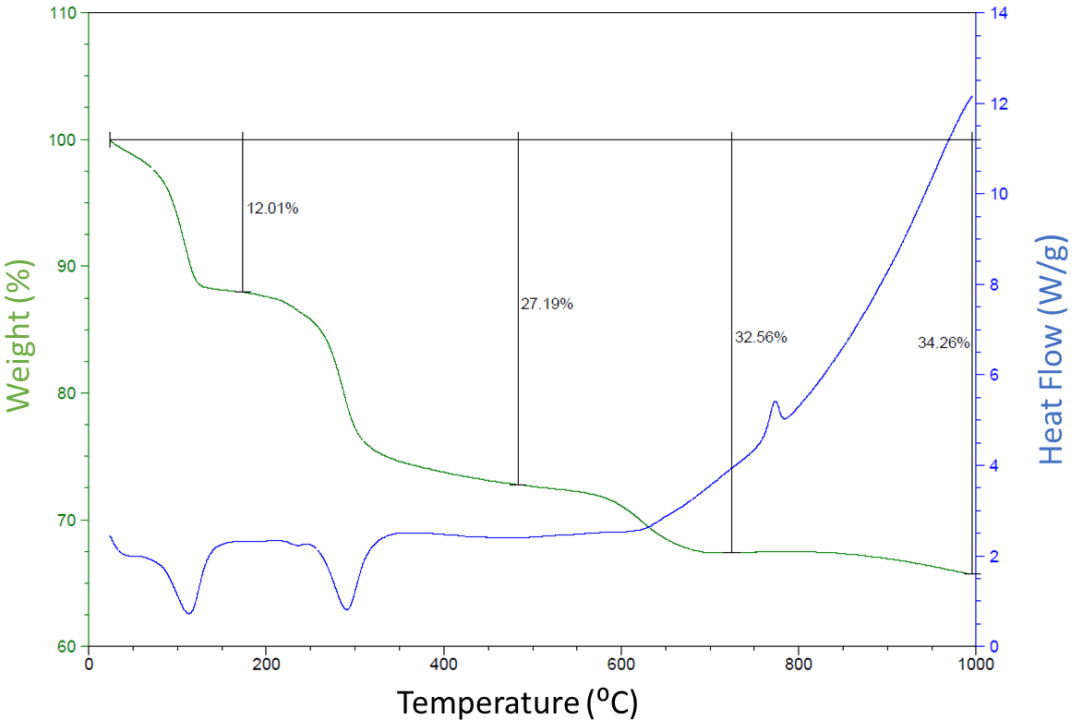

Figure 4. ATD-TG curves of hydrocalumite prepared in the mechanochemical reactor during 5 minutes (HC_5min_RL)

