ON THE IMPORTANCE OF VARIATION OF ALKALISATION CONDITIONS ON CELLULOSE ETHER SYNTHESIS

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With a multivariate approach, we investigate and correlate the effect of mercerization conditions on the properties of a cellulose ether. We have chosen to work with carboxymethylcellulose (CMC) for analytical reasons. As expected, the *DS* was found to increase when the NaOH/AGU (anhydroglucose unit) stoichiometric ratio (r) was increased (range 1.0–1.3) and [NaOH] was decreased (range 50-30%). However, such changes also favoured the formation of unwanted side products. Decreased (r) and increased [NaOH] resulted in increased heterogeneity, and thus the quantities of insoluble particles and unreacted chemicals also increased. As another result, the prediction between mercerisation and synthesis weakens. Consequently, a *DS* of 0.18–0.7 was obtained; the measured solubility was much lower than expected. A non-statistical distribution of substituents was further found. Interestingly, the relative importance of substitution at $\bar{X}_3$ increases with an increased [NaOH].

Keywords: mercerization, alkalisation, cellulose ethers, carboxymethylcellulose, sodium glycolate, sodium diglycolate

INTRODUCTION

A broad spectrum of commercial cellulose ethers (CEs) is available, such as ionic carboxymethylcellulose (CMC) and nonionic ethyl hydroxyethyl cellulose (EHEC) and methyl ethyl hydroxyethyl cellulose (MEHEC), which can be used as thickening, stabilizing, water-retaining and dispersing agents in, for example, water-based paints and in the building industry.[1,2] CEs can be made by the reaction of alkali cellulose with monochloroacetic acid to produce CMC, and with ethyl chloride and ethylene oxide to produce EHEC *etc*.[3-5] The production of alkali cellulose (Na-Cell) is often called mercerization. It is common knowledge that the activation achieved during mercerization affects the degree of substitution (*DS*), which is an important quality parameter of CEs.[2,6] In the traditional mercerization process (TAM), the Na-Cell is obtained by steeping the cellulose with a relatively low concentration (20–30% w/w) of NaOH solution.[7] The advantage of this TAM process is a quick and complete reaction.[8] The wet Na-Cell is then squeezed to remove excess H_2O and NaOH.[7,9] The H_2O and NaOH still left after pressing form unwanted side products, like sodium glycolate (in CMC production) or ethylene glycols, methanol and ethanol (in EHEC and MEHEC production). They are formed by the reaction of etherifying agents with the remaining H_2O and excess OH^- ions.[3] To circumvent the problem with unwanted reactions, the mercerization of cellulose for CEs production is shifted towards low-water-content (LWC) mercerization. In this kind of process, a NaOH/AGU (anhydroglucose unit) stoichiometric ratio, denoted herein as (r), of 1.1–5.0 is used, with the concentration of the added NaOH between 40–55% (w/w) and in the presence of an organic liquid. The mercerization time is variated between ≈15–60 min, depending on the produced CE.[2,10,11]

Most of the available mercerization literature for CEs use organic liquids, and a long mercerization time, *e.g.* one h. Some of these studies have indicated an alteration of the reaction yield and rate when alcohols, *e.g.* 2-propanol or ethanol, are used.[12,13] Their influence on the characteristics of the final products has also been shown.[14,15] In this context, the influence of (r) between ≈0.65–5.4 and [NaOH] between ≈8–45%

on the CMC properties has also been presented.[16-20] In the last-mentioned studies, the amount of accessible NaOH was always controlled by the [NaOH] and independent ratio variation was never done. Thus, (r) and [NaOH] interaction/dependency and its effect on CE properties were not thoroughly investigated. Studies carried out by our research group have shown that LWC mercerization has somewhat other dependencies upon parameters such as temperature, ratio, concentration, and mercerization time than the above studies.[21,22] In this paper, we connect these dependencies to etherification. Furthermore, studies focusing on the influence of mercerization parameters on the formation of side products are few.[6] In the present work, we also attempt to fill this gap.

Ideally, we would be able to analyse the effect of different alkalisation conditions on both ionic and nonionic CEs directly. However, the production of nonionic CEs yields a rather complex mixture of products. The reaction of NaOH with, *e.g.* ethylene oxide, introduces new reactive hydroxyl-groups, which form the basis for further reactions. The analysis of this complex mix complicates the analytical work at the molecular level. To circumvent this problem, we have instead synthesised CMC in the present work, which made it easier to analyse the influence of the mercerization conditions on a molecular level. Another advantage of this decision is that the studied process mimics the nonionic CEs, but gives the analytical benefits of working with CMC. CMC is usually produced in a process that includes alcohol, which is valid for lab-scale as well as for commercial production.[7,20] The current study was made on CMC synthesised without alcohol. We decided to get a reliable relation of mercerization conditions (and avoid the possible influence of the use of alcohol on the outcome) on CE properties and side products. Also, the aim is to achieve results applicable not only for CMC, but for all CEs, where LWC mercerization is used as the first step in the production process. Very importantly, we always had in mind to be able to relate the current results to previous studies, which focused on mercerization at LWC and where we used no alcohol.[21,22] It is worth clarifying that the present work does not aim to optimize mercerization at LWC in any way.

