*CELLULOSE CHEMISTRY AND TECHNOLOGY*

# NOVEL CELLULOSE AND STARCH-BASED MATERIALS

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The experiences on cellulose research in our region, first in Teltow and later in Potsdam-Golm, have extended over many years since the 1920s with the foundation of the Vereinigte Glanzstoff-Fabriken in Teltow-Seehof, followed by the Institut für Faserforschung and the Institut für Polymerforschung of the Academy of Sciences of the GDR, up to the Fraunhofer Institute for Applied Polymer Research IAP, which is now situated in Potsdam-Golm. While the original fiber production in Teltow-Seehof was based on the viscose process, which is still the dominating process for producing man-made cellulose fibers, alternative ecologically friendly procedures have been developed in the course of the years. One of these developments concerns the so called CarbaCell process, whereby the chemical modification of cellulose with urea (instead of carbon disulphide in the viscose process) leads to cellulose carbamate, which can be spun and regenerated. Another alternative is the direct solution procedure in N-methylmorpholine-N-oxide monohydrate (NMMNO*$H_2O$). This non-derivatizing solvent for cellulose can also be used for several homogeneous chemical reactions, whereby in comparison with the classical heterogeneous slurry processes, a completely different distribution of substituents in the anhydroglucose unit and also along the polymer chain is achieved. The substitution pattern has a high influence on the properties of the products, especially on the solution behavior. Also, anorganic cellulose esters like phosphates and sulfates can be synthesized regioselectively at positions C6 or C2/C3. Especially the cellulose sulfate with substitutions at position C6 is a suitable material for the micro-encapsulation of living cells for clinical applications.

Slightly substituted cellulose derivatives are also the starting point for the formation of nanocellulose, which is prepared as a clear and opalescent dispersion after a mechanical treatment.

Another subject matter is the development of starch-based materials. Starting from thermoplastic starch by adding a plasticizer, highly substituted starch esters are developed, which show mechanical properties like petrochemical-based thermoplastic materials.

A short overview of some research activities on the topics of cellulose and starch at the Fraunhofer Institute for Applied Polymer Research IAP over the last 20 years is presented.

***Keywords***: cellulose carbamate, N-methylmorpholine-N-oxide monohydrate (NMMNO*$H_2O$), homogeneous synthesis, cellulose sulfate, microencapsulation, nanocellulose, thermoplastic starch mixed esters

## INTRODUCTION

Cellulose constitutes the most abundant, renewable polymer resource available today worldwide. It can be available in a rather pure form, e.g. in the seed hairs of the cotton plant, but mostly occurs combined with lignin and other polysaccharides (so-called hemicelluloses) in the cell wall of woody plants. Starch is an important energy reserve of plants. It is synthesized as microscopic granules in the tissue of many plant species (e.g. pollen, leaves, stems, roots, tubers, bulbs, rhizomes, fruits, flowers, and seeds), and provides dietary energy for animals and humans.

Before proteins, fats and oils, saccharides and polysaccharides – especially cellulose and starch – are quantitatively the most important product group of the photoinitiated biosynthesis. Under the legitimate assumption that biomass consists of about 40% polysaccharides, the annual production output of photoinitiated biosynthesis of cellulose and starch amounts to approximately 70 billion tons, an enormously high yield when compared with the finite world reserves of the major non-recurrent raw materials, such as petroleum, natural gas, coal, metals and ores.[1]

Both, cellulose and starch are polymers composed of specific glucose units. Cellulose is a polydisperse linear homopolymer, consisting of regio- and enantioselective β-1,4-glycosidic linked D-glucopyranose units (so-called anhydroglucose units [AGU]).

Starch granules are composed of two major α-glucans, amylose and amylopectin. The ratio of the two components varies according to the botanical origin. Amylose is an essentially linear α-glucan containing around 99% α-1,4- and 1% α-1,6-linked anhydroglucose units. Most grain derived starches like corn starch are characterized by an A-type X-ray spectrum and root or tuber derived starches like potato by a B-type spectrum.

Native cellulose and starch are insoluble in water and in most organic solvents at ambient temperature, which is caused by their supermolecular structures and the hydrogen bonding network, which is more distinctive in cellulose. The properties in general and especially the solubility of these polysaccharides can be influenced by a chemical modification of the free OH-groups within the AGU's. For solubility, a hydrophilic/hydrophobic balance is necessary, which can be adjusted by different chemical modifications like etherification or esterification processes.

The research activities on the topic of cellulose at the location of Teltow-Seehof started long before the founding of the Fraunhofer Institute for Applied Polymer Research.[2] Already during the 1920s, the Vereinigte Glanzstoff-Fabriken (VGF) worked on the viscose process. Here cellulose pulp is converted with sodium hydroxide and carbon disulfide to cellulose xanthogenate first. This metastable intermediate is soluble in aqueous sodium hydroxide, and can be formed as a viscose solution in a wet process. Under decomposition of the xanthogenate, a high-purity cellulose is regenerated in the precipitation bath.

Further research on cellulose was continued over the years at the Institut für Faserforschung and the Institut für Polymerforschung (IPOC), both predecessor institutions of the Fraunhofer Institute.

The wide range of preparative and structure-analytical studies over the past 20 years includes the development of an environmentally friendly alternative to the viscose process, which is given by the CarbaCell process, whereby cellulose is transformed to cellulose carbamate by the reaction with urea (replacing carbon disulphide in the viscose process) and afterwards a solution of this derivative in NaOH lye is precipitated and cellulose is regenerated in the precipitation bath.[3] On the other hand, the direct solution procedure in NMMNO offers another alternative to the viscose process.[4] Beyond that, a lot of research topics like the synthesis and deformation of cellulose carbamate, the melt like processing of cellulose NMMNO solutions into fibers, blown films and nonwovens, the conversion of native cellulose into nanocellulose, homogeneous and heterogeneous reactions, and regioselective etherifications and esterifications of cellulose and also of starch in the AGU and along the polymer chains, were examined.

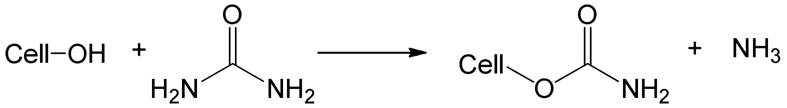
## CELLULOSE

### Cellulose carbamate

In cooperation with the Zimmer AG, Frankfurt/M, the CarbaCell process based on a special cellulose carbamate synthesis was developed at Fraunhofer IAP. In the center of the development work stood the improvement of the procedural economy as a basis for a pilot plant process. Besides the spinning process and the structure-property examinations, the optimization of the synthesis was one subtask.

For the synthesis of cellulose carbamate, cellulose is converted with urea after alkalization to achieve a product that is soluble and shapeable in dilute sodium hydroxide solutions.

The patented CarbaCell technology is based on a synthesis of the cellulose carbamate (Scheme 1) in xylene as an inert organic solvent, which acts as a transfer medium.[3]Cellulose carbamate is relatively stable at room temperature over a long period of time near pH 7, which permits storage times of more than a year without loss of quality. For a further processing (e.g. spinning or shaping), the solubility of cellulose carbamate is very important. Generally, the solubility of cellulose derivatives is influenced by the degree of substitution (DS) and by the distribution of the substituents amongst others. In the case of cellulose carbamates, it means that a DS value of about 0.2 or higher with a homogeneous substituent distribution and without or with low degree of cross-linking is necessary. Against this background and under economic aspects, several synthesis steps were investigated. On the one hand, the activation step and urea treatment (alkalization, washing, intercalation with urea) was simplified by a one-step activation using a mixture of sodium hydroxide solution and urea.[5] On the other hand, the activation and intercalation was homogenized by using an aceotropic water alcohol mixture[6] or organic solvents with high boiling-points.[7] As a further variation, a synthesis with *in-situ* activation was developed, whereby all discontinuous preparation steps could be omitted.[8]



Scheme 1: Formation of cellulose carbamate by transformation of cellulose with urea

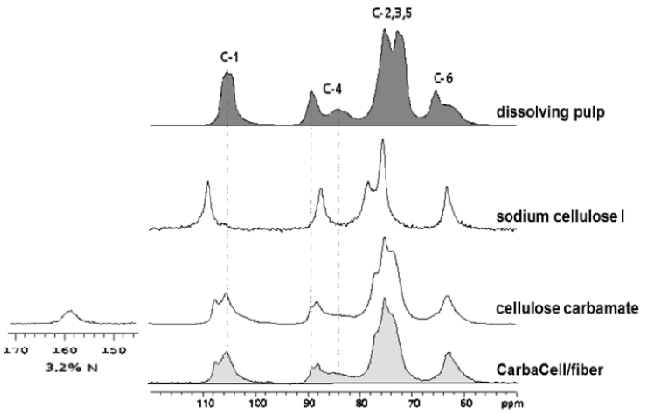


Figure 1: Structural changes of cellulose in the carbamate process as observed with $^{13}$C-CP/MAS NMR spectroscopy

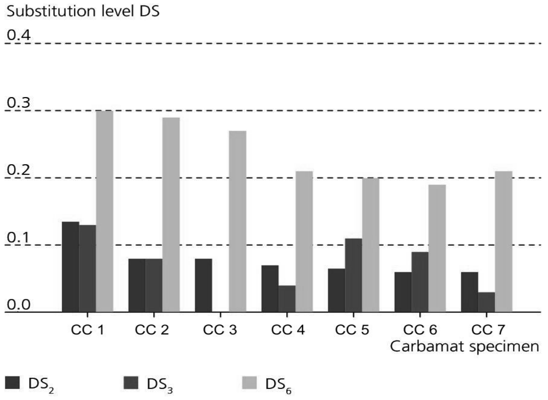


Figure 2: Distribution of substituents of different cellulose carbamates inside the anhydroglucose units

Among these improvements, some other variations of the synthesis conditions were investigated by using an extruder[5] or a kneader[7] as a reaction vessel or by using electromagnetic radiation as a heat source.[9] The synthesized products, as well as the structural changes of cellulose during processing, were characterized by $^{13}$C-CP/MAS solid-state NMR. As shown in Figure 1, the dissolving pulp with the structure of cellulose I in the activation stage was alkalized to sodium cellulose I, transformed to cellulose carbamate and regenerated to the fiber structure (cellulose II).

The transformation of the alkalized cellulose with urea to cellulose carbamate leads to structures that are similar to the cellulose modifications II and IV, and that have either block like or statistic distributions of the substituents along the cellulose chain.[10, 11] After the shaping process and removal of the carbamate groups, the typical structure of regenerated cellulose II is obtained.

