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Synthetic polymers functionalized by carbohydrates: a review

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Abstract

Polymers based on carbohydrates have re-emerged as exciting topics of polymer research, due to a worldwide focus on sustainable materials. However, multi-step synthesis of these polymers have made their use as commodity plastics uneconomical, and currently their applications are restricted to biomedical fields. Functionalization of polymers has emerged as another important area of polymer science and technology. Chemically linking sugar moeities onto synthetic polymers is a unique method of functionalization of synthetic polymers, whereby not only is the polymer functionalized, but it can also get other desirable properties such as biodegradability—a property much debated and researched in modern times. This paper reviews several methods of anchoring carbohydrates onto polymers and the advantages and the disadvantages associated with each method, their current and potential applications, and their characterization methods.

Keywords: Polymers; Carbohydrates; Monosaccharides

1. Introduction

There has been a worldwide realization that nature-derived monosaccharides, disaccharides, oligosaccharides and polysaccharides can provide us the raw materials needed for the production of numerous industrial consumer goods (Kunz, 1993; Pacitti, 2003; Varma, 2003). While functionalization of polymers (especially polyolefins) is a particularly attractive area of polymer research today (Chung, 2002), using sugar functionalized petrochemical polymers such as polystyrene for use as biodegradable polymers is a newly discovered application of a sugar-linked synthetic polymer (Galgali, Puntambekar, Gokhale, & Varma, 2004; Galgali, Varma, Gokhale, Puntambekar, & Khire, 2002). The class of sugar based polymers, generally known as poly(vinylsaccharide)s, have also been investigated in some detail for a variety of applications, particularly in the biomedical field (Caneiro, Fernandes, Figneiredo, Fortes, & Freitas, 2001; Fraser & Grubbs, 1995; Kallin, Lonn, & Norberg, 1989; Kobayashi, Sumitomo, & Ina, 1985; Nishimura et al, 1991; Nishimura, Matsuoka, & Kurita, 1990).

Structurally, the poly(vinylsaccharide)s have a synthetic C–C backbone with pendant carbohydrate molecules, whereas modified polysaccharides have a carbohydrate backbone with synthetic molecules attached as pendants. Since sugars are a good source of food for micro-organisms, many poly(vinylsaccharide)s have the potential to be utilized as biodegradable polymers. There are four general methods of preparing synthetic polysaccharides: polymerization of vinyl sugars (polyvinylsaccharide)s, polymerization of anhydro-sugars (polyanhydrosugar)s, enzyme-mediated synthesis of carbohydrate polymers, and grafting of sugars onto functionalized synthetic polymers by polymer analogous reactions. In few cases, olefin metathesis reactions have also been employed for synthesis of poly(vinylsaccharide)s.

Poly(vinylsaccharide)s are most commonly synthesized by either homopolymerization of the vinyl sugars or by copolymerization of the vinyl sugar with other polymerizable vinyl monomers. Anhydro sugars have been polymerized cationically by ring-opening polymerization to obtain stereoregular synthetic polysaccharides. This strategy has been extended to the synthesis of synthetic polymers with pendant sugars by graft copolymerization of anhydro sugars

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onto halogenated polymers. Enzymatic reactions have been used to synthesize linear polymers with sugar as part of the main chain (Patil, Rethwisch, & Dordick, 1991). Enzymatic reactions are very specific and do not involve any protection and deprotection of the sugar hydroxyls, but are extremely slow (Martin, Ampofo, Linhardt, & Dordick, 1992). Hence chemo-enzymatic methods, or in other words, enzyme mediated polymerizations, have been used to synthesize poly(vinylsaccharide)s and were found to be better alternatives, wherein the polymerizable vinyl saccharides were synthesized enzymatically and the polymerizations had been carried out by conventional chemical methods. Another method of obtaining polymers of carbohydrates is by grafting saccharides onto synthetic polymers.

The advantages and limitations of all the above mentioned four methods of synthesis of carbohydrate polymers will be discussed in this paper, along with the applications (current and potential) of the polymers so synthesized.