Secondly, the study aimed to examine the formation of unwanted side products and relate their formation to the assumed mercerization. We also investigated the effects of the co-variation of the added [NaOH], (r), and reaction time at LWC mercerization conditions on the measured *DS*, insoluble particles, side products, and unreacted chemicals, using a multivariate data approach. We addressed the variation of both the added [NaOH] and (r) independently. We then compared the resulting parameters to the similar parameters addressed earlier for LWC mercerization. Furthermore, to provide information on a molecular level, we have analysed both the substitution pattern within the AGU (position C2, C3, C6) using ^{1}H NMR, along the polymer chains (molar fraction) of the synthesised CMC samples by High-Performance Liquid Chromatography (HPLC), and compared how we could relate the increase of unwanted side products to *DS*.

EXPERIMENTAL

Materials

A softwood sulphite dissolving cellulose pulp from pine and spruce was provided by Domsjö Fabriker AB, Örnsköldsvik, Sweden. The average molecular weight of this pulp was 3.92×10^5 g mol^{-1} (internal method, KA 10.312), and an intrinsic viscosity of 544 mL g^{-1} (ISO 2470:1999), as supplied by the manufacturer. The alkaline solutions for S samples were prepared using NaOH pellets (ACS reagent, ≥97.0%, Sigma-Aldrich) and boiled MilliQ H_2O, while N samples were prepared with a stock solution of 50% [NaOH] (Across Organics), diluted using deionised H_2O when 30% and 40% [NaOH] was added. After being prepared, all alkaline aqueous solutions were kept in vessels protected from atmospheric CO_2. Sodium chloroacetate powder (denoted as Na-MCA) (assay ≥98.0%, Merck) was used for carboxymethylation of the alkali cellulose. D_2SO_4 and D_2O were acquired from Sigma-Aldrich.

Experimental design for carboxymethylcellulose production

The design of experiments (DoE) consisted of simultaneous variation of mercerization parameters; (r), added [NaOH], and time, using two levels each: (r) = 1 and 1.3 mol/mol; [NaOH] = 9.9 N (30% w/w) and 19.1 N (50% w/w); mercerization time = 10 and 60 min. The middle points (*i.e.* replicates) were at (r) = 1.15, 14.2 N (40%, w/w [NaOH]) and 35 min mercerization time. In all the experiments, we kept the mercerization temperature at 26 °C. We set the experimental mercerization parameters related to previous studies,[21,22] and within ranges used in the industry.[2,10]

In this study, we define (r) as a stoichiometric ratio between NaOH and AGU. Added [NaOH] refers then mainly to the concentration of water at any given (r). The response variables, *i.e.* analyses, were: the *DS*

(calculated from both substitution patterns within the AGU and along the polymer chains), sodium glycolate (%) (denoted as Na-glycolate), sodium diglycolate (%) (denoted as Na-diglycolate), remaining Na-MCA (%), remaining NaOH (%), NaCl (%), pH, and insoluble particles (%). We performed two DoEs using MODDE (v.9.1.1.0, Umetrics AB, Umeå, Sweden). Firstly, we did a Fractional Factorial Design, which consisted of 4 experiments plus two central points; samples are labelled as N1-N6. Secondly, we applied an extended model, *i.e.* a Full Factorial Design, where we increased the number of experiments to 10, including two central points. These samples are labelled as S1-S10.

Synthesis of carboxymethylcellulose

We synthesised CMCs at two locations, with different types of equipment (mentioned here also as a kneader). Firstly, we synthesised the samples labelled "N" using an IKA HKD-T 0.60 kneader for CMC synthesis at Nouryon (formerly AkzoNobel), Arnhem, the Netherlands. Secondly, we produced the samples labelled "S" in a kneader usually used to shred alkali cellulose in viscose production at MoRe Research, Örnsköldsvik, Sweden. The latter equipment is detailed in the supplementary material of Albán Reyes, Gorzsas, Stridh, de Wit and Sundman.[21]

CMC production involved several steps. Firstly, the sheet of dissolving pulp was ground at Nouryon (AkzoNobel), Örnsköldsvik, Sweden, in a pilot plant fine cutting mill (Netzsch, Germany), using a 280 µm mesh. Secondly, we added the milled cellulose pulp to the kneader (24.3 g in N and 15 g in S kneader). We sprayed the NaOH(aq) into the kneader using an airbrush (Biltema AB, Sweden, unit nr. 17372), as described by Albán Reyes, Gorzsas, Stridh, de Wit and Sundman.[21] Important to note is that the kneader continuously mixed the pulp and the NaOH(aq) throughout the process. After mercerization, *i.e.*, after 10–60 min, at 26 °C (see Table 1), we added powdered Na-MCA (equimolar to the NaOH). We varied the Na-MCA/AGU ratio and NaOH/AGU ratio similarly to synthesise CMC with similar settings as used in the CE industry. The use of a lower Na-MCA/AGU ratio results in less CMC-reaction, while a higher Na-MCA/AGU ratio could lead to more unreacted chemicals. The industry does not desire these two outcomes for economic reasons.