Comprehensive NMR-studies of cellulose carbamates in solutions of zinc chloride have shown that the substitution in the AGU occurs predominantly at position C-6 prior to C-3 and C-2 (Figure 2).

In all the described syntheses, the nitrogen contents of the carbamates were in the range between 2.0 and 4.5%, corresponding to DS values from about 0.26 to 0.63. Besides the spinning process of cellulose carbamate, some other possibilities of shaping with different applications were found. For example, it is possible to use cellulose carbamate particles together with detergents as a carpet cleaner.[12] Thereby, the polluted carpet can be cleaned by the treatment with wet cellulose-based powder, which can be vacuum-cleaned after drying. Other possible applications of cellulose carbamate are the use as high-absorbent nonwovens, hollow fibers, sponges, or as a membrane for blood detoxification, haemofiltration and/or plasmapheresis.[13]

## Cellulose ethers and esters – homogeneous versus heterogenous synthesis/regioselectivity

Cellulose ethers are amongst the most important water soluble polymers. They are produced on a large scale and applied in a variety of fields. Accordingly, there are many different types of commercial cellulose ethers varying with respect to type of substitution, as well as to the average degree of polymerization and substitution. However, chemical and physical properties of these materials are determined not only by the averaged substitution, but also by the positions of the substituents at the AGU and by the distribution of the substituents along the cellulose chain.

Nowadays, the industrial-scale production of cellulose ethers takes place exclusively under heterogeneous reaction conditions, whereby cellulose is initially activated with alkali hydroxide solutions and then reacted with alkyl halides or epoxy alkyl compounds at elevated temperature.[14] Activation is required to loosen the partially crystalline structure of cellulose and to increase the accessibility of the hydroxyl groups for the reaction. In order to improve the uniformity of substituent distribution and hence to improve the product properties, the reaction is often carried out in the presence of inert organic solvents, such as e.g. iso-propanol. A preferred manufacturing route of e.g. carboxymethyl cellulose (CMC), the most important cellulose ether, is given by the slurry method. In the slurry process, cellulose is mostly suspended in an isopropanol-water-NaOH system. The molar ratio of NaOH/AGU is chosen as necessary for the reaction with monochloroacetic acid (MCA). It was found that the effect of a slurry alkalization with the usual aqueous-alcoholic NaOH solution corresponds to that of a highly concentrated aqueous NaOH solution.[15] With regard to CMC preparation, highly uniform cellulose ether is obtained from a fully alkalized cellulose characterized by a very low supramolecular order and a lattice type resembling Na-cellulose II.

By variation of the reaction conditions, the substitution along the cellulose chain can be influenced. For example, it was shown that it is possible to substitute the cellulose only at non-crystalline regions. Thus, a block-like distribution of substituents was strongly indicated. Its characteristics can be controlled through the choice of the etherification reagent, by the adjusted degree of substitution and by various pre- and post-treatments.[16] On the other hand, to reach a more homogeneous distribution along the cellulose chain, it is necessary to decrystallize the cellulose structure or better to make the modification under homogeneous conditions. The comparison of different activation methods (dissolution of cellulose in molten inorganic salts, also in NMMNO*$H_2O$ with subsequent precipitation under non-crystallizing conditions and the treatment by electron beam irradiation) and their influence on the following derivatization is described by Fischer *et al.*[17]

For homogeneous reactions, different non-derivatization solvent systems for cellulose and their use to prepare cellulose derivatives have been suggested in the literature,[18, 19] such as aqueous solutions of quaternary ammonium bases,[20] sodium hydroxide/urea,[21] or Ni(tris(2-aminoethyl)amine]$(OH)_2$,[22] non-aqueous mixtures of sulfur dioxide/dimethyl-amine/dimethyl sulfoxide,[23]dimethyl sulfoxide/paraformaldehyde,[24] N,N-dimethyl-acetamide/lithium chloride,[25] 1,3-dimethyl-2-imidazolidinone,[26] or N-methyl-pyrrolidone/lithium chloride.[27] Also, molten inorganic salts[28] and ionic liquids[29, 30] are potential solvent systems and reaction media for the derivatization of cellulose. A special possibility for the dissolution and/or decrystallization of cellulose is given by the NMMNO*$H_2O$, which is also the only industrialized solvent for spinning of cellulose fibers (Lyocell process), being used instead of the viscose process.[31] The NMMNO*$H_2O$ system was in the research focus at Fraunhofer IAP for homogeneous derivatization of cellulose. The comparison of different synthesis conditions and their influence on the distribution of substituents, as well as on the properties of the products were investigated for a variety of cellulose ethers, like CMC, hydroxyethyl cellulose (HEC), hydroxypropyl cellulose (HPC), sulfoethyl cellulose (SEC),[32] and for cyanoethyl cellulose.[33] In general, an improvement of the solution qualities and an increasing viscosity of synthesized cellulose derivatives were observed from heterogeneous with native cellulose to heterogeneous with amorphous cellulose to homogeneous reaction conditions. By investigations regarding carboxymethylation, a certain addition sequence of the reagents in the system cellulose/NMMNO/DMSO/MCA/Triton B was optimal, and this produced a homogeneous synthesis of clearly water soluble products already by a DS > 0.2. This was never found for any other homogeneous carboxymethylation reaction in cellulose solvent systems before.

For strictly homogeneous systems with a solid-phase catalysis and without NaOH, we found a uniform distribution of the substituents along the polymer chains without multiple substitution in the AGU.[34] High solution viscosities, e.g. of 41500 MPa s (2% aq. solution $DS = 0.24$, $\gamma = 2.55\ s^{-1}$), indicate a low depolymerization when gallic acid propyl ester was used as stabilizer. In comparison, a commercially available reference sample, produced by a heterogeneous process ($CMC_{het}$, DS = 1.0), has a viscosity of $\gamma = 28000$ mPa s as a 2% aqueous solution (Figure 3).

It is also recognized that the substitution along and between the polymer chains is more equal with the homogeneous conversion, compared to classical procedures. As shown in Table 1, there is a remarkable difference between the heterogeneously produced cellulose ethers with a DS distribution C2 > C6 > C3 and the homogeneous etherification in NMMNO*$H_2O$/organic solvent systems with a DS distribution of C3 > C2 >> C6.

This high regioselectivity at the secondary OH-groups of the AGU may be caused by the strong solvation behavior of NMMNO*$H_2O$, thus protecting the C6-OH-group.

Furthermore, a broad range of other synthetic routes for regioselective derivatizations were examined.[35-40] Starting from soluble cellulose derivatives like cellulose acetate or trialkylsilyl cellulose, these substituents were used as protecting or leaving groups during the following homogeneous derivatization, which is shown in Scheme 2 and Scheme 3 exemplarily.

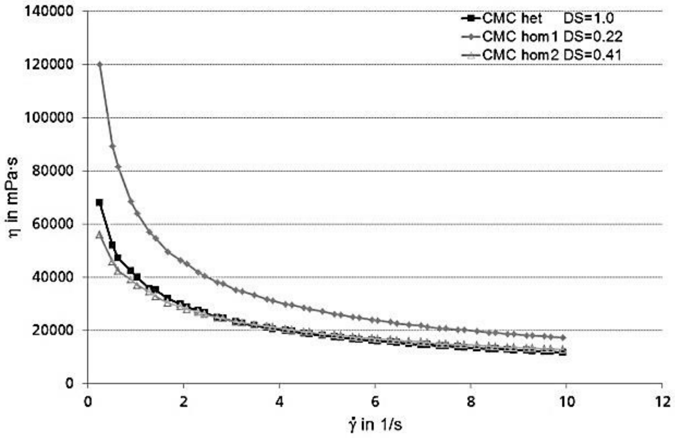
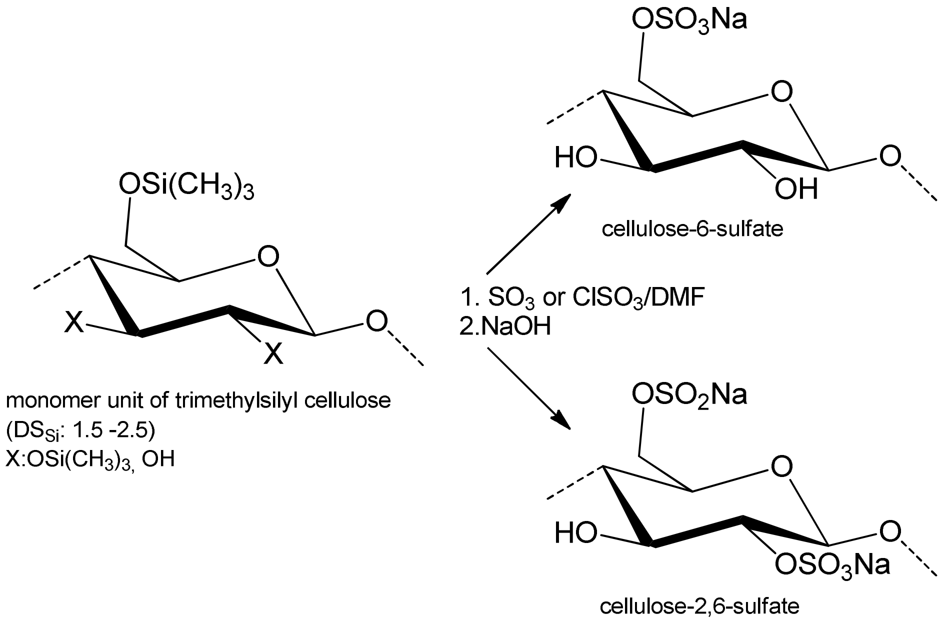
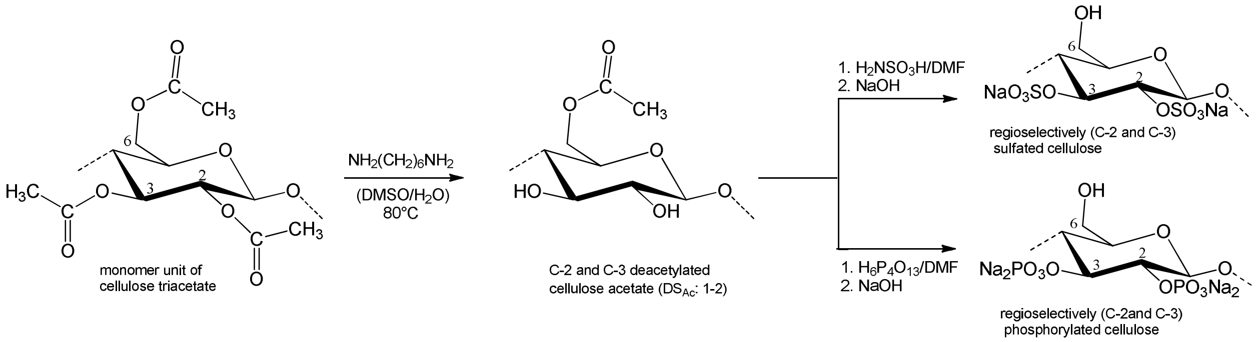