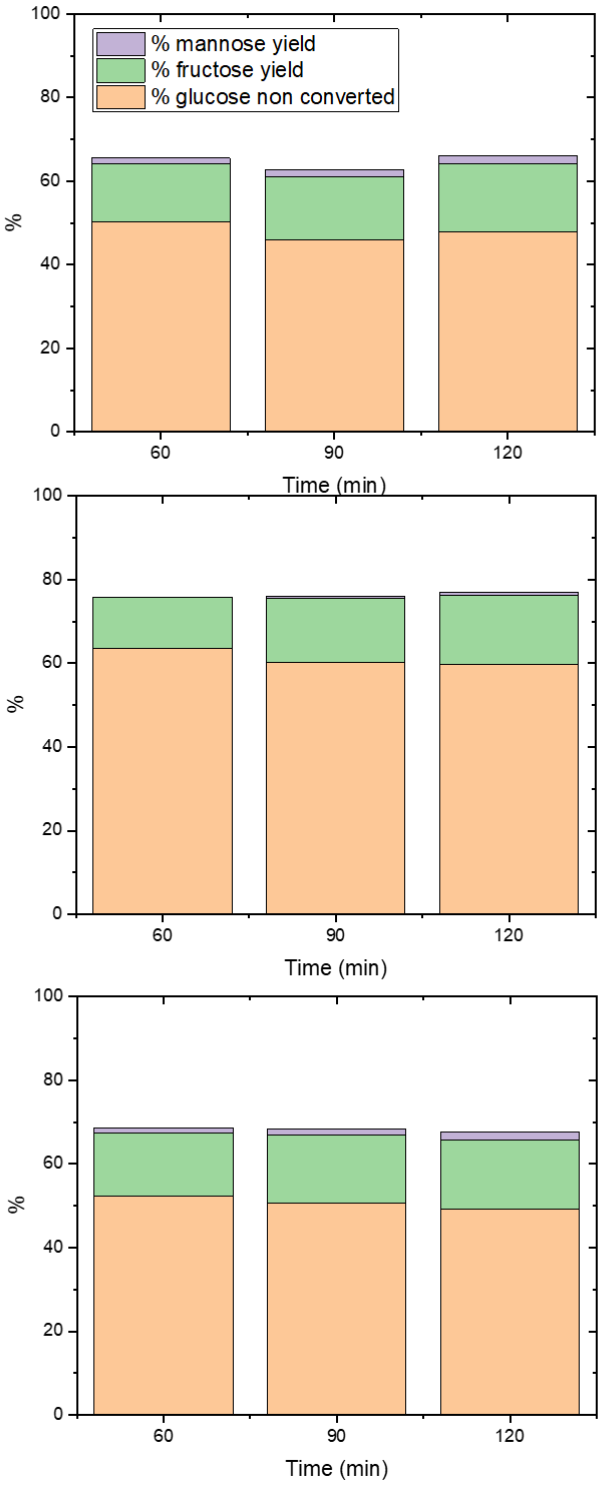

Figure 5. Fructose yield and percentage of non-converted glucose in the isomerization of glucose in the presence of calcined hydrocalumite prepared in the mechanochemical reactor with different times: c_HC_60min_RL (A), c_HC_15min_RL (B) and c_HC_5min_RL (C). Experimental conditions: 17 wt% glucose (20 g glucose in 100 mL H_2O); Glucose/catalyst weight ratio: 12; Temperature: 50 ºC.

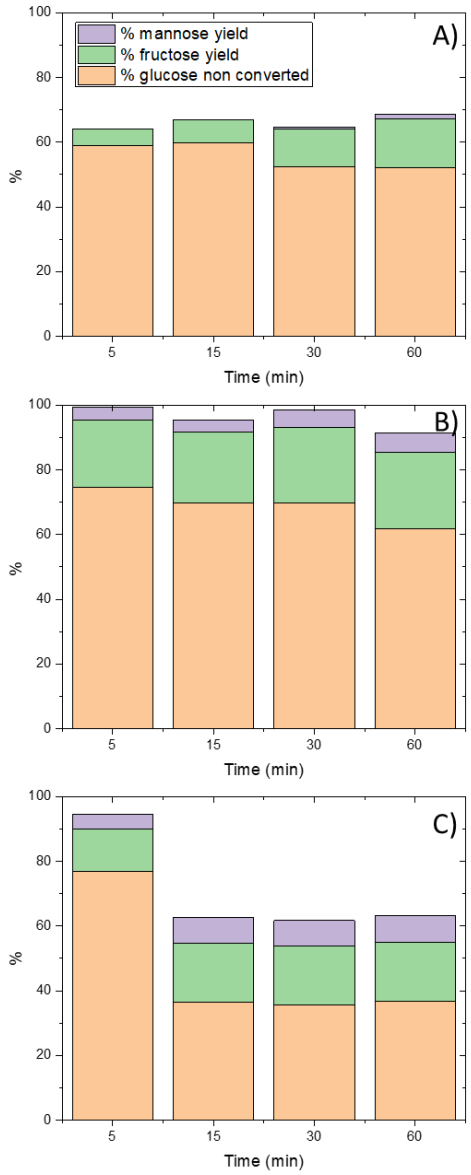

Figure 6. Influence of the glucose/catalyst weight ratio (R) on fructose and mannose yields and percentage of non-converted glucose in the isomerization of glucose in the presence of c_HC_5min_RL: R= 12 (A), R= 6 (B) and R= 3 (C). Experimental conditions: 17 wt% glucose (20 g glucose in 100 mL H_2O); Temperature: 50 ºC.