Since the primary purpose of the present work is to study the effect of LWC mercerization on CMC properties and side products, we kept all the parameters in the etherification step constant, except the Na-MCA/AGU, which was varied according to (r), as has been explained. In the etherification step, we increased the temperature to 70 °C of the kneader and kept it there for 60 min with continued "kneading". The etherifying agent monochloroacetic acid ($CH_2ClCOOH$, MCA) is usually used in CMC industrial production.[14,15,23] Since this chemical is a carboxylic acid, however, it consumes added NaOH. In the present study, we add only 1-1.3 mol NaOH per mol of AGU. If we had used monochloroacetic acid, we would have to add 2-2.6 mol of NaOH in the mercerization step. Since we wanted to study the effect of the LWC mercerization, we avoided this by using the Na-salt of monochloroacetic acid ($CH_2ClCOONa$). Subsequently, after cooling to room temperature, we placed the products in sealed plastic bags before further treatment. The samples were not purified due to the subsequent analysis of side products. Finally, the samples were dried, ground and stored at room temperature until analysis. Equations 1 to 5 show the chemical reactions for mercerization, etherification, and side reactions. Mercerization conditions for each sample are detailed in Table 1.

Mercerization:

$$\text{Cell-OH} + \text{NaOH (aq)} \rightarrow \underset{\textit{Alkali cellulose}}{\text{Cell-ONa}} + H_2O \quad (1)$$

Etherification reaction:

$$\text{Cell-ONa} + ClCH_2COONa \rightarrow \underset{\textit{Carboxymethylcellulose sodium}}{\text{Cell-O-}CH_2COONa} + NaCl \quad (2)$$

Side reactions in CMC synthesis:

$$NaOH\ (aq) + ClCH_2COONa \rightarrow \underset{\textit{Sodium glycolate}}{HOCH_2COONa} + NaCl \quad (3)$$

$$NaOH\ (aq) + HOCH_2COONa \rightleftharpoons \underset{\textit{Disodium glycolate}}{NaOCH_2COONa} + H_2O \quad (4)$$

$$ClCH_2COONa + NaOCH_2COONa \rightarrow \underset{\textit{Sodium diglycolate}}{NaOOCCH_2OCH_2COONa} + NaCl \quad (5)$$

where Cell-OH represents the functional hydroxyl groups (OH-C2; OH-C3; OH-C6) in the AGU.

Multivariate data analyses

A Partial Least Squares (PLS) regression method was used[24,25] to model the overall effect of (r), added [NaOH], and mercerization time on the studied responses mentioned above. In the PLS analysis, we used a unit variance scaling to avoid the effects of different numerical values of the variables. We performed the PLS analysis using MODDE (v.9.1.1.0, Umetrics AB, Umeå, Sweden).

Table 1
Overview of conditions used during mercerization with low-water-content (LWC) and etherification steps

Sample name	Added [NaOH] (%, w/w)	NaOH/AGU (mol/mol)	Merc. time (min)	Na-MCA/AGU (mol/mol)	Water/AGU (mol/mol)
N1	30	1	60	1	5.19
N2	50	1	10	1	2.22
N3	30	1.3	10	1.3	6.74
N4	50	1.3	60	1.3	2.89
*N5	40	1.15	35	1.15	3.83
*N6	40	1.15	35	1.15	3.83
S1	30	1	60	1	5.19
S2	50	1	10	1	2.22
S3	30	1.3	10	1.3	6.74
S4	50	1.3	60	1.3	2.89
*S5	40	1.15	35	1.15	3.83
*S6	40	1.15	35	1.15	3.83
S7	30	1	10	1	5.19
S8	50	1	60	1	2.22
S9	30	1.3	60	1.3	6.74
S10	50	1.3	10	1.3	2.89

Replicates are marked with asterisks (*)

Measurements

Nuclear Magnetic Resonance (NMR) Spectroscopy

We recorded the NMR spectra on a Bruker 400 MHz spectrometer at the "NMR for life" core facility at Umeå University, with a total of 32 scans typically obtained per sample. As a standard, we used 4,4-dimethyl-4-silapentane-1-sulfonic acid (DSS). We carried out the ^{1}H NMR analysis similarly, as reported in a previous study.[20] We dialysed the synthesised CMC samples against running deionised H_2O to remove impurities before the NMR measurements. We then freeze-dried and hydrolysed (in 72 % (v/v) D_2SO_4/D_2O) the samples for 60 min at 30 °C. We then diluted the hydrolysed sample to 25% (v/v) and continued the hydrolysis for 120 min, at 90 °C. If necessary, we filtered the samples before NMR analysis.

Monomer composition analysis

We performed an HPLC analysis of the molar ratios of unsubstituted (*i.e.*, glucose), 2-; 3-; 6-mono-*O*-carboxymethyl glucose (mono), 2,3-; 2,6-; 3,6-di-*O*-carboxymethyl glucose (di), and 2,3,6-tri-*O*-carboxymethyl glucose (tri) in each of the CMC samples, similarly to Heinze, Erler, Nehls and Klemm,[26] briefly described as follows. The protocol followed is an internal protocol used by Noyroun (Arnhem, the Netherlands) and may not be displayed publicly. Very briefly, the samples were completely hydrolysed to monomers by subsequent treatment with 70% and 15% sulfuric acid at ambient and elevated temperatures, respectively. The mixture of monomers was then analysed using HPLC.

Measurements of side products and unreacted chemicals

Glycolates, sodium hydroxide and sodium chloride were determined using methods comparable to, or validated according to the industrial standardised protocol ASTM D1439.