2. History of carbohydrate based polymers

The synthesis of the poly(vinylsaccharide)s dates back to as early as the 1930s. Reppe (1930) was the first person to synthesize vinyl saccharide monomers. He synthesized vinyl ethers from glucose and fructose by alkali catalyzed addition of protected sugars to acetylene. He synthesized two vinyl saccharide monomers viz. 1-*O*-vinyl1,2:5, 6-disopropylidene fructopyranose and 3-*O*-vinyl1,2:5, 6-diisopropylidene glucofuranose which he later polymerized (Reppe & Hecht, 1936) to obtain insoluble polymers.

In the 1940s, Yanovsky worked on the synthesis of poly(vinylsaccharide)s (Nichols & Yanovsky, 1944, 1945; Treadway, 1945). However, he was successful in getting only crosslinked polymers since the polymerization involved glucose pentamethacrylate and glucose allyl ether monomers. Haworth, Gregory, and Wiggins (1946) polymerized substituted carbohydrates, containing two acrylate or methacrylate groups to obtain hard products, which were also crosslinked. The reactions were carried out in absence of a catalyst. Helferich and Hofmann (1952) and Helferich and Jung (1958) were successful in synthesizing water soluble poly(vinylsaccharide)s viz poly(*p*-hydroxystyrene-α-D-galactoside) and poly(*p*-hydroxy β-D-glucoside). They studied the adsorption of three enzymes viz. β-D-glucosidase, α-D-galactosidase and β-D-galactosidase, all of which are present in sweet almonds, on these polymers. (Wolfrom, Swan, Ennor, & Chaney, 1959) reported the polymerization of 3-methacryloyl-D-mannitol pentanitrate into a hard solid. Until the 1950s more stress was laid on synthesizing monomer derivatives and checking their polymerizability rather than obtaining polymers with properties for specific applications.

The synthesis of a linear vinyl saccharide polymer was seldom reported until 1960. The fist high molecular weight

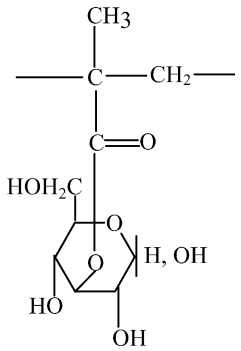

Fig. 1. Poly(methacryloyl D-glucose).

poly(vinylsaccharide) which was also soluble in water was poly(methacryloyl glucose), which was first reported by Bird, Black, Dewar, and Rutherford (1960). Poly(methacryloyl glucose) has been synthesized as both a homopolymer (Black, Dewar, & Rutherford 1963; Imoto & Kimura, 1962; Kimura & Hirai, 1962) and as a copolymer (Kimura & Imoto, 1961). In the1960s two groups Bird et al. (1960) and Kimura and Imoto (1961) were simultaneously working along similar lines to synthesize poly(methacryloyl glucose) (Fig. 1).

They polymerized 1,2:5,6 di-*O*-isopropylidene-D-glucofuranose methyl methacrylate by free radical polymerization to obtain poly(3-*O*-methacryloyl 1,2:5,6 di-*O*-isopropylidene-D-glucofuranose) (Fig. 2).

Removal of the isopropylidene groups afforded poly(methacryoyl glucose). These polymers could be dyed by a water-soluble dyestuff. 1-acrylamido and 1methacryl amido-1-deoxy-D-glucitol were synthesized and polymerized to obtain a new type of vinyl polymer with pendant sugar residues (Panzer & Whistler, 1959). Poly(*N*-acryloyl-D-glucamine) which was synthesized in 1961 (Whistler, Panzer, & Roberts, 1961) displayed a high tolerance for electrolyte. In the early 1960s 6-*O*-vinyl ether of 1,2:3,4 di-*O*-isopropylidene-D-galactopyranose (Fig. 3) (Black et al., 1963; Whistler, Panzer, & Goatley, 1962) and the corresponding 6-*O*-vinyl ether of 1,2:5,6 di-*O*-isopropylidene glucofuranose (Black, Dewar, & Rutherford, 1962) have been reported which were polymerized by cationic polymerization.