Figure 3: Viscosity of 2% aqueous solution of CMC vs. shear rate (reaction process, het.: heterogeneous, hom.: homogeneous)



Scheme 2: Synthesis of regioselective cellulose sulfates via trimethylsilyl cellulose



Scheme 3: Synthesis of regioselective cellulose sulfates and phosphates via cellulose triacetate

Table 1
DS and DS distribution of homogeneous synthesized CMC in comparison with a commercial available sample

| Sample | DS | Distribution | | | |
|---|---|---|---|---|---|
| | ($^{13}$C-NMR) | $DS_2$ | $DS_3$ | $DS_6$ | %$DS_3$ |
| $CMC_{hom1}$ | 0.22 | 0.1 | 0.12 | 0 | 55 |
| $CMC_{hom2}$ | 0.41 | 0.12 | 0.27 | 0.02 | 66 |
| $CMC_{het}$ Ref. | 1.02 | 0.45 | 0.21 | 0.36 | 21 |

Table 2
Membrane forming and separation properties of sodium cellulose sulfate/poly(DADMAC) membranes (pervaporation test with ethanol/water, T = 50 °C)

| Membrane | Stability | Flow rate$J_V$ (kg/h·m$^2$) | Separation factor α(%) |
|---|---|---|---|
| PEC membrane cellulose-6-sulfate | good | 1.5-3.5 | 140-210 |
| PEC membrane cellulose-2,3-sulfate | not stable | - | - |
| Alginate membrane* | good | 2.2 | 40 |
| Chitosan membrane* | good | 0.4 | 125 |

PEC = polyelectrolyte complex; *reference

Table 3
Blood clotting of cellulose sulfate as a function of distribution of substitution
(TT = thrombin time [s], PTT = partial thromboplastin time [s])

| DS(NMR) | Distribution | | | TT (s) 25 μg/ml | PTT (s) 25 μg/ml |
|---|---|---|---|---|---|
| | $DS_2$ | $DS_3$ | $DS_6$ | blood | Blood |
| 0.95 | 0.00 | 0.00 | 0.95 | 18.9 | 80.8 |
| 0.95 | 0.30 | 0.30 | 0.35 | 20.0 | 136.5 |
| 0.95 | 0.55 | 0.20 | 0.20 | no clotting | 294.3 |

The pattern of substitution has a strong influence on the properties of the products. For example, cellulose sulfates with a substitution on position C6 in combination with cationic poly-(diallyldimethyl-ammonium chloride) (poly (DADMAC)) preferably show a good simplex membrane formation. This could be used for the separation of water/ethanol mixtures via a pervaporation membrane (Table 2) or the forming of capsules (see below). On the other hand, cellulose sulfate with a preferred substitution at position C2/3 shows a high anticoagulant potential (Table 3).[41]

## Cellulose sulfate

Cellulose sulfates have so far received rather little attention within cellulose esterification reactions, as compared, for example with cellulose acetates or nitrates. However, the preparation of cellulose sulfate and its application research has a long tradition at the Fraunhofer IAP, as indicated by the large number of patents.[42]

Possible application areas of cellulose sulfates depending on their properties can be: film-forming material, viscosity regulator, anionic polyelectrolyte component and substance with biological activity.[41, 43-45] The properties of cellulose sulfates depend on the degree of polymerisation (DP), the degree of the substitution (DS), the distribution in the anhydro-glucose unit (AGU) and the distribution along the chains.

Naturally occurring sulfated biopolymers, such as heparin, chondroitin sulfate are widely spread in nature and demonstrate important functions in the regulation of cellular proliferation and differentiation.[46, 47] Even polysaccharides without sulfate groups exhibit biological activities after sulfation, e.g. cellulose sulfate shows anticoagulant and antiviral functions.[46, 48, 49]

***Synthesis of cellulose sulfate***

The sulfation of hydroxyl groups of cellulose generallyresults in the half-ester. These half-esters can be converted into the neutral sodium salts, which are soluble in water depending on the synthesis condition from a DS value of 0.2-0.3. Generally, the term cellulose sulfate will be used to denote the acid half-ester or its sodium salt.

As fundamental routes of synthesis of cellulose sulfates can be considered:[43]

(i) sulfation of hydroxy groups of unmodified cellulose, usually starting under heterogeneous reaction conditions, (ii) sulfation of hydroxy groups in partially functionalized cellulose esters or ethers with the primary substituent acting as a protecting group, (iii) sulfation by displacement of an ester or ether group already present in the macromolecule.

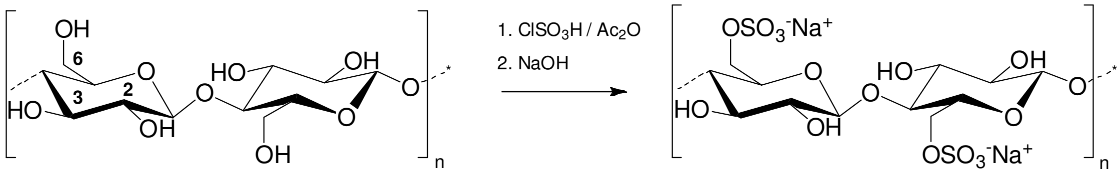
Along the second and the third routes regioselectively functionalized cellulose sulfates can be obtained. The sulfation of cellulose in a strictly heterogeneous system (first route) was discussed in a series of papers.[50-52]

The sulfation of hydroxy groups of partially modified cellulose esters and ethers can be realized in dipolar aprotic solvents (route two). Besides, the primary substituent presents itself as a protecting group and is not attacked by the sulfating agents. The acetyl group of partially esterified cellulose acetate proved to be a suitably stable protecting group in a subsequent sulfation.[53]

The influence of the sulfating agent, e.g. chlorosulfuric acid, amidosulfuric acid or sulfuryl chloride, on the distribution of the sulfuric half-ester within the AGU was investigated by Philipp *et al.*.[35, 36] The formation of labile ester or ether groups, which are easily displaced by sulfating agents from their position in the AGU, is typical of the third route. Such labile groups can be used, e.g. the nitrite group as an ester or the trialkysilyl group as ether.[54-57]

The acetosulfation is a quasi-homogenous synthesis proceeding under gradual dissolution of the cellulose by using different reactivity of the primary and secondary OH-groups, resulting in cellulose acetate sulfate as an intermediate. The synthesis route consists of the competitive esterification of cellulose suspended in N, N-dimethylformamide (DMF) with a mixture of a sulfating and acetylating agents. After precipitation of the polymer, the acetyl groups are cleaved in alkaline solution (Scheme 4). The acetosulfation is a convenient method for the preparation of regioselectively C6 substituted cellulose sulfates.[35, 43]

The investigation of the acetosulfation in different polar aprotic solvents with various sulfating and acetylating agents is shown in another study.[58] By varying of the sulfation and acetylating reagents, a number of water-soluble cellulose sulfates with DS values from 0.2 to 2.3 were obtained. As solvents N,N-dimethylformamide (DMF), N,N-dimethyl-acetamide (DMAC), dimethyl sulfoxide (DMSO) and N-methyl-2-pyrrolidone (NMP) were used. Water soluble products were received in all solvents, except for DMSO.



Scheme 4: Synthesis of sodium cellulose sulfate by acetosulfation

The synthesis of cellulose sulfate in ionic liquids and DMF as co-solvents was described by Gericke *et al.*[59]As a result,water-soluble cellulose sulfates were obtained and after a complex purification, their use for biomedical applications was investigated.

The synthesis of sulfoacetate derivatives of cellulose was described by Chauvelon *et al.*.[60] The synthesis was performed in glacial acetic acid as a solvent, and acetic anhydride and sulfuric acid as reagents. The water soluble products were distinguished by a $DS_{acetate}$ between 1.6 and 2.4 and $DS_{sulfate}$ of 0.3. The characterization of the products was carried out after cleavage of the acetate group and enzymatic hydrolysis.[61]

## Spectroscopic characterization of the cellulose sulfate

The regioselectivity of the cellulose sulfate was determined by means of $^{13}$C-NMR-spectroscopy, according to Nehls *et al.*[62]Figure 4 shows a selection of cellulose sulfates with DS up to 1.1 in comparison with a nearly completely substituted cellulose sulfate. The substitution of the sulfate half ester on position C6 appears by shifting of the C6 signal from 61 to 67 ppm. The substitution on position C2 can be found by a shift of the C1 signal from 103 to 101 ppm. The DS values were calculated after analysis of the surface integrals. The regioselectivity of the acetosulfation can be definitely conformed by the NMR data.

Raman spectroscopy is also an efficient method for structural characterization of native polymers. Thus, the investigation of the different cellulose polymorphs was conducted by Raman spectroscopy.[63, 64]

Figure 5 shows FT-Raman spectra of a series of cellulose sulfates in the range of 700 and 1600 cm$^{-1}$ with different DS. Noticeably, the increase of the Raman intensity at 1025 and 1070 cm$^{-1}$ (OSO and COS stretching vibration) was observed with the increase of the $DS_{sulfate}$.