Content of insoluble particles

The content of insoluble particles in each of the CMC samples was measured by gravimetric measurement as described further. A known amount of the dry CMC sample was dissolved in deionised H_2O to 2% concentration. The solution was divided into two, and one solution was centrifuged. The centrifuged and non-centrifuged solutions were dried at atmospheric pressure at 105 °C, and the weight of insoluble particles was calculated.

RESULTS AND DISCUSSION

Carboxymethylcellulose produced by low-water-content (LWC) mercerization

We ground the dissolving cellulose pulp sheet to obtain a "powder" that enabled the mixing of

the pulp with a small amount of aqueous NaOH and powdered Na-MCA. However, the blending of such a dry system is problematic. The performance of the kneader is vital for the outcome, which leads to varying results and unsatisfactory reproducibility. Thus, to increase the significance of our results and assay the influence of the mixing system, we performed the CMC synthesis using two different kneaders, N and S kneaders (*i.e.*, N and S samples), which differ in mixing capacity and efficiency. This makes it possible to detail the impact of mixing efficiency on the achieved results. Although the experimental conditions were the same in N and S kneaders (see Table 1), the results differ. The N kneader has greater efficiency in mixing than the S kneader. We carried out replicates for each kneader, thus showing the reproducibility for each separately, see Table 2 and Table 3. In general, samples produced in the N kneader show better reproducibility of the results, a higher DS_{calc} (Table 2), slightly lower % of Na-glycolate and insoluble particles (Table 3), compared to samples produced in S kneader.

However, it is worth mentioning that, even though there are differences in the results obtained for each kneader, the data trend for the DS_{calc} is mostly the same. Due to the few data points included in the DOE for N samples, we do not see any variation of the responses concerning mercerization time. Thus, regarding the influence of the mercerization time on the studied responses, we have solely focused on S samples, where we use an extended model.

Correlation between mercerization parameters and the resulting degree of substitution

As mentioned in the introduction, mercerization, as well as the etherification step, affect the *DS*.[3] *DS* is defined as the average number of substituted functional OH groups in the AGU (at positions C2, C3 and C6).[27] We analysed the *DS* in the CMC samples using both HPLC and ^{1}H-NMR (see methods above). Different hydrolysis methods give similar *DS* values for a particular analysed sample. We find an example of this in the study reported by Heinze and Pfeiffer,[20] where they analysed CMC samples produced in the presence of alcohol by ^{1}H-NMR and HPLC methods and had similar *DS*s. However, in the present study, even though the *DS* derived by ^{1}H-NMR and HPLC mostly show the same data trends (see Table 2), the values differ slightly. Unfortunately, we think this is due to incomplete hydrolysis of the unreacted cellulose present in the highly heterogeneous CMC samples. Thus, we use the *DS* calculated by HPLC, here referred to as DS_{calc}, in the present study to describe the CMC properties related to *DS*. We chose these values since HPLC is a standardised method used internally daily and thus considered more accurate for total *DS* calculations in our case.

Our results show that at LWC mercerization, DS_{calc} has a marginal positive correlation to (r), while it has a statistically significant negative correlation with the added [NaOH], as illustrated in Figure 1. This agrees with a previous study from our group, where the degree of activation of sulphite cellulose pulp increases as the (r) increases and added [NaOH] decreases under our experimental conditions.[21] An example is that, under our experimental conditions, we obtained the highest DS_{calc} value ($DS_{calc} \approx 0.7$) at 30% added [NaOH] and (r) = 1.3 (*i.e.*, water/AGU molar ratio of 6.74). The positive correlation with the amount of NaOH is, on the one hand, well established in the literature. As examples, Ramos, Frolllini and Heinze also found an increase in the *DS* with (r) when they performed the carboxymethylation of cellulose in dimethyl sulfoxide/tetrabutylammonium fluoride trihydrate solution.[28] Hedlund and Germgård also observed such positive correlation when they prepared CMC samples in the presence of 2-propanol.[17]

On the other hand, the decrease in *DS* with an increase in added [NaOH] differs from the observations given by Almlöf, Kreutz, Jardeby and Germgård,[18] where the authors observed a positive correlation of the *DS* of the CMC produced with a relatively low concentration of NaOH ([NaOH]= 9- 27.5%) and (r) from 0.65 to 2.55, in the presence of isopropanol. In agreement with our observations, a decrease of *DS* was also observed by Yeasmin and Mondal,[19] when the [NaOH] increased from 30 to 40% for CMC samples prepared with cellulose extract from corn husk in the presence of ethanol. Thus, the previously mentioned discrepancy seems to be due to the lower [NaOH] and low (r) used in the study by Almlöf, Kreutz, Jardeby and Germgård.[18] From the literature, we also know that, at room temperature, we need at least 10% [NaOH] for an adequate activation of cellulose at TAM conditions.[29,30] Furthermore, in earlier publications, we show that in LWC mercerization, the degree of activation increases with increased NaOH from 10% to 20%. It then decreases when

NaOH concentration increases from 30% to higher concentrations.[21]

We have also shown earlier that sub-stoichiometric (r) gives a low degree of activation.[21,22] According to known facts and in our view, increased [NaOH] and (r) above 9% and 0.65, respectively, will lead to an increased *DS*.[18] However, under our current study conditions, with higher added [NaOH] (and (r) = 1-1.3 mol/mol), any further increase of [NaOH] leads to a decrease in the amount of water, resulting in poorly swollen cellulose, with highly heterogeneous activation, as described in our earlier study, and consequently a low *DS*.[21]