However, no special attention was paid to the characterization of the resulting polymers and solution properties of

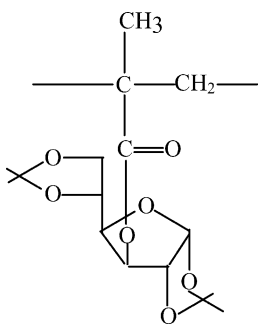

Fig. 2. Poly(3-*O*-methacryloyl 1,2:5,6-diisopropylidene D-glucofuranose).

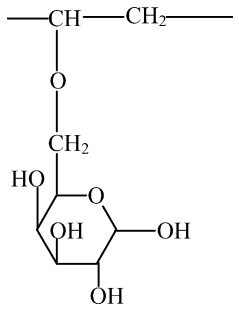

Fig. 3. Poly(6-*O*-vinyl 1,2: 3,4-di-*O*-isopropylidene D-galactopyranose.

the deprotected water-soluble products until 1986. Klein (1986) prepared poly(6-*O*-vinyl-1,2:3,4-di-*O*-isopropylidene-D-galactopylanose) by cationic polymerization and characterized it by ^{13}C-NMR. He also studied the solution viscosities of the polymers formed after the deprotection of the isopropylidene groups viz. poly(6-*O*-vinyl-D-galactopyranose).

Polymers having molecular weights upto 100,000 were successfully synthesized in 1963 (Black et al., 1963). Klein (1982) obtained molecular weights upto 715,000 by solution polymerization. The same group of workers (Klein, Herzog, & Hajibegli, 1985) extended their work on the synthesis of poly(vinylsaccharide)s to obtain further higher molecular weights by emulsion polymerization wherein they obtained molecular weights upto 2.9×20^7. The methodolgy of grafting onto synthetic backbones, however, has since not been pursued vigorously, due to synthetic challenges. Polymeric derivatives of methacrylic acid containing aromatically substituted glycopyronoside side chains were reported for the first time by (Carpino, Ringsdorf, & Ritter, 1976).

Another strategy was adopted for obtaining poly(vinylsaccharide)s by the ring openinig polymerization of the anhydro sugars using macromolecular halides as initiating systems (Uryu, Kitano, Ito, Yamanouchi, & Matsuzaki, 1981a). Refer to note on cationic polymerizations. In the 1990s the importance of poly(vinylsaccharide)s in biological systems was elucidated. It was only in the 1990s that the role of poly(vinylsaccharide)s in biological systems gained impetus. Many articles dealt with the use of these polymers in cell recognition processes, for binding of hepatocytes, synthetic antigens etc. They were mainly useful for elucidating the role of carbohydrates in the biochemical processes. Poly(vinyl alcohol) containing glucose linked by adipic acid as a spacer was shown to be biodegradable (Tokiwa et al., 2000). Furuike, Nishi, Tokura, & Nishimura (1995), Matsuoka & Nishimura (1995), Nishimura et al. (1991, 1994), Nishimura et al. (1990), were instrumental in synthesizing a number of glycoconjugates. They studied their binding specificities with lecithins and they found that glycopolymers having related disaccharide derivatives in their side chains (Nishimura et al., 1991) showed enhanced binding capacity with lecithins based on a polymer sugar cluster effect whereas synthetic trisaccharide or smaller sugar derivatives showed only weak affinity to the hemaglutinin molecules (Sauter et al., 1989). Kobayashi, Akaike, Kobayashi, and Sumitomo (1986) have reported the synthesis of polystyrene having pendant lactose residues by polymerizing the oligosaccharide lactones with *p*-vinylbenzylamine by using radical polymerization methods and its application as substratues for liver cell cultures. They also synthesized poly (*N*-(*p*-vinyl benzyl)-4-*O*-β-D-galactopyranosyl D-gluconamide) as a substratum for culture of hepatocytes (Kobayashi, Goto, Kobayashi, & Akaike, 1994c; Kobayashi, Kobayashi, & Akaike, 1994a; Kobayashi, Kobayashi, Tobe, & Akaike, 1994b). Several pseudopolysaccharides, or in other words, synthetic polymers with pendant carbohydrates have been synthesized and their potentials as polymeric drugs and in solid phase synthesis have been exploited (Andresz, Richter, & Pfannemuller, 1978; Horejsi, Smolek, & Kocourek, 1978; Kraska & Mester, 1978; Nishio, Nakaya, & Imoto, 1978; Nolte, Zomeren, & Zwikker, 1978). An amphiphilic glycopolymer was synthesized (Kobayashi et al., 1994) consisting of a poly(acryl(aminophenyl)) backbone and chemoenzymatically synthesized oligosaccharides (Kobayashi et al., 1994). A recent review article by Kobayashi (2001) describes various applications of glyconjugate polymers in biological and biomedical fields. He also studied the micellar behaviour of glycoconjugates in water by various techniques such as fluorescent spectroscopy, dynamic light scattering and fluorescence energy transfer experiments and also measured the average particle size of these micelles (Goto et al., 2001). Glycoproteins have been synthesized in the Uryu laboratory to study the binding of oligosaccharide chains to enzymes and immune active proteins to study the activation and stabilization of natural proteins. They also studied low molecular weight AIDS drug carrying carbohydrate moieties.A very recent article, reported the synthesis and its hydrolysis under physiological environment, of poly(ester amide)s based on arabinose (Pinilla, Martinez, Mata, & Galbis, 2002).