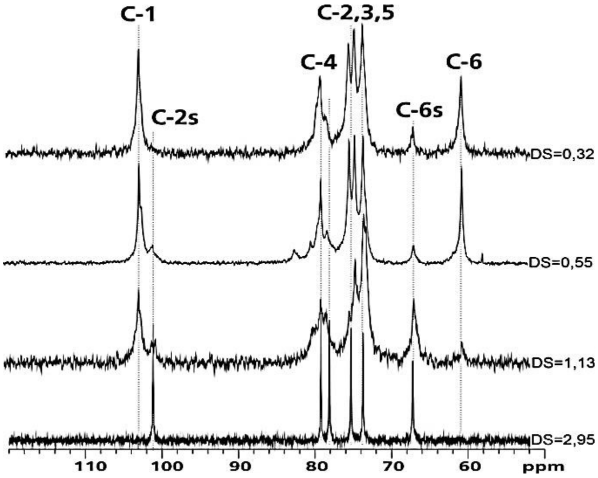


Figure 4: $^{13}$C-NMR spectra of selected cellulose sulfate in comparison with nearly completely substituted cellulose sulfate (DS > 2.9)

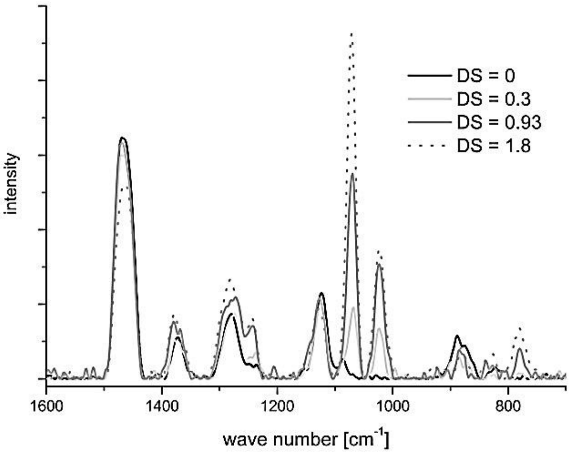


Figure 5: Raman spectra of selected cellulose sulfate in comparison with a non-substituted cellulose

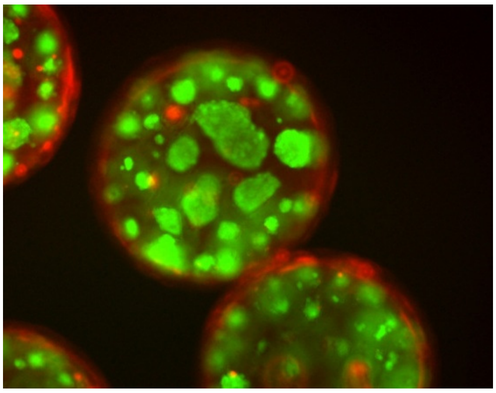


Figure 6: Fluorescence microscopic image of cells in sodium cellulose sulfate and poly(diallyl dimethyl ammonium chloride) microcapsules (Adapted with permission from Brian Salmons[65])

One new peak appeared at 780 $cm^{-1}$ (bending vibration) as well. The modes between 1200 and 1400 $cm^{-1}$ involved methine, methylene and hydroxyl group bending motions. The signal at this range was decreased until it disappeared with the increase of $DS_{sulfate}$ (1378, 1279 and 1240 $cm^{-1}$). Further shifts in the range of the stretching vibration were identified between 1000 and 1200 $cm^{-1}$.

### *Encapsulation of cells – biomedical application*

The capsules were prepared by a precipitation technique. The cellulose sulfate samples were dissolved in physiological sodium chloride solution (0.9 mass-percent, w/w). The concentration of the polymer was adjusted between 1.0 and 1.8 mass-percent (w/w). Capsules were formed by dropping sodium cellulose sulfate solution into a cationic poly(DADMAC) solution. The capsules were washed with physiological sodium chloride solution.

Although great progress has been made over the last few decades in antitumor therapy, many forms of cancer, including pancreatic cancers, hepatocellular carcinomas, gliomas/glioblastomas and ovarian cancers, remain only manageable, rather than curable. Gene therapy, e.g. utilizing encapsulated cells, has been proposed as a means to treat cancer and consequently some of the first gene therapy trials were aiming at this purpose. A possibility for cancer treatment is the utilization of the "gene-directed enzyme prodrug therapy" (GDEPT). The therapy uses 'suicide genes', encoding enzymes in donor cells, which convert inactive prodrugs into tumor-toxic metabolites.[65] The genetically modified cells are implanted nearby the tumor.[66] The cells have to be protected from the patient's immune system and have to be physically confined to the site where they are needed, and both of these prerequisites can be achieved by encapsulating the cells in micro beads (Figure 6).[67-69]

The major advantage of the use of encapsulated cells for the treatment of cancers (as well as other diseases) is that aprodrug can be activated in a sustained manner from implanted cells, since the cells are enclosed in microcapsules, cannot divide and, since most activated prodrugs exert their effects only on dividing cells, the nondividing prodrug producing cells are protected from the effects of the therapy.[68]

The microencapsulation of living cells and the subsequent implantation of these encapsulated cells into patients as a strategy to treat diseases were pioneered 30 years ago.[69] One of the first materials used to encapsulate cells was the seaweed derived substance alginate and this substance is still in use today, mainly for the encapsulation of islet cells to treat diabetes.[70] A good alternative encapsulation material is cellulose sulfate, where the sulfate group is attached to cellulose in a heterogenous reaction.[45] Most recently, sub sieve agarose beads have also been used for encapsulation.[71] Capsules consisting of polymers of sodium cellulose sulfate (SCS) and poly(DADMAC) offer a number of advantages, including the relative ease to reproducibly produce the SCS starting material, greater robustness of the capsules (permitting delivery by syringe or by a catheter without cell bursting), good biocompatibility both for the cells in the microcapsule and with the surrounding tissue upon implantation, and lack of an immune or inflammatory response. Moreover, GMP manufacturing of an encapsulated cell medicinal product based on SCS and poly(DADMAC) has recently been established.[72]

In mouse preclinical studies, encapsulated cells were injected directly into preformed tumors.[66] In a phase I/II clinical trial of encapsulated cells in patients with pancreatic cancer, the encapsulated cells were delivered by supra-selective catheterization of blood vessels leading from the inguinal region to vessels that flowed into the tumor.[73] The 1-year survival rates were 2- and 3-fold greater than those for benchmark drug treated patients and the control group, respectively.[65]

## Nanocellulose

Nanotechnology can be described as the continuation and expansion of the microtechnique. However, the miniaturization of the microstructure is demanding mostly absolutely new unconventional approaches. Generally, nanotechnology is concerned with the constitution, the properties and the effects of the structure in the nanoscale area ($10^{-9}$ m). Nanomaterials are produced as yet with chemical or mechanical methods.

The focus of this study is the verification of routes to nanostructural cellulose and the characterization of the product properties.

Nanoscaled particles of cellulose and its derivatives are obtained in different ways. The preparation is carried out in principle by mechanical treatments. On the one hand, amorphous cellulose prepared by dissolving and precipitation is used. Subsequently, the sample is hydrolyzed, if necessary, and the mechanical treatment of the sample is started. The mechanical treatment contains a combination of dispersing instruments of the rotor-stator typ, e.g. ultra turrax® (UT), as well as the micro fluidizer® (MF) type.[74] On the other hand, the preparation of nanocellulose is carried out by MF treatment of low substituted cellulose derivatives, e.g. MC, CMC or oxidized cellulose.[75] Thereby the degree of substitution (DS) is less than 0.5.

The resulting nanoscaled cellulose dispersions have solid contents from 0.5 up to 3.0%. They are clear, opalescent and stable without protective colloids (Figure 7).

The samples are air-dried and characterized by SEM. No microfibrils of cellulose are shown on the image. A typical morphology of oxidized nanocellulose is characterized as ball-shaped particles, which form chains of stringed beads (Figure 8).

An interesting rheological effect can be verified for dispersions of nanocellulose. Different samples of TEMPO-oxidized cellulose, CMC and MC show thixotropic behavior (Figure 9).

Figure 7: Dispersion of nanocellulose with a solid content of 1% (w/w)

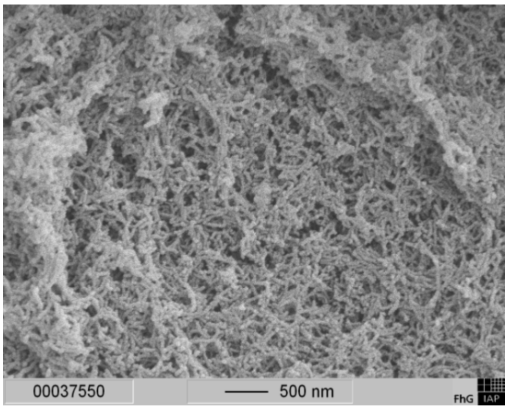


Figure 8: SEM image of oxidized nanocellulose

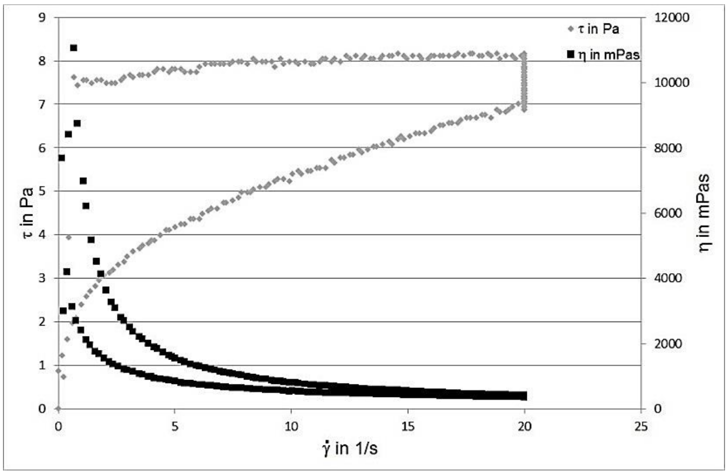


Figure 9: Thixotropic behavior of a CMC nanodispersion with DS = 0.3 (shear rate $\dot{\gamma}$, shear viscosity η, shear stress τ)

Some selected nanodispersions (oxidized cellulose and CMC) are dried by freeze drying, solvent exchange and spray drying. The dried samples are characterized by porosity determination. Afterwards the dried samples are dispersed again in water and the rheological behavior is compared with the starting dispersion. The viscosity of the original samples can be reached only after use of higher shear force. The investigations demonstrate that redispersion of nanocellulose is possible independent from the cellulose sample (oxidized cellulose or CMC) and the drying method.

The nanocellulose dispersions can form films very easily. Such film forming can be an interesting application for nanocellulose. Depending on the appearance of the dispersion, the films are transparent, turbid, colourless, white or yellow. The films are characterized by SEM.

Further application areas of nanocellulose are imaginable, e.g. for reinforcement of physical stability of paper, for adjustment of certain barrier properties in packing materials, for improvement of material properties as additive in polymer composites, as hydrogel in pharmaceutical and cosmetic industry, as rheology modifier in food.

