Synthesis and Applications of Cellulose Sulfates

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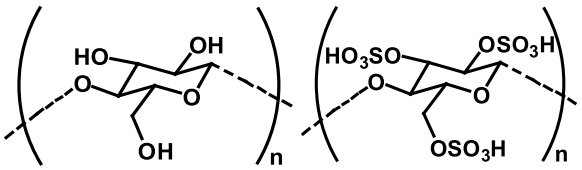
Cellulose is the most naturally abundant renewable polymer with the formula $(C_6H_{10}O_5)_n$, n ranging from 10,000 to 15,000. The monomer of cellulose biopolymer is anhydroglucose unit (AGU) and it has three hydroxyl groups (Figure 1(a)). These –OH groups form network of hydrogen bonds between individual cellulose polymer molecules and convert them into complex structures. Therefore, cellulose becomes less soluble in common organic and inorganic solvents. Cellulose can be used as a green source to develop biodegradable and biocompatible materials with attractive properties by chemical modifications or mixing with other components. Cellulose sulfate is such a modified material which is an inorganic ester of cellulose. Sulfation of cellulose replaces the hydrogen atoms of the primary and secondary hydroxyl groups of cellulose monomer (β-D-glucopyranosyl units) by $–SO_3H$ groups (Figure 1.(b)).



(a) (b)

Figure 1. Structure of (a) Cellulose and (b) Cellulose Sulfate

The level of substitution is generally expressed in terms of degree of substitution (DS) and it can have a value between 0 and 3. Cellulose sulfate polymer molecule is a combination of tri-, di-, mono- and un-substituted monomers. Unlike cellulose, sulfated cellulose derivatives are much more soluble in water and the solubitily depends on the DS, the number of unreacted free hydroxyls and the degree of polymerization of the cellulose backbone.

There are many sulfation agents such as sulfuric acid, sulfur trioxide-pyridine, sulfur trioxide-dimethylformamide and chlorosulfonic acid-pyridine-formamide which can be used for sulfation. Though both SO_3 and chlorosulfionic acid are powerful sulfation agents, the major drawback of these reagents is the moisture sensitivity. Therefore, both reagents strongly react with water. In order to reduce risk during the synthesis, chlorosulfonic acid and SO_3 are used with organic bases such as triethylamine (TEA), pyridine (Py) or aprotic dipolar solvents such as dimethylformamide (DMF). Further, SO_3-DMF and SO_3-Py complexes are commercially available as white solids.

Most of the previous syntheses of cellulose sulfates have been carried out in either heterogeneous or homogeneous systems. Heterogeneous system starts with activated cellulose suspension and a major problem is the unequal approachability between the -OH groups in the amorphous regions and those in the crystalline regions. Bhatt & Gupta prepared cellulose sulfate from α-Cellulose isolated from *Lantana camara* by sulfation in a heterogeneous medium (Figure 2). According to the article an azeotrope of 19.8 – 34.2 N Sulfuric acid and 33 % 1-butanol containing 1.65 % ammonium sulfate (20 - 60 mL) was added slowly to cellulose powder (1 g) and stirred at -10 ^{0}C to 10 ^{0}C for 30 – 120 minutes to form viscous solution. Then that solution was poured in to 3 volumes of acetone to precipitate cellulose sulfuric acid ester. Next it was neutralized with 5% NaOH solution at 0 ^{0}C, precipitated, washed with acetone and dried to collect sodium cellulose sulfate ester. The optimized conditions to obtain cellulose sulfate ester with a DS of 0.392 were identified as 60 min reaction time at 0 ^{0}C aqueous sulfuric acid with the normality of 34.2 N.

$$H_2SO_4 + H_2O \longrightarrow HSO_4^- + H_3O^+ \quad (1)$$

$$(C_6H_7O_2)_x\,(OH)_{3x} \xrightarrow{HSO_4^-} (C_6H_7O_2)_x\,(OH)_{3x-a}\,(OSO_3H)_a$$