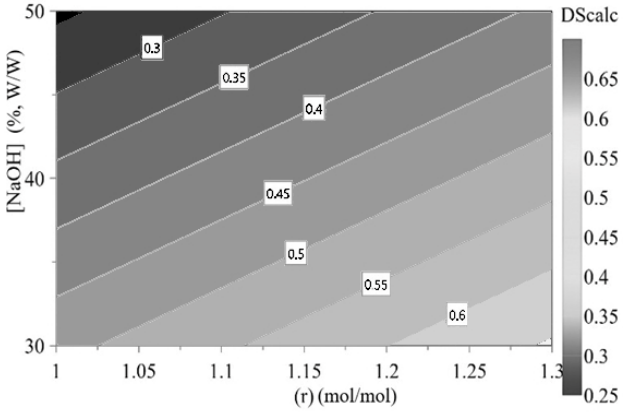

Figure 1: Contour plot showing the DS_{calc} for S samples, as a simultaneous function of NaOH/AGU stoichiometric ratio ((r), X-axis) and added [NaOH] (in % w/w, Y-axis) at 35 min

To address the effect of mercerization time on the DS_{calc}, we have mercerised samples from 10 min to 60 min. The modelled effect of mercerization time shows no statistically significant influence on the overall DS_{calc}. This result agrees with the previous study reported by our group, where we found no statistically significant effect of prolonging time on the degree of activation of cellulose pulp for samples treated by LWC mercerization and with highly concentrated NaOH solution (45%–55%, w/w).[21] Nevertheless, we can mention that we observed a slight increase of DS_{calc} over time for CMC samples prepared in the S kneader at 30% w/w [NaOH]. This goes in line with an earlier study, where we observed an increase of the degree of activation under similar LWC mercerization conditions ((r)=0.8 at 30% [NaOH]), suggesting a possible continuous formation of Na-Cell.[22] However, the relative change in DS_{calc} with prolonged time for the synthesised CMC samples is lower than the reported degree of activation therein. Also, as further reported in that paper, at 50% w/w [NaOH], where the amount of water is limited, the samples herein show high heterogeneity and poor *DS*s. To sum up, with this heterogeneous system, any change is too small, and we chose to state that we did not see any significant change of *DS* with mercerization time in our study.

It is a well-established fact that the average *DS* is not the only factor influencing the properties of cellulose ethers. The substitution pattern within the AGU (positions C2, C3, C6) also plays a critical role.[31] In the present study, we have analysed such patterns, as well as the patterns of the repeating AGUs (*i.e.*, molar fraction) of the polymer chain. We present the obtained results below.

Substitution pattern within the anhydroglucose unit (AGU)

The hydroxyl groups located at C2, C3 and C6 positions in the glucose ring are substituted to a different degree during the etherification of the alkali cellulose.[4,32] We refer to these different (individual) degrees of substitution in each carbon as $\overline{X}_2$, $\overline{X}_3$ and $\overline{X}_6$, and we calculate them from ^{1}H-NMR spectra of hydrolysed CMC, as described in the literature. We calculated the DS_{SUM} of the CMC, as shown in Equation (6). We present the calculated partial degree of substitution of the individual $\overline{X}_i$ (i = 2, 3, 6), together with the DS_{SUM} in Table 2.

$$DS_{SUM} = \overline{X}_2 + \overline{X}_3 + \overline{X}_6 \quad (6)$$

Our results show the expected order $\bar{X}_3 < \bar{X}_2 \approx \bar{X}_6$ for the substitution in C3, C2, and C6 positions, respectively. These observations are well consistent with previously reported reactivity patterns for the three hydroxyl groups in the AGU.[33-36] Interestingly, as the added [NaOH] increases from 30 to 50%, the relative contribution to DS_{SUM} of $\bar{X}_3$ increases. Samples produced in the N kneader show that when we added 30% [NaOH] during the mercerization step, the average values of the relative contribution (given in %) for $\bar{X}_2$, $\bar{X}_3$ and $\bar{X}_6$ was 41, 15 and 44, respectively. When we increased the added [NaOH] to 50%, these values changed to 39%, 22% and 39%, respectively. Samples produced in the S kneader show similar behaviour in the average relative contribution in % for the three $\bar{X}_i$.

Table 2
Partial degree of substitution ($\bar{X}_i$) at positions C2, C3 respectively C6 in the anhydroglucose unit for the carboxymethylcellulose samples, determined using ^{1}H NMR spectroscopy

Sample name	$\bar{X}_2$	$\bar{X}_3$	$\bar{X}_6$	DS_{SUM}
N1	0.2	0.06	0.22	0.48
N2	0.24	0.13	0.25	0.62
N3	0.33	0.15	0.35	0.83
N4	0.28	0.16	0.26	0.7
*N5	0.24	0.16	0.25	0.65
*N6	0.25	0.12	0.25	0.62
S1	0.26	0.09	0.26	0.61
S2	0.14	0.06	0.14	0.34
S3	0.3	0.13	0.29	0.72
S4	0.15	0.08	0.17	0.4
*S5	0.18	0.07	0.2	0.46
*S6	0.19	0.08	0.18	0.45
S7	0.25	0.08	0.24	0.57
S8	0.06	0.02	0.05	0.12
S9	0.28	0.1	0.3	0.68
S10	0.26	0.13	0.24	0.64