The history of the success of anhydro sugar polymerizations dates back to the mid 1960s. Ruckel and Schuerch (1966) were the first to successfully synthesize a regular polysaccharide by anhydro sugar polymerizations. Lin and Schuerch (1972), Ruckel and Schuerch (1966, 1967), Uryu and Schuerch (1971) and Zachoval and Schuerch (1969) studied the synthesis of D-glucan (Fig. 4) in different solvent systems, at different temperatures and effect of various electrophilic reagents in detail. They polymerized

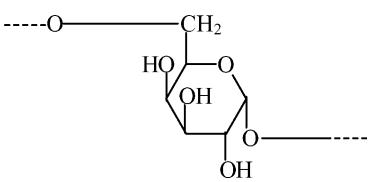

Fig. 4. 1,6 D-Glucan.

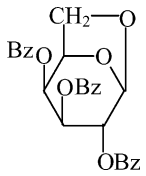

Fig. 5. 1,6-Anhydro-β-D-glucopyranose tri benzyl ether.

1,6-anhydro-β-D-glucopyranose tribenzyl ether (Fig. 5) followed by its debenzylation to obtain high yields and stereoregular polymers.

Schuerch was also instrumental in the synthesis of D-galactan (Lin & Schuerch, 1972; Uryu, Libert, Zachoval, & Schuerch, 1970; Uryu & Schuerch, 1971) and D-mannan (Frechet & Schuerch, 1969; Lin & Schuerch, 1972; Tkacz, Lampen, & Schuerch, 1972). Glucomannans were also synthesized which were linear and stereoregular (Kobayashi, Eby, & Schuerch, 1977). The strategy of ring-opening polymerization of anhydro sugars was extended to the synthesis of glycoconjugates, wherein, disaccharides were linked to various proteins (Eby & Schuerch, 1982).

The anhydro sugars which can be synthesized and polymerized are 1,2-, 1,3-, 1,4-, and 1,6- anhydropyranoses and 1,2-, 1,3-, 1,5- and 1,6- anhydrofuranoses.

The first attempt at polymerizing a 1,6-anhydro sugar dates back to 1918 (Pictet, 1918). Ever since then several attempts, particularly in the late 1950s, were made to synthesize linear polysaccharides but were not fruitful (Goldstein & Hullar, 1959; Wolfrom, Thompson, & Ward, 1959). Bredereck and Hutten (1963), were first successful in polymerizing perbenzyl ether and peracetate of levoglucosan using organic halides and silver perchlorates. Comb-like glucans were synthesized from 1,6 anhydro-maltose and 1,6-anhydro cellobiose (Masura & Schuerch, 1970; Veruovic & Schuerch, 1970). The polymerization reactivities (polymerizabilities) of isomeric forms of 1,6-anhydroaldoxoses were studied and the rate was found to be maximum for the mannose sugar (Schuerch, 1981; Uryu, Sakamoto, Hatnaka, & Matsuzaki, 1984). The 1,6-anhydro sugars (1,6-anhydro-2, 3,4-tri-*O*-benzyl-β-D-glucopyranose and the corresponding tri-*O*-methyl derivative) were not only homopolymerized but also have been successfully copolymerized with other monomers like epichlorohydrin, 3,3-bis (chloromethyl) oxetane, and 1,3-dioxolane (Uryu, Hatanaka, & Matsuzaki, 1980). 1,6 anhydro-β-D-galactopyranose and 1,6 anhydro-β-D-mannopyranose were also copolymerized to obtain branched heteropolysaccharides viz. α-[1®3] branched dextrans (Ito & Schuerch, 1979). Precipitin activity of synthetic mannan synthesized by polymerization of 1,6-anhydro mannose derivative was compared with mannan isolated from S. cerevisiae and their activities were corelated to their phosphate contents (Okubo et al., 1980). Ring opening polymerization of 1,6 anhydro sugars were carried out using macromolecular halides, Lewis acids or silver hexafluorophosphate to generate carbenium or oxonium ions which initiated the polymerization of anhydro sugars (Uryu et al., 1981a,b).