Cellulose Cellulose sulfate (2)

$$(C_6H_7O_2)_x\,(OH)_{3x-a}\,(OSO_3H)_a \xrightarrow{NaOH} (C_6H_7O_2)_x\,(OH)_{3x-a}\,(OSO_3^-Na^+)_a \quad (3)$$

Figure 2. Synthesis of sodium cellulose sulfate

In contrast, homogeneous system starts with partially substituted cellulose derivatives in an aqueous solution. In the homogeneous system, although the -OH groups are more accessible for reaction, the DS of product is often low because some -OH groups have already been substituted by other groups. The sulfation of un-substituted cellulose in a homogenous system with prior cellulose dissolution may overcome the drawbacks of both approaches. Currently ionic liquids (IL) are used for dissolution process, and 1-ethyl-3-methyl imidazolium acetate [EmimAc], 1-allyl-3-methylimidazolium chloride ([Amim]Cl and 1-butyl-3-methylimidazolium chloride ([C_4mim]Cl are common ILs reported in literature. Wang & Li have reported the homogenous sulfation of bagasse cellulose in an ionic liquid, in this research bagasse cellulose has been dissolved in an ionic liquid, 1-butyl-3-methylimidazolium ([C_4mim]Cl and then sulfated by using chlorosulfonic acid – dimethylformamide. The sulfated bagasse cellulose product had DS between 0.52 – 2.95 and possesed significant anticoagulation activity.

Cellulose sulfate derivatives have important chem-

ical and physical properties such as solubility in water, high viscosity, outstanding compatibility with metal ions, enzyme resistance, shear resistance, temperature stability, suspension stability, film formation ability, protein reactivity, solvent tolerance *etc*. These properties will vary on the DS of cellulose sulfate and on the degree of polymerization (DP). Cellulose sulfates are used as a thickener in tertiary oil recovery, water-based paint, printing pastes in textiles, photographic applications and food industry. High viscosity, solubility, suspension stability and tolerance to organic solvents are desirable properties of sulfated cellulose which are useful in cosmetics. The formulations of toothpaste, hair conditioner and shampoo contain cellulose sulfate to control appearance, viscosity, flow characteristics and shelf life. In textile industry, it becomes not only a thickener but also a dye anti-migration agent in back-coatings. Moreover, cellulose sulfates are used in slurry explosives due to high viscosity and gel formation ability by crosslinks.

In addition, there are cellulose sulfate analogues with a range of bioactivities such as antiviral, antibacterial, anti-adhesive and anticoagulation. Heparin is a highly-sulfated glycosaminoglycan which is effectively used as an anticoagulant in medicine. According to a recent study carried out by the Research Institute of Chemical Engineering in China, the anticoagulation activity of sodium bagasse cellulose sulfate has a positive correlation with DS and some of the activity indexes exceed those of heparin.

Moreover, cellulose sulfate is used in biomedical applications for encapsulation of cells. The capsules have been prepared by precipitation technique using physiological sodium chloride solution (0.9 w/w). The cellulose sulfate was dissolved in NaCl solution and dropped into a cationic poly(diallyl dimethyl ammonium chloride) solution to form capsules. These encapsulated cells have been proposed to use in the Gene therapy to treat cancer. The therapy uses "suicide genes" encoding enzymes in donor cells which convert inactive pro-drugs into tumor-toxic metabolites.

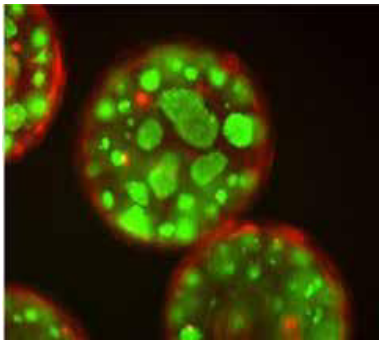


Figure 3. Fluorescence microscopic image of cells in sodium cellulose sulfate and poly(diallyl dimethyl ammonium chloride) microcapsules

According to the literature there is a wide range of applications of cellulose sulfates in different fields. If cellulose sulfate can be synthesised from agricultural and industrial wastes such as banana plant stems, pineapple leaves and cotton wastes in Sri Lanka, it can support our economy in future.

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