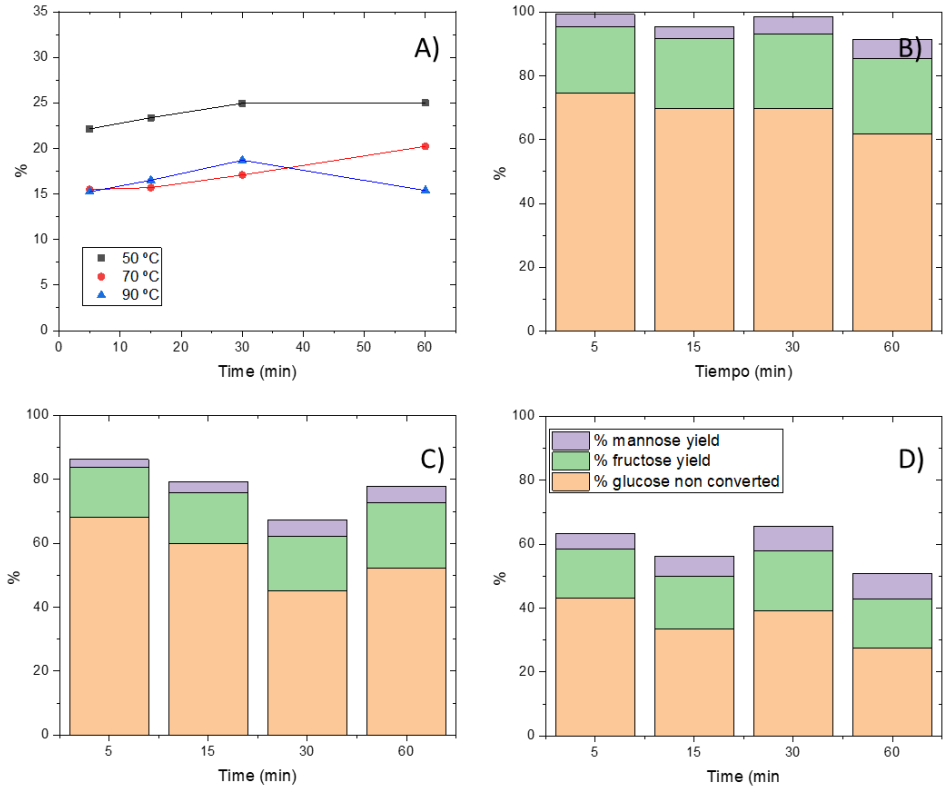

Figure 7. Fructose yields at different reaction temperatures (A), fructose and mannose yields and percentage of non-converted glucose in the isomerization of glucose with c_HC_5min_RL at 50 °C (B), 70 °C (C) and 90 °C (D). Experimental conditions: 17 wt% glucose (20 g glucose in 100 mL H_2O); Glucose/catalyst weight ratio: 6.