## STARCH

Besides cellulose, the derivatization and processing of starch is also a core competence at Fraunhofer IAP. Also, based on starch, different ethers and esters were synthesized, e.g. highly substituted carboxymethylstarch as a polyelectrolyte,[76] cationic starch as a flocculation agent[77] or regioselectively substituted acetates and sulfates.[78]The development of starch-based materials was another research focus area, which is described in the following sections.

### Thermoplastic material made from starch

Renewable resources are used widely in day-to-day living, foremost in the form of food. Renewable resources have also been used as sources of energy and as construction material (wood) since ancient times. For various reasons ($CO_2$ neutrality, decrease of oil reserves, etc.), substantial use of renewable resources in other areas is becoming ever more important. Creating thermoplastic materials using biomass materials here is a central focus. Native materials like cellulose, starch or lactic acid are the most widely analyzed raw materials in the development of biobased thermoplastic polymers. Lactic acid, obtained by fermenting starch or sugar, can be condensed to polylactic acid and has similar properties to those of polypropylene or polyethylene.[79] As a thermoplastic material, cellulose acetate is – in addition to cellulose acetate propionate and cellulose acetate butyrate – the best known ester that is used in industrial applications.[80] In most cases, starch-based thermoplastic materials are native starches that can be processed on an extruder after adding a plasticizer. All of these materials can be processed using conventional equipment (extruder/injection molding machine), which makes them easier to launch onto the market.

Starch-based thermoplastic materials hitherto have been mainly used in the packaging industry. Their advantages are that they are biodegradable, as well as inexpensive. Many papers have been published in the last 15 years describing how to modify starch in order to turn it into a thermoplastic material. It can be plasticized with different low molecular weight organic compounds in order to produce, for example, films,[81] foams or plastic parts by thermoplastic processing routes.[82] These starch-based materials have poorer mechanical properties than synthetic polymers. The main problems are related to the hydrophilic nature and therefore the relatively high water uptake of starch-based materials, as well as to the brittleness of the resulting products.[83]

As compared with synthetic polymers, little is yet known about the structure-property relationships in extruded starch. To control the properties of extruded starch materials, a better understanding of the structure-property relationships, including the general limitations of the property profile of these materials, seems to be necessary. In a project, the structure-property relationships of extruded starch were investigated in detail to provide parameters for an optimum processing window to make films of plasticized starch. Another way to produce starch-based thermoplastic materials is derivatization of starch, which gives the possibility to improve the mechanical behavior of the produced specimens.

### Structure-property relationships of extruded starches

#### *Extrusion experiments*

The starting starch materials were compounded with a plasticizer system and were processed in a PTW 25 twin-screw extruder (Haake, Germany) with 7 temperature zones. Mainly flat films were extruded using a 50 mm long flat-film die. For a comparison of the extrusion behavior of the different starch types, we used a plasticizer system with the following composition (wt% of the plasticizer-starch compound): 6.2% urea, 9.4% glycerol, 10.4% water. The starch to plasticizer ratio was 74:26. Otherwise, for investigating the influence of the extruder temperature profile on the structure formation of the starch films, the different starting starch types (with the exception of wrinkled pea starch) were always used with the same plasticizer content of 28.6% and a constant plasticizer composition (31.8% urea, 28.3% glycerol, 33.9% water, 5.3% stearic acid, and 0.7% polyethylene glycol). After extrusion, in a second stage, these granular materials were processed into flat films with the temperatures of extruder zones 4 and 5 being increased in steps of 10 °C from 120 to 180 °C (wheat starch, Hylon VII, amylopectin) or even to 210 °C (potato and maize starches).

## Extrusion behavior and mechanical properties of films

### *Influence of the starting starch type*

Under the given conditions it was possible to extrude rather clear films (the best from potato) from the different starch types. The measured mechanical properties of the extruded starch films are shown in Table 4. They do not differ greatly but, surprisingly, films with amylopectin as the starting material exhibit the highest modulus and strength.

### *Structural characterization of the extruded films*

The determined parameters (crystal type, degree of crystallinity $x_c$, lattice disorder factor k, and crystallite dimensions $D_{hkl}$) obtained by WAXS investigations in relation to variations in extruder zone temperature are given in Table 5. To analyze the effects of extruder temperature on film structure, we investigated selected film samples produced from each of the starting starch types at low, moderate and high extruder zone temperatures (i.e. three film samples per starch type). Comparing the crystallinity of the different starch types, the values for potato starch films are found to be slightly lower than those for the other materials. With the exception of maize starch, the crystallinity values of the samples do not vary significantly with changes in extruder temperature. However, except for the amylopectin film, the crystallite $V_H$ dimensions of the different starch films increase considerably (up to a factor of two in some cases) with rising temperature of extruder zones 4 and 5.

Table 4
Mechanical properties strength σ, elongation ε and Young's modulus E of starch films extruded from different starting starch polymers

| Starch type | σ (MPa) | ε (%) | E (MPa) |
|---|---|---|---|
| Potato starch | 22.0 | 11.7 | 880 |
| Maize starch | 20.3 | 9.1 | 800 |
| Wheat starch | 22.1 | 7.6 | 1140 |
| Amylo maize starch Hylon VII | 21.5 | 10.4 | 1015 |
| Wrinkled pea starch | 17.7 | 4.8 | 740 |
| Amylopectin | 23.4 | 5.4 | 1200 |
| Wrinkled pea starch/amylopectin 9:1 | 20.0 | 4.6 | 940 |
| Wrinkled pea starch/amylopectin 4:1 | 17.6 | 5.7 | 730 |

Table 5
X-ray scattering results for starch films processed at different temperatures of extruder zones 4 and 5 (cristallinity$x_c$, lattice disorder parameter $k$, crystallite dimensions $D_{hkl}$)

| Starch type | Amylose content (%) | T of zones 4 and 5 (°C) | $x_c$( %) | $k$ x10² (nm²) | $D_{hkl}$(nm) | | | Portion type B (%) |
|---|---|---|---|---|---|---|---|---|
| | | | | | $V_H D_{110/020}$ | $V_H$ $D_{200/130}$ | $V_H D_{310/240/150}$ | |
| Potato | 21 | 120 | 36 | 2.3 | 14.6 | 12.3 | 18.3 | |
| | | 170 | 35 | 2.8 | 17.2 | 20.1 | 23.2 | |
| | | 200 | 33 | 2.6 | 26.4 | 26.5 | 34.0 | |
| Wheat | 23 | 120 | 39 | 2.8 | 15.6 | 13.3 | 17.2 | |
| | | 150 | 39 | 2.7 | 21.5 | 15.9 | 24.7 | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 180 | 38 | 2.7 | 24.6 | 23.8 | 34.7 | |
| Maize | 21.7 | 120 | 41 | 3.1 | 15.6 | 12.2 | 12.9 | |
| | | 160 | 39 | 2.3 | 26.3 | 21.2 | 22.8 | |
| | | 210 | 35 | 2.9 | 31.0 | 33.0 | 26.3 | |
| Hylon VII | 54 | 120 | 39 | 2.6 | 16.0 | 15.3 | 16.5 | 18 |
| | | 150 | 39 | 2.9 | 28.4 | 20.6 | 26.8 | 4 |
| | | 180 | 41 | 2.2 | 28.9 | 31.2 | 29.4 | (0) |
| Amylo-pectin | 0 | 130 | 38 | 2.6 | | type A | | Small content B |
| | | 150 | 34 | 2.9 | | 1.8-3.3 | | |
| | | 170 | 36 | 2.9 | | | | |

There is an increase in the crystallite dimensions of the potato film samples. This behavior is typical of that exhibited by the other starch films, except for amylopectin. The film samples in Table 5 discussed up to this point are crystallized preferentially in the $V_H$ polymorph. Only the Hylon film additionally exhibits a content of B-type starch, which diminishes with increasing extruder temperature.

## Synthesis of thermoplastic starch mixed esters catalyzed by *in situ* generation of imidazolium salts

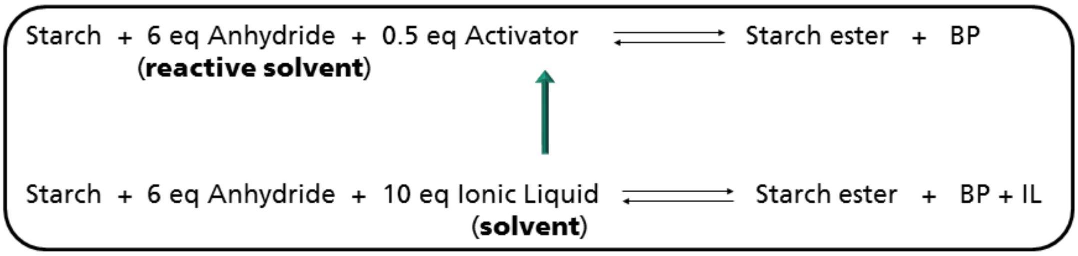
### *Preparation of starch esters using ionic liquids as catalysts*

Polysaccharide esters have been extensively studied over the last two decades and many methods have been developed in order to meet certain requirements. Starch acetates based on a sustainable native polymer, for example, can be used as a thermoplastic material. The classical reaction of starch with acetic anhydride as esterifying agent for 15 h at 140 °C does, however, only result in a starch acetate with a low degree of substitution.

An activator is essential for achieving highly-substituted starch. A lot of work in this field was carried out by various groups in the US around the middle of the last century. There has been a major focus on ionic liquids in polysaccharide chemistry over the last few years. A widely used ionic liquid is 1-N-butyl-3-methylimidazolium chloride ($[C_4mim]^+Cl^-$) as a solvent and reaction medium for starch to carry out homogeneous derivatization. Quite interesting properties are resulting, for example, starch acetate synthesized in $[C_4mim]^+Cl^-$ in terms of the substituent distribution, when compared to cellulose acetate.[84] A new idea was to investigate the method of esterifying starch (Scheme 5) with carboxylic acid anhydrides by using an ionic liquid as a catalyst in just small amounts and not as a solvent.

First we investigated the influence of different ratios of starch (high amylose content corn starch was used) to esterification agent, as well as reaction time and amount of IL. $[C_4mim]^+Cl^-$ was chosen as IL to catalyze the esterification of starch for these investigations. Table 6 demonstrates the resulting catalytic effect of $[C_4mim]^+Cl^-$.