(*) indicates replicates

In general, it is known the substitution on C2 is more kinetically favoured, while substitution on C6 is more thermodynamically stable during chemical modification of cellulose.[37] Furthermore, the literature suggests that accessibility is a cause of differences in the distribution of substituents.[4] Thus, we hypothesise that as the conditions become dryer, the spatial hindrance for substitution at C3 is less pronounced, since this position is hard to reach anyway. It becomes logical since the introduced "diffusion-controlled" limitation most likely also affects at C2, as well as at C6. Thus, this results in a larger relative contribution of $\bar{X}_3$ with increased added [NaOH]. It could seem that the literature found something else, *e.g.* the findings reported by Heinze and Pfeiffer[20] show a slight increase in the $\bar{X}_6$ with [NaOH]. We do not observe any such correlation in our data. A slurry method with isopropanol was used, with much lower [NaOH] (5–30% w/v), a variation of (r) between ≈0.5 and 3.2, and longer reaction time (2–6 h) in their study, however. Thus, our explanation for this discrepancy could be that, under our experimental conditions, the system is so dry that any decrease of water by increased [NaOH] hindered the accessibility to the functional OH groups, causing the decrease in the relative contribution of $\bar{X}_6$ (and also a slight decrease in $\bar{X}_2$). This agrees with the hypothesis.

Substitution patterns along the polymer chains

We present the mol fractions of glucose (*i.e.* unsubstituted AGU), mono-, di- and tri-*O*-carboxymethyl glucose for the hydrolysed CMC samples, and DS_{calc} in Figure 2. We calculated the DS_{calc} according to Equation (7):

$$DS_{calc} = \frac{glucose*0 + mono*1 + di*2 + tri*3}{SUM\ (glucose + mono + di + tri)} \quad (7)$$

Statistical models for calculating the distribution of substituents of cellulose derivatives as a function of *DS* were presented as early as in 1939, by Spurlin. The models are made based on the assumption that all functional OH-groups are equally accessible and that their reactivity stays constant through the reaction. Despite these simplifications, statistical calculations of the distribution of substituents have proven to be relevant.[20,28] The mono-substituted glucose in our hydrolysed CMC samples was of a lower mol fraction, compared to what we would expect from these statistics. Meanwhile, the fractions of glucose, di- and tri-substituted carboxymethyl glucose were slightly higher, as shown in Figure 2. The explanation of such non-statistical distribution is that, along the polymer chain in the CMC samples, there are areas of lower and higher substitution than the average DS_{calc}. The observed deviation, therefore, suggests a high heterogeneity in the synthesised CMC samples.

Heterogeneity in carboxymethylcellulose produced by low-water-content mercerization

Ideally, CE manufacturing is a well-distributed functionalisation that occurs equally throughout the cellulose molecule. The success of the reaction is, however, dependent on the antecedent activation of the cellulose. In our studies mentioned above on cellulose activation, we have noted the LWC mercerization does not fully activate cellulose. Therefore, we did not expect perfectly well-distributed CMC either. An idea of the inhomogeneity in the CMC samples can be derived from: i) a comparison between the obtained distribution of the substituents with the statistically calculated, as has been mentioned above, and also ii) considering the solubility of the samples related to the average *DS*. Low solubility in relation to the average *DS* indicate areas in the sample of much lower *DS* than what the average reveals. Thus, it seems that LWC mercerization causes incomplete activation because of poor distribution. Ramos, Frollini and Heinze[28] pointed out a similar reasoning. Heterogeneous reactions are, however, less reproducible and hence complicate multivariate correlations.

According to literature, good water solubility of typically produced CMC is achieved at *DS* values around 0.5–0.8.[7,27] In the synthesised CMC samples, we reached a DS_{calc} of up to 0.7. Despite these high *DS* values, we never reached a solubility above 86% (14% insoluble particles, Fig. 3). Ramos, Frollini and Heinze[28] explained such insolubility by the non-statistical distribution of the monomer units. Our samples seemed to show less deviation from the statistical distribution (see Fig. 2), but as described above, the deviation is not negligible. The non-statistical distribution of the monomers is a clear indication of significant heterogeneity.

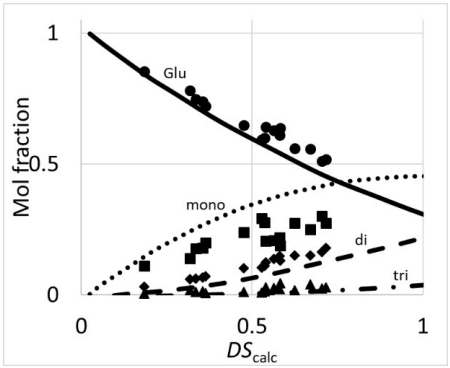

Figure 2: Molar fraction of glucose (Glu, solid line and circles), 2-; 3-; 6-mono-*O*-carboxymethyl glucose (mono, dotted line and squares), 2,3-; 2,6-; 3,6-di-*O*-carboxymethyl glucose (di, dashed line and diamonds), and 2,3,6-tri-*O*-carboxymethyl glucose (tri, dashed-dotted line and triangles) in hydrolysed CMC samples versus DS_{calc} (symbols represent the samples, lines – statistical distribution proposed by Spurlin.[41] DS_{calc} – *DS* derivate through the HPLC method)

The levels of insoluble particles in CMC samples decrease with increased DS_{calc}, but does not follow the dependence expected from the literature for any given DS_{calc} (Fig. 3). The high percentage of insoluble particles thus indicate the existence of larger areas of unreacted cellulose.