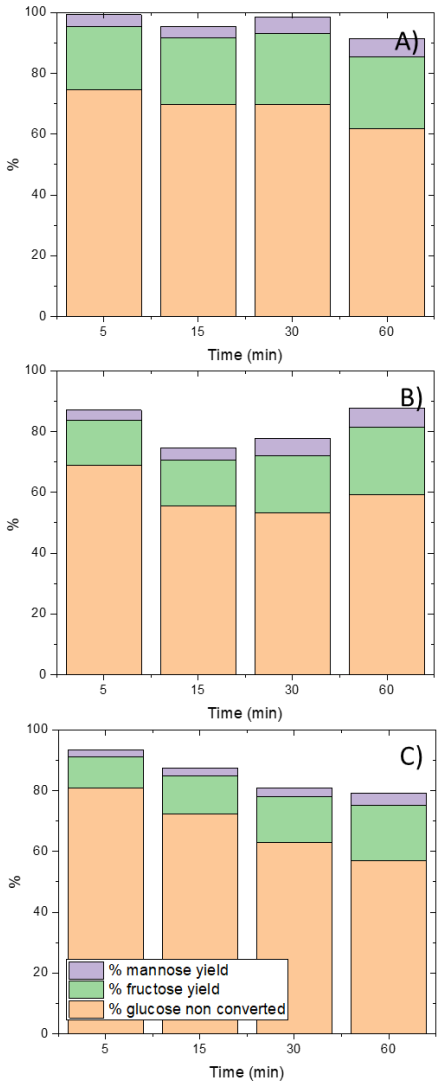

Figure 8. Influence of the percentage of glucose in solution on fructose and mannose yields and percentage of non-converted glucose in the isomerization of glucose in the presence of c_HC_5min_RL: wt% glucose= 17 (A), 33 (B) and 50 (C). Experimental conditions: 100 g H_2O; Glucose/catalyst weight ratio: 6; Temperature: 50 ºC.

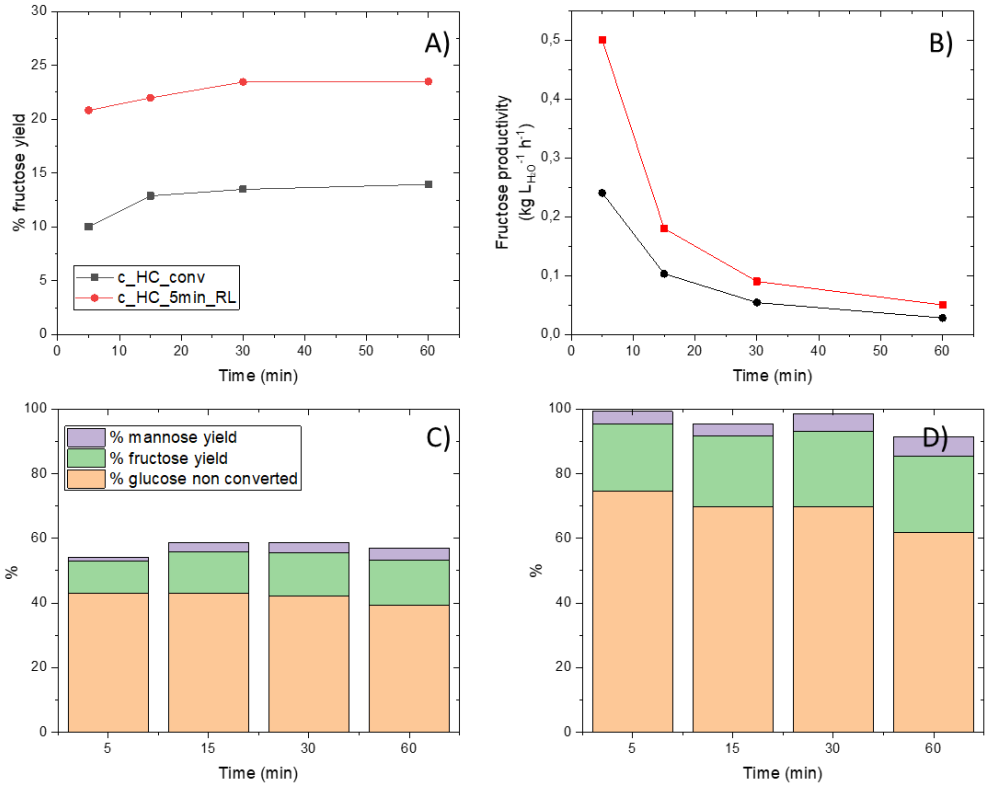

Figure 9. Isomerization of glucose at different reaction times in the presence of calcined hydrocalumite prepared with different methods: fructose yield (A), productivity expressed as concentration (kg/L) of fructose formed per hour (B), fructose and mannose yields, and percentage of non-converted glucose with c_HC_conv (C) and c_HC_5min_RL (D). Experimental conditions: 17 wt% glucose (20 g glucose in 100 mL H_2O); Glucose/catalyst weight ratio: 6; Temperature: 50 ºC.