Using 1.2-0.20 moleq of $[C_4mim]^+Cl^-$ per AGU under the mentioned reaction conditions results in highly-substituted starch acetates or propionates. When applying less $[C_4mim]^+Cl^-$, the reaction time must be increased in order to achieve starch esters with a high degree of substitution. A starch diacetate can be isolated if air-dried starch (water content ~11 wt% means 1.2 moleq per AGU) is used as starting material, whereas the degree of substitution is lower than that of the starch acetate produced from dried starch.



Scheme 5: Comparison between the synthesis of starch acetate in acetic anhydride as a reaction medium and ionic liquid as a solvent; BP=by-product

Table 6
Degree of substitution and molar mass averages of saponified starch esters of starch acetates and propionates in dependency on the molar ratios; reaction temperature was 130 °C for all samples

| Starch ester | moleq $[C_4mim]^+Cl^-$ per AGU | moleqAnhydrid per AGU | $t_{Reaction}$ (h) | $DS_{Ester}$ | $M_w$ $x10^6$(g/mol) |
|---|---|---|---|---|---|
| Acetate | 0.33 | 4.5 | 4 | 2.81 | 0.52 |
| Acetate | 0.20 | 4.5 | 4 | 2.73 | 0.36 |
| Acetate | 0.15 | 4.5 | 4 | 1.62 | 0.33 |
| Acetate | 0.075 | 4.5 | 4 | 1.53 | 0.34 |
| Acetate | 0.075 | 4.5 | 24 | 2.96 | 0.33 |
| Acetate | 0.0375 | 4.5 | 24 | 2.61 | 0.14 |
| Acetate | 0.0188 | 4.5 | 24 | 0.61 | 0.16 |
| Acetate | 0.33 | 3.25 | 4 | 2.83 | 0.24 |
| Acetate | 0.20 | 2.5 | 4 | 2.54 | 0.18 |
| Acetate | 0.20 | 1.5 | 4 | 1.68 | 0.16 |
| Propionate | 1.2 | 4.5 | 4 | 2.86 | 1.48 |
| Propionate | 0.5 | 4.5 | 4 | 2.76 | 0.75 |
| Propionate | 0.33 | 4.5 | 4 | 2.22 | 1.01 |
| Propionate | 0.15 | 4.5 | 4 | 1.47 | 0.47 |
| Propionate | 0.075 | 4.5 | 4 | 0.77 | 0.32 |
| Propionate | 0.33 | 4.5 | 4 | 2.06 | 0.82 |

Water from starch decreases the concentration of non-hydrated chloride ions in the reaction system and therefore the effectiveness of breaking the starch's H-bonds. Furthermore, the water can react with acetic anhydride to create acetic acid. This decreases the amount of acetic anhydride, which can esterify the starch. The esterification of starch with propionic anhydride results in lower degrees of substitution than for acetylation under the same reaction conditions. A reason for this is the lower activity of the carbonyl carbon for the propionyl group.

Table 7
Average degree of substitution of starch acetates prepared at 130 °C for 4 h with 4.5 moleq $Ac_2O$ and 0.2 moleq of IL per AGU, as well as molar mass averages of saponified starch acetates

| Significance of alkyl chain | | | Significance of $[C_2mim]^+X^-$counterion | | |
|---|---|---|---|---|---|
| Ionic liquid | DS | $M_w(x10^6$ g/mol) | Counter ion | DS | $M_w(x10^6$ g/mol) |
| $[Hmim]^+Cl^-$ | 2.93 | 0.24 | $Cl^-$ | 2.81 | 0.48 |
| $[C_2mim]^+Cl^-$ | 2.81 | 0.48 | $Br^-$ | 2.98 | 0.28 |
| $[C_4mim]^+Cl^-$ | 2.73 | 0.36 | $AcO^-$ | 0.62 | 0.79 |
| $[C_6mim]^+Cl^-$ | 1.34 | 0.83 | $(MeO)(H)PO_2^-$ | 0.14 | 0.98 |

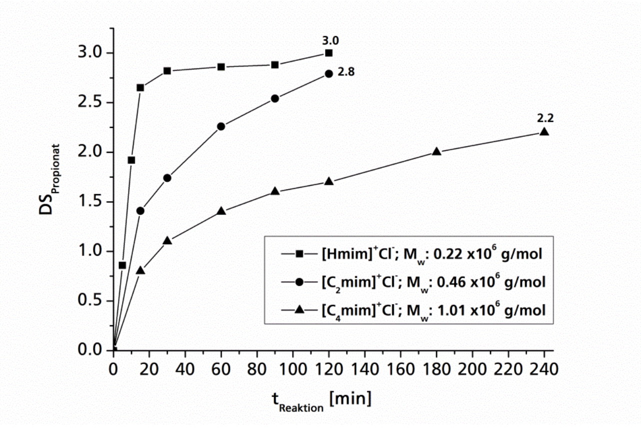


Figure 10: Esterification rate and average molecular weights for starch propionates synthesized with 4.5 moleq of propionic acid anhydride per AGU, 0.33 moleq of different ionic liquids per AGU, and $T_{reaction}$ = 130 °C

### *Using different ILs for the esterification of starch*

We investigated the influence of different ionic liquids on the acetylation of starch and its molecular degradation. The applied ionic liquids differed in the length of the alkyl side chain, as well as in the type of the counterion (Table 7).

The DS value decreases slightly when the chain length of the imidazolium-based ionic liquids with chloride as counterion increases, and it decreases considerably when $[C_6mim]^+Cl^-$ is used. Swatloski *et al*. described how the solution power of 1-N-alkyl-3-methylimidazolium chlorides for biopolymers decreases with increasing chain length caused by the reduction ineffective chloride concentration.[85]

The partial solubilization or swelling of starch might be the lowest for $[C_6mim]^+Cl^-$ and less for $[C_4mim]^+Cl^-$ than for $[C_2mim]^+Cl^-$ and $[Hmim]^+Cl^-$. Halogenides as counterions for the positively charged imidazolium ring lead to highly-substituted starch acetates. Furthermore, the question of how the different ionic liquids influence the speed of the esterification of starch was investigated by preparing starch propionate with $[Hmim]^+Cl^-$, $[C_2mim]^+Cl^-$ and $[C_4mim]^+Cl^-$ respectively and comparing these (Figure 10). Using $[C_4mim]^+Cl^-$ as a catalyst for the esterification of starch along with propionic anhydride, a $DS_{Propionate}$ of 2.2 is reached after 4 h. Using $[Hmim]^+Cl^-$ instead of $[C_4mim]^+Cl^-$ results in a degree of substitution of 2.6 after 0.25 h, and after 2 h the hydroxyl groups of starch are completely esterified.

Furthermore, a nearly fully substituted starch propionate can be isolated after 2 h when $[C_2mim]^+Cl^-$ is used. The much faster reaction time for $[Hmim]^+Cl^-$, compared to the other two ionic liquids, maybe due to the additional acidic character of $[Hmim]^+Cl^-$, which can also be seen in the values of the molar mass averages.

Finally, it can be said that for the first time ionic liquid in low amounts can catalyze esterification reactions of starch to produce starch acetate and propionate. Therefore, the requirements that the catalyst be recyclable, decrease activating energy and be used in small amounts are fulfilled. Products from esterification with a degree of substitution ~2.5 exhibit a low average molecular weight. A relationship between the type of ionic liquid used as a catalyst for esterification and properties like degree of substitution and average molar mass of starch esters could be shown.

### *Synthesis of thermoplastic starch mixed esters catalyzed by* **in situ** *generation of imidazolium salts*

With the results shown so far, it is possible to produce starch esters by using ionic liquids just in small amounts. The resulting starch esters (starch acetate or propionate) presented only poor mechanical properties. Anyway, starch acetate stands out because of its extreme brittleness regardless of how it is prepared.[86]

This may be the main reason why it is not used in industrial applications. Longer chain substituents can be used in order to avoid brittleness in the starch acetate. An increase in the alkyl chain length of the ester substituents results in an increase in the elongation at break in the specimens, but also in a major loss of stiffness.[87]

The synthesis of mixed esters is one way of trying to keep the stiffness, while increasing the elongation at break, which is prevalent in literature.

This work describes the new synthesis of novel thermoplastic starch mixed esters. In this process, the ionic liquid in the form of imidazolium salts is generated during the reaction in low amounts and catalyzes this esterification.[88] After plastification of these derivatives with triacetin (TA; glycerol triacetate), they were processed in an extruder followed by injection molding to produce specimens. Their tensile strength, E-modulus and elongation at break were determined in an initial characterization of their mechanical properties.

Different esterification agents have to be used to produce mixed esters. When using two types of carboxylic acid anhydrides, the declining carbonyl activity with increasing chain length causes several problems. This is because the carboxylic acid anhydride with the shorter chain length will always produce the highest degree of substitution. An answer to this might be to work with different classes of esterification agents, like carboxylic acid anhydrides and carboxylic acid chlorides. For example, propionic chloride exhibits a higher carbonyl activity caused by the electron withdrawing effect of the chloride, in comparison with acetic acid anhydride. Here the problem for starch chemistry is the by-product hydrochloric acid, which causes a strong degradation of starch by breaking the α-1,4 linkages of the anhydroglucose unit. Because of this, an acid scavenger has to be used. Possible acid scavengers are imidazole derivatives, which produce the corresponding chloride salt by reacting with hydrochloric acid.

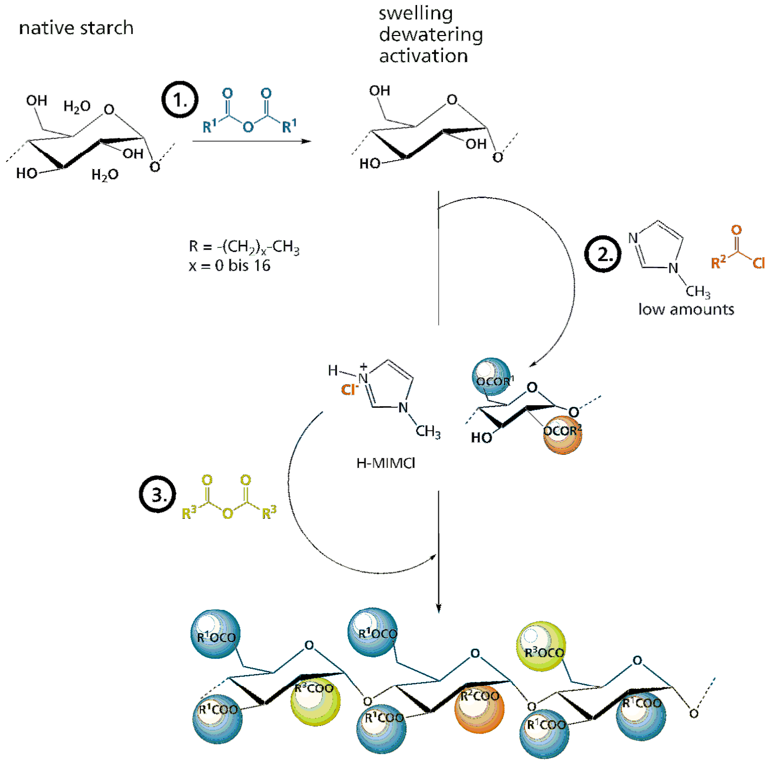
These organic salts can be classified as imidazolium salts or ionic liquids and have a catalyzing effect on the esterification of starch, as shown before.