We found the highest percentage of insoluble particles (>50%) in samples prepared in the S kneader at 50% added [NaOH]. We had prepared the sample with the least percentage of insoluble particles (<14%) in the S kneader too, but at 30% of added [NaOH], thus adding significantly more H_2O. These results suggest that the mixing efficiency, as well as the experimental conditions, affect the insoluble particles, see the % of insoluble particles obtained for N and S samples in Figure 3. The heterogeneity is thus on a macroscopic level too. As a consequence, this prevents excellent correlations.

The nature and processing conditions of the raw materials can also be considered an influencing factor for the insolubility of the CMC. Earler studies by Jardeby *et al.*[38,41] pointed out that undissolved residuals in CMC are closely related to the thin-walled fibres. They explained that during the drying of the cellulose pulp sheet, such fibres compressed together, making the accessibility of cellulose difficult. In our study, however, we did not perform these analyses. To avoid the influence from any such factors, the same raw material, *i.e.*, the same batch of pulp, was used throughout the current study to reduce the number of uncertainties that might influence the results.

Influence of mercerization conditions on side products formation

In theory, LWC mercerization should produce fewer side products, compared to TAM.[3,40] In accordance with that, N samples synthesised using 50% added [NaOH] and (r) = 1.0 show lower amounts of side products than those with lower added [NaOH] and higher (r) (Table 3). When the influence of the added [NaOH] and (r) on side products is modelled for N samples, these two variables show a statistically significant effect on the measured Na-glycolate (not shown). Thus, the best mercerisation conditions used herein (based on the knowledge from previous studies, *e.g.* Forsberg, Stridh, de Wit and Sundman[22]) give many side products (Fig. 4a-b). However, excellent correlation is prevented by overly large inhomogeneity.

As displayed in Equations 2-5, the formation of sodium diglycolate requires the prior formation of sodium glycolate and disodium glycolate. If (r) is reduced (*i.e.* also the Na-MCA/AGU molar ratio), the amount of NaOH (aq) available for the formation of side products is low.

This would then be more reflected in the sodium diglycolate because of the dependence on previous side product formation and free NaOH(aq).

Table 3
Side products, NaCl, remaining Na-MCA and NaOH, and pH of a 2 % (w/w) solution of carboxymethylcellulose samples

Sample name	Na-glycolate (%, w/w)	Na-diglycolate (%, w/w)	Na-MCA (%, w/w)	NaOH (%, w/w)	NaCl (%, w/w)	pH	Insolubles (%, w/w)
N1	5.36	2.64	1.56	0	18.8	6.5	21.8
N2	3.97	2.61	4.32	1.03	15.7	11.4	29.7
N3	6.21	4.25	0.45	0	22.1	6.3	17.7
N4	5.21	4.26	8.38	2.52	15.9	11.7	24.9
*N5	5.35	3.39	5.53	0.88	17.6	11.2	19
*N6	5.33	3.1	6.45	1.02	17.1	11.3	20.1
S1	4.67	3.72	1.88	0.01	18.4	9.1	13.7
S2	5.81	5.34	4.5	1.1	17.1	11.5	54.4
S3	5.47	5.36	0.3	0	21.9	6.2	30
S4	2.31	2.4	22.44	6.4	9.3	12.3	35.3
*S5	6.74	2.67	9.28	2.35	14	11	22.6
*S6	6.28	4.08	8.94	1.76	15.8	11.7	42.2
S7	5.65	4.93	0.24	0	19.8	7.2	38
S8	7.06	1.89	14.07	4.8	10.8	12.1	51.3
S9	6.3	4.42	0.02	0	22.2	5.5	25.2
S10	6.68	6.45	1.91	0.02	20.9	9.3	23.7

(*) indicate replicates

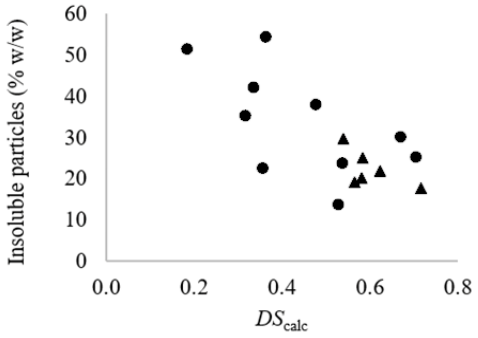

Figure 3: Amount of insoluble particles (%, w/w) as a function of DS_{calc} for carboxymethylcellulose samples prepared in N (triangles) and S (circles) kneaders, respectively