Table 1. Textural properties of fresh and calcined hydrocalumite prepared under conventional and mechanochemical methods.

Sample	S_{BET} (m^2/g)	S_{micro} (m^2/g)	S_{ext} (m^2/g)	V_p[a] (cm^3/g)	d_p[b] (nm)
HC_conv	17.05	1.62	15.42	0.036	12.0
c_HC_conv	7.70	4.69	3.01	0.013	9.1
HC_5min_RL	23.05	1.79	21.26	0.057	10.4
c_HC_5min_RL	6.45	1.14	5.31	0.013	7.9

[a] at P/P_0= 0.95; [b] average pore width from BJH desorption

Table 2. Catalytic data in the isomerization of glucose to fructose in the presence of c_HC_5min_RL. Experimental conditions: Glucose/catalyst weight ratio: 12; wt% glucose: 17 (20 g glucose in 100 mL H_2O); Temperature: 50 ºC.

Time (min)	% Yield (fructose)	% Selec (fructose)	% Conv (glucose)	Fructose productivity ($kg_{fructose}\ L_{H_2O}^{-1}\ h^{-1}$)
5	5.0	12.2	40.9	0.12
15	6.9	17.2	40.1	0.06
30	11.7	24.5	40.1	0.05
60	15.0	31.5	47.7	0.03
90	16.2	32.9	47.8	0.02
120	16.5	32.6	49.4	0.02

Table 3. Catalytic activity in the isomerization of glucose with c_HC_5min_RL. Experimental conditions: Glucose/catalyst weight ratio: 6; wt% glucose: 17 (20 g glucose in 100 mL H_2O); Temperature: 50 ºC.

Time (min)	% Yield (fructose)	% Selec (fructose)	% Conv (glucose)	Fructose productivity ($kg_{fructose}\ L_{H_2O}^{-1}\ h^{-1}$)
5	20.8	82.3	25.3	0.50
15	22.0	72.4	30.3	0.18
30	23.5	77.4	30.3	0.09
60	23.5	61.7	38.1	0.05
90	23.7	58.0	40.9	0.03
120	24.5	62.4	39.3	0.03

Table 4. Data of catalytic activity in the isomerization of glucose to fructose of different basic catalysts, using water as solvent

Catalyst	Experimental conditions	% Conv (glucose)	% Selec (fructose)	% Yield (fructose)	Productivity ($kg_{fructose}\ L_{H_2O}^{-1}\ h^{-1}\ Kg_{catalyst}^{-1}$)	Eco-friendly[c]	Cost	Separation	Ref.
$CaO\text{-}Al_2O_3$ (Ca/Al= 3)	Continuous, 10 wt% glucose, 0.5 g cat, Flow rate= 2 mL/h, 45ºC, TOS= 4 h	68	80	54	27000	+	+	+	[38]
LDH_CO_3	Batch, 1 wt% glucose, 0.33 wt % cat, 90ºC, 48 h	58	73	42	27	+	+	+	[45]
PAO[a]	Batch, 0.9 wt% glucose, 0.1 wt cat %, 85ºC, 5 h	49	99	49	882	+	-	+	[46]
IRA-900	Batch, 10 wt% glucose, 10 cat wt%, 80ºC, 30 min	36	75	27	540	+	-	+	[47]
Thermus Ohsimai[b]	Batch, 40 wt% glucose, 25 g/L wet cells biocatalys, 85ºC, 5 h	-	-	52	1664	-	-	-	[48]
Calc_HC	Semi-continuous, 17 wt% glucosa, 2.8 % cat, 50ºC, 5 min	25	82	21	15300	+	+	+	This work

[a] Amidoximed polyacrylonitrile;
[b] glucose isomerase