***Preparation of a trifunctional starch mixed ester***

Using the new reaction type (Scheme 6), it is easy to create a trifunctional starch mixed ester, which contains three different ester groups and is fully substituted.

So far, this paper has described the use of one kind of carboxylic acid anhydride. The fact that the carboxylic acid anhydride is added in two portions allows different carboxylic acid anhydrides to be used. Through this, the current problem of the carbonyl activity can be avoided. A detailed analysis of the preparation of starch acetate propionate laurates clearly proved that the carboxylic acid anhydride, which is added to the reaction mixture from the beginning, always esterifies the starch by converting nearly 100% of the corresponding carboxylic acid anhydride. This allows $DS_{Propionate}>DS_{Acetate}$ to be achieved even when the same molar amounts of each acid anhydride are used.

Many starch mixed esters with different substitution patterns within the AGU can be synthesized using the described synthesis method (Table 8). An analysis of the influence of the different ester groups, as well as their amount, on the glass transition temperature was performed on starch mixed esters. With an increasing amount of bulkiness substituents, the glass transition temperature decreases.



Scheme 6: Schematic reaction mechanism for the synthesis of trifunctional starch mixed esters

Table 8

DS values of trifunctional starch mixed esters from high amylose starch, used acid chloride and resulting glass transition temperatures; DS values were determined by $^{13}C$ NMR spectroscopy

| Derivative | Acid chloride | ΣDS | $DS_{1st\ ester}$ | $DS_{2nd\ ester}$ | $DS_{3rd\ ester}$ | $T_g$(°C) |
|---|---|---|---|---|---|---|
| StAcProp | propionyl | 2.96 | 2.06 | 0.90 | / | 146.8 |
| StAcPropHex | hexanoyl | 2.98 | 2.26 | 0.63 | 0.11 | 134.3 |
| StAcPropLau | lauroyl | 3.0 | 2.28 | 0.62 | 0.10 | 127.5 |
| StAcPropPalm | palmitoyl | 3.0 | 2.24 | 0.69 | 0.07 | 142.1 |
| StAcPropStea | stearoyl | 3.0 | 2.03 | 0.93 | 0.04 | 141.6 |
| StAciBuLau | lauroyl | 3.0 | 2.35 | 0.53 | 0.12 | 129.2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| StPropAcLau | lauroyl | 3.0 | 2.32 | 0.55 | 0.13 | 99.2 |
| StPropiBuLau | lauroyl | 3.0 | 2.34 | 0.46 | 0.20 | 96.9 |
| StPropBuLau | lauroyl | 3.0 | 2.05 | 0.82 | 0.13 | 95.2 |
| StPropHexLau | lauroyl | 3.0 | 2.20 | 0.65 | 0.15 | 83.5 |

***Mechanical properties of samples from trifunctional starch mixed esters***

By the described synthesis method for the production of trifunctional starch mixed esters different starch acetate-based mixed esters, which are not brittle can be achieved. The alkyl chain of propionate, as well as hexanoate as third ester groups seems to be too short to avoid the brittleness of the plasticized specimens. As soon as laurate and longer alkyl chain acid chlorides are used for the third ester group, materials with an increased stiffness are possible without being brittle (Figure 11).

Even if the degree of substitution of the long chain third ester group (StAcPropLau, StAcPropPalm, StAcPropStea) decreases slightly with an increasing chain length (see Table 8), the values for the elongation at break nearly remain unchanged. The increased chain length levels the decreased degree of substitution regarding the behavior of elongation at break.

The effect of the second ester group on the mechanical properties was investigated by starch propionate-based mixed esters. The higher content of propionate groups for StPropAcLau (Figure 11) in comparison with StAcPropLau (Figure 12) leads to a loss of strength and stiffness, but to an increase of the flexibility of this material.

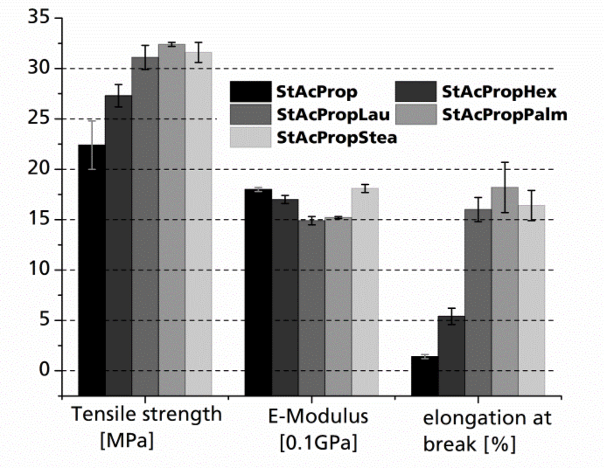


Figure 11: Mechanical properties of trifunctional starch acetate-based mixed esters plasticized with 10 wt% triacetin

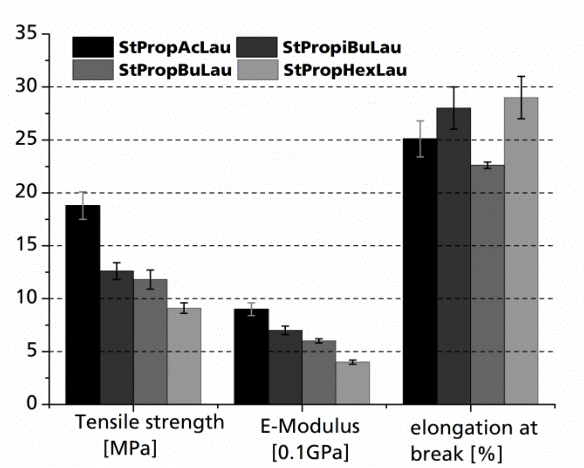


Figure 12: Mechanical properties of trifunctional starch propionate-based mixed esters plasticized with 10 wt% triacetin

The increase of the chain length of the second ester group leads in general, as it was suspected, to higher values for the elongation at break, but therewith to decreased values for tensile strength, as well as E-modulus. A detailed consideration of the mechanical properties for StPropiBuLau and StPropBuLau shows a difference for the achieved values of the behavior for elongation at break. The higher sterical demand of the iso-butyrate substituent might be the reason of this effect, because the expansion of the chain segments is higher than for butyrate as second ester. This behavior can also be found for hexanoate as second ester. The specimens from StPropiBuLau and StPropHexLau are characterized by a good flexibility. Besides these properties, the low water uptake (less than 0.5 wt%) is noteworthy.

Summarizing, it can be said that starch mixed esters, carrying up to three different ester groups, were prepared by a new synthesis method. This type of reaction is catalyzed by imidazolium salts, which are formed during the reaction in low amounts. The resulting materials show very good mechanical properties, which are unique to until now known starch-based materials.

## CONCLUSION

The described examples of derivatization and processing of cellulose and starch are only a small choice of all the projects worked on. All the obtained results were developed and funded in cooperation with a range of industry partners, as well as by public funding. The research included chemical modification, as well as shaping of cellulose to reach properties for certain applications, such as man-made cellulose fibers, encapsulation materials, thickening agents, and starch-based thermoplastic materials.

The future research and development in the field of polysaccharide chemistry will focus on the demand of increasing usage of renewable resources for chemical and technical sustainable applications.

## REFERENCES

[1] H. A. Krässig, "Cellulose – Structure, Accesibility and Reactivity", Gordon and Breach Science Publishers, Yverdon, 1993.

[2] B. Philipp, D. Paul, Achtzig Jahre Polymer kolloid forschung in Teltow-Seehof, Verlag Reinhard Knof, Nehmten, 2001.

[3] M. Voges, M. Brück, H.-P. Fink, J. Gensrich, *Procs. The Akzo-Nobel Cellulosic Man-made Fibre Seminar*, Stennungsund, 2000.

[4] H. Firgo, M. Eibl, D. Eichinger, *Lenzinger Ber.*, **75**, 47 (1995).

[5] F. Loth, H.-P. Fink, P. Weigel, German patent DE 10223172 (2004).

[6] F. Loth, H. Lang, H. Schleicher, German patent DE 19940393 (2001).

[7] F. Loth, E. Schaaf, P. Weigel, H.-P. Fink, J. Gensrich, German patent DE 10223171 (2003).

[8] F. Loth, E. Schaaf, H.-P. Fink, J. Kunze, J. Gensrich, German patent DE 10253672 (2004).

[9] F. Loth, German patent DE 10162791 (2002).

[10] J. Gensrich, H.-P. Fink, J. Kunze, E. Schaaf, *Procs. Zellcheming-Konferenz*, Baden-Baden, June 24-27 (2002), CD (Papier 2003,5) [Chem. Abstr., 139, 215686 (2003)].

[11] J. Kunze, H.-P. Fink, *Macromol. Symp.*, **223**, 175 (2005).

[12] F. Loth, H. Lang, German patent DE 19928333 (2000).

[13] J. Gensrich, H.-P. Fink, G. Weidel, German patent DE 102004023410 (2005).

[14] H. Thielking, M. Schmidt, "Ullmann'sEncyclopedia of Industrial Chemistry: Cellulose Ethers" (online publication date), 2006.

[15] H.-P. Fink, E.Walenta, J.Kunze, G.Mann in "Cellulose and Cellulose Derivatives: Physico-chemical Aspects and Industrial Applications", edited by J. F. Kennedy, G. O. Phillips, P. A. Williams and L. Piculeu, Woodhead, Abington, Cambridge, 1995, p. 523.

[16] G. Mann, J. Kunze, F. Loth, H.-P. Fink, *Polymer*, **39/14**, 3155(1998).