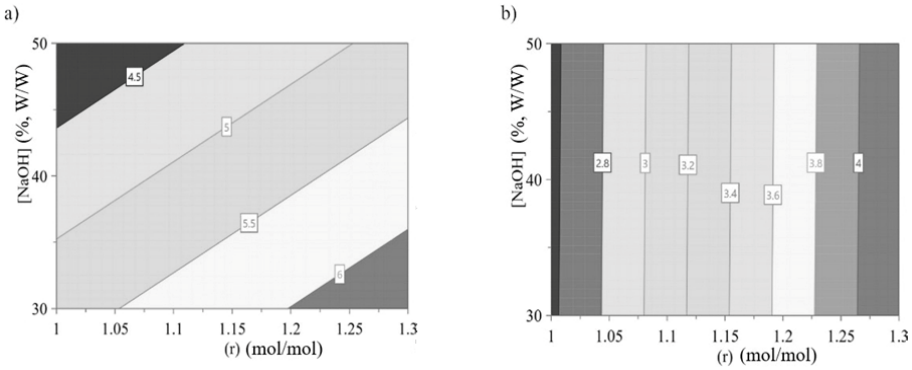

Figure 4: Contour plots showing (a) % of Na-glycolate, and (b) % of Na-diglycolate for N samples, as a simultaneous function of NaOH/AGU stoichiometric ratio (r) and added [NaOH] (%) at 35 min

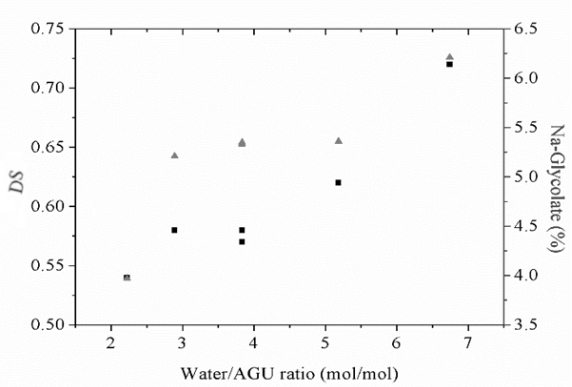

Figure 5: Water/AGU mol/mol ratio (X-axis) versus both DS_{calc} (squares, left hand Y-axis) and (%) Na-glycolate (triangles, right hand Y-axis) for N samples

For samples prepared in the less efficient S kneader, the effects of the varied added [NaOH] or (r) on Na-glycolate and Na-diglycolate does not show any statistical significance.

Next, we asked how the mercerization time influences the amount of these side products. Mercerization time shows no significant influence for samples produced in the N kneader. This is because (r) and the added [NaOH] varied for each of the synthesised N samples. Thus, there are too few data points in N samples for reliable comparison concerning mercerization time. For the S kneader, decreased Na-diglycolate with mercerization time was the only statistically significant result (Table 2). This may be due to the slow and continued alkali cellulose formation with the time that likely decreased the amount of NaOH(aq) available for side reactions.

Interestingly, according to these data, the increase in water affects the *DS* and Na-glycolate

formation differently. Figure 5 shows these changes for N samples at the lowest and highest studied water/AGU mol/mol ratios. For comparative reasons, we show the relative change for both in *DS* and Na-glycolate. In the figure, we can see that an increase of water/AGU mol/mol ratio from the lowest value (2.2) to 2.9 increases Na-glycolate by about 31%, while the *DS* only increases by 7%. At further increasing water/AGU mol/mol ratio, a Na-glycolate increase is barely visible, while *DS* shows a significant increase as we increase the ratio. When the water/AGU mol/mol ratio is increased to 6.7, both Na-glycolate and *DS* increase. Therefore, it seems that the side reaction is more sensitive to the water availability than the primary reaction is (under very dry process conditions). We do not know, however, if it is chemical thermodynamics or purely different physical accessibilities (due to diffusion) that is the reason for this.

Unreacted chemicals in the carboxymethylation of cellulose

The unreacted NaOH (%), and resulting pH in a 2% solution CMC sample, as well as the unreacted Na-MCA, correlates positively with the added [NaOH], while they correlate negatively to the water/AGU mol ratio (see Table 3). These results once more indicate that the LWC mercerization causes a very heterogeneous NaOH/H_2O/cellulose/Na-MCA mixture, and this heterogeneity becomes more pronounced as we decrease the amount of water by increasing the added [NaOH].

CONCLUSION

A multivariate data analysis approach proves to be suitable, but not perfect, for finding correlations between mercerization variables, CMC substitution properties, amounts of side products and unreacted chemicals. This allows us to draw correlations between earlier mercerization studies and the present one. We see that increased mercerization increases *DS*, but not to the expected degree. However, we also see that optimum mercerization conditions lead to increased side product formation, while increased merccerisation time could decrease one of the side products. Moreover, we did not achieve complete solubility in the synthesised CMC samples. We conclude that the high heterogeneity in the synthesised samples, evidenced by a non-statistical distribution of substituents, is the reason for this. The problem of a well-distributed mercerisation under LWC conditions has been shown previously and became obvious. This lack of homogeneity also causes a weakening of the multivariate correlations. With regard to the distribution of substituents within the AGU, our results show a lower value for $\bar{X}_3$, compared to $\bar{X}_2$ and $\bar{X}_6$, thus indicating that the LWC mercerization in the absence of alcohols results in a similar distribution as often found in the CMC processes. Interestingly, our data also show that the relative importance of the substitution in $\bar{X}_3$ increases when [NaOH] increases from 30% to 50%. Moreover, we show that CMC properties and the formation of side products are greatly affected by the mixing equipment used.

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