Uryu, Koyama, and Matsuzaki (1979) and Uryu et al. (1981a,b) reported the synthesis of 2,3-*O*-benzylidene[1®5]-α-D-ribofuranan and 2,3-*O*-benzylidene[1®4]-α-D-ribopyranan by ring opening polymerization of the corresponding 1,5-anhydro2,3-*O*-benzylidene-β-D-ribofuranose and 1,4-anhydro-2,3-*O*-benzylidene-α-D-ribopyranose.

The earliest reports of polymerization of 1,4-anhydrosugar was by Kops and Schuerch (1965). They polymerized 1,4-anhydro-2,3,6-tri-*O*-methyl-β-D-galactopyranose and 1,4-anhydro-2,3-di-*O*-methyl-α-L-arabinopyranose. 1,4-Anhydro-2,3,6-tri-*O*-benzyl-α-D-glucopyranose was also synthesized in 1974 using different catalysts like phosphorous pentafluoride, antimony pentafluoride (Micheel, Brodde, & Reinking, 1974) and triethyl oxonium tetrafluoroborate (Micheel & Brodde, 1974). Difficulties are encountered while polymerizing 1,4-anhydro sugars since these sugars contain fused 1,3-dioxolane, tetrahydrofuran and tetrahydropyran ring systems (Mark & Bikales, 1988). (1 → 4)-β-D-ribopyranan was synthesized using the benzylidene derivative of 1,4- anhydroribose (Uryu et al., 1981a,b), whereas, the furanan form was synthesized from dibenzyl ether of 1,4-anhydro-α-D-ribopyranose (Uryu, Yamanouchi, Kato, Higuchi, & Matsuzaki, 1983). More recently arabinofuranan and xylofuranan were prepared by corresponding 1,4-anhydro sugar polymerizations and sulfonated to various extents (Yoshida et al., 2000). The highly sulfonated ones (having degrees of sulfonation of 1.4–1.9) showed potent anti HIV activities and also exhibited higher blood anticoagulant activities.

1,3 Anhydro 2,4,6-tri-*O*-benzyl and 1,3 anhydro-2,4,6-tri-*O*-(*p*-bromobenzyl)β-D-mannopyranose were synthesized by Varma and Schuerch (1981) which were later polymerized to obtain stereoregular mannans by Kong and Schuerch (1984). Stereoregular (1 → 3) α-D-glucopyranan and mannopyranan were also synthesized using using triflic anhydride or silver triflate as the catalyst (Good and Schuerch (1985) and Kong and Schuerch (1984)).

Schuerch reported synthesis of glucopyranans and mannopyranans by polymerization of corresponding 1,2- anhydro sugars (Sharkey, Eby, & Schuerch, 1981; Yamaguchi & Schuerch, 1980). 1,2 anhydro mannose derivative was also polymerized by Trumbo and Schuerch (1985) and their results were compared with other 1,2 anhydro sugar polymerizations and mechanisms were proposed.

Other than these few other anhydro sugar polymerizations have been carried out. 5,6-Anhydro-1,2-*O*-isopropylidene-α-D-glucofurnose (Uryu, Kitano, Tachikawa, Ito, & Matsuzaki, 1978) was polymerized by ring opening of