[17] S. Fischer, W.Wagenknecht, B. Volkert, *229th ACS National Meeting*, San Diego, Abstracts of papers CELL 173(2005).

[18] B. Philipp, B. Lukanoff, H. Schleicher, W. Wagenknecht, *Z. Chem.*, **26**, 50(1986).

[19] T. Heinze, T. Liebert, *Prog. Polym. Sci.*, **26**, 1689 (2001).

[20] D. H. Powers, L. H. Bock, A. L. Houk, US Patent, US 2,087,549 (1937).

[21] Q. Zhou, L. Zhang, M. Li, X. Wu, G. Cheng, *Polym. Bull.*,**53**, 243(2005).

[22] J. Burger, G. Kettenbach, P. Klüfers, *Macromol. Symp.*, **99**, 113(1995).

[23] A. Isogai, A. Ishizu, J. Nakano, *J. Appl. Polym.Sci.*, **31**, 341(1986).

[24] M. D. Nicholson, US Patent, US 4,034,335(1977).

[25] C. L. McCormick, D. K.Lichatowich, *J. Polym.Sci. Lett. Ed.*, **17**, 479 (1979).

[26] A.Takaragi, M. Minoda, T. Miyamoto, H. Q. Liu, L. N. Zhang, *Cellulose*,**6**, 93(1999).

[27] M. Diamantoglou, H. Kuhne, *Papier*, **42**, 690(1988).

[28] S. Fischer, *Lenzinger Berichte*, **83**, 71(2004).

[29] R. P. Swatloski, S. K. Spear, J. D. Holbrey, R. D. Rogers, *J. Am. Chem. Soc.*, **124**, 4974 (2002).

[30] G. Laus, G. Bentivoglio, H. Schottenberger, V. Kahlenberg, H. Kopacka *et al.*, *Lenzinger Berichte*, **84**, 71(2005).

[31] H.-P. Fink, P. Weigel, H. J. Purz, J. Ganster, *Prog. Polym. Sci.*, **26**, 1473(2001).

[32] B. Volkert, W. Wagenknecht, *Macromol. Symp.*, **262**, 97(2008).

[33] B.Volkert, W.Wagenknecht, M. Mai, in "Cellulose Solvents: For Analysis, Shaping and Chemical Modification", edited by T. Liebert, ACS Symposium Series, American Chemical Society, Washington, DC, 2010, Chapter 18, p. 319.

[34] E.-H. Klohr, J. Neubauer, W. Koch, K. Szablikowski, D. Redeker*et al.*, German patent DE 19730090(1999).

[35] B. Philipp,W. Wagenknecht, M. Wagenknecht, I. Nehls, D. Klemm*et al.*, *Das Papier*, **49**, 3(1995).

[36] B. Philipp,W. Wagenknecht, M. Wagenknecht, I. Nehls, D. Klemm*et al.*, *Das Papier*, **49**, 58(1995).

[37] B. Philipp,W. Wagenknecht, M. Wagenknecht, I. Nehls, D. Klemm*et al.*, *Das Papier*, **49**,102 (1995).

[38] B. Philipp, W. Wagenknecht, I. Nehls, D. Klemm, A. Stein*et al.*, *Polymer News*, **21**, 155 (1996).

[39] D. Klemm, Th. Heinze, B. Philipp, W. Wagenknecht, *Acta Polym.*, **48**, 277(1997).

[40] W. Wagenknecht, *Das Papier*, **50**, 712(1996).

[41] T. Groth, W. Wagenknecht, *Biomaterials*, **22**, 2719 (2001).

[42] a) H. Thielking *et al.*, German patent DE19837673 (1998); b) H. Dautzenberg*et al.*, German patent DE 4021050 (1992);c) W. Wagenknecht, H.-H.Schwarz, German patent DE 4435180 (1996);d) S. Fischer*et al.*, German patent DE 102005011367 (2006).

[43] D. Klemm, B. Philipp, Th. Heinze, U. Heinze, W. Wagenknecht, “Comprehensive Cellulose Chemistry”, Wiley VCH, 1998, p.115ff.

[44] R. G. Schweiger, *Carbohyd. Res.*, **21**, 219(1972).

[45] H. Dautzenberg,U. Schuldt, D. Lerche, H. Woehlecke, R. Ehwald, *J. Membr.Sci.*, **162**, 165 (1999).

[46] I. Capilla, R. J. Linhardt, *Angew. Chem. Int. Ed.*, **41**, 391 (2002).

[47] U. Hacker, K. Nybakken, N. Perrimon, *Nat. Rev. Mol. Cell. Biol.*, **6**, 530(2005).

[48] M. Kunou, M. Koizumi, K. Shimizu, M. Kawase, K. Hatanaka, *Biomacromolecules*, **1**, 451 (2000).

[49] Z. Wang, L. Li, K. Xiao, J. Wu, *Bioresource Technol.*, **100**, 1687 (2009).

[50] H. Bracannot, *Ann. Chim. Phys.*, **12**, 185 (1819).

[51] B. Philipp, W. Wagenknecht, *Cellulose Chem. Technol.*, **17**, 443(1983).

[52] B. Lukanoff, H. Dautzenberg, *Papier*,**48**, 287(1994).

[53] W. Wagenknecht, I. Nehls, J. Kötz, J. Ludwig, *Cellulose Chem. Technol.*, **25**, 343 (1991).

[54] W. Wagenknecht, I. Nehls, B. Philipp, *Carbohyd. Res.*, **240**, 245(1993).

[55] R. G. Schweiger, *Tappi J.*, **57**, 86(1974).

[56] W. Wagenknecht, I. Nehls, A. Stein, D. Klemm, B. Philipp, *Acta Polym.*, **43**, 266(1992).

[57] A. Richter, D. Klemm, *Cellulose*, **10**, 133(2003).

[58] K. Hettrich, W. Wagenknecht, B. Volkert, S. Fischer, *Macromol. Symp.*, **262**, 162(2002).

[59] M. Gericke, T. Liebert, T. Heinze, *Macromol. Biosci.*, **9**, 303 (2009).

[60] G. Chauvelon, A. Buleon, J.-F.Thibault, L. Saulnier, *Carbohyd. Res.*, **338**, 743 (2003).

[61] M. Thomas, G. Chauvelon, M. Lahaye, L. Saulnier, *Carbohyd. Res.*, **338**, 761 (2003).

[62] I. Nehls, W. Wagenknecht, B. Philipp, B. Stscherbina, *Prog. Polym. Sci.*, **19**, 29 (1994).

[63] R. H. Atalla, *J. Appl. Polym. Sci.*, **37**, 295 (1983).

[64] K. Schenzel, S. Fischer, *Cellulose*, **8**, 49 (2001).

[65] B. Salmons, E. M. Brandtner, K. Hettrich, W. Wagenknecht, B. Volkert *et al.*, *Curr. Opin. Mol. Ther.*, **12**, 450 (2010).

[66] M. Löhr, P. Müller, P. Karle, J. Stange, S. Mitzner *et al.*, *Gene Ther.*, **5**, 1070 (1998).

[67] R. M. A. Hernández, G. Orive, A. Murua, J. L. Pedraz, *Adv. Drug Deliv. Rev.*, **62**, 711 (2010).

[68] B. Salmons, O. Hauser, W. H. Günzburg, W. Tabotta, in “The Bioartificial Pancreas and Other Biohybrid Therapies”, edited by P.Hallé, P. de Vos, L.Rosenberg, Research Signpost Publishing, 2009, p. 595.

[69] F. Lim, A. M. Sun, *Science*, **210**, 908(1980).

[70] G. Orive, R. M. Hernández, A. R. Gascón, R. Calafiore, T. M. S. Chang*et al.*, *Nat. Med.*, **9**, 104(2003).

[71] S. Sakai, I. Hashimoto, S. Tanaka, B. Salmons, K. Kawakami, *Cell. Transplant*, **18**, 933 (2009).

[72] B. Salmons, O. Hauser, W. H. Günzburg, W. Tabotta, *Bioprocess. J.*, **4**, 36 (2007).

[73] M. Löhr, J. C. Kröger, A. Hoffmeyer, M. Freund, J. Hain *et al.*, *Cancer Ther.*, **1**, 121 (2003).

[74] K. Nachtkamp, Ch. Krueger, J. Engelhardt, V. Kriegisch, S. Fischer*et al.*, European patent, EP 000002022801 (2009).

[75] K. Nachtkamp,Ch. Krueger, J. Engelhardt, S. Fischer, M. Pinnow*et al.*, European patent, EP 000002022802(2009).

[76] B. Volkert, F. Loth, W. Lazik, J. Engelhardt, *Starch/Stärke*, **56**, 307(2004).

[77] R. Kortemeyer, Untersuchungen zur Herstellung, Charakterisierung und Verwendung kationischer Stärken, Diploma thesis, Universität-Gesamthochschule Paderborn(1995).

[78] A. Richter, W. Wagenknecht, *Carbohyd. Res.*, **338**, 1397 (2003).

[79] U. Hiroschi, M. Chenghuan, K. Yoshiharu, *Macromol. Mater.Eng.*, **288**, 562 (2003).

[80] K. Balser, L. Hoppe, T. Eicher, M. Wandel, H.-J. Astheimer *et al.*, in “Ullmann’s Encyclopedia of Industrial Chemistry”, Wiley-VCH VerlagGmbH& Co.KGaA, Weinheim, 2005, p. 22.

[81] E. Walenta, H.-P. Fink, P. Weigel, J. Ganster, E. Schaaf, *Macromol. Mater. Eng.*, **286**, 462 (2001).

[82] X. Qiao, W. Jiang, K. Sun, *Starch/Staerke*, **57**, 581(2005).

[83] R. Shogren, *Carbohyd. Polym.*, **19**, 83 (1992).

[84] A. Lehmann, B. Volkert, *J. Appl. Polym.Sci.*, **114**, 369 (2009).

[85] R. P. Swatloski, S. K. Spear, J. D. Holbrey, R. D. Rogers, *J. Am. Chem. Soc.*, **124**, 4974 (2002).

[86] B. Volkert, A. Lehmann, T. Greco, M. Hassan Nejad, *Carbohyd. Polym.*, **79**, 571 (2010).

[87] C. Fringant, M. Rinaudo, M. F. Foray, M. Bardet, *Carbohyd. Polym.*, **35**, 97(1998).

[88] A. Lehmann, B. Volkert, M. Hassan Nejad, T. Greco, H.-P. Fink, *Green Chem.*, **12**, 593 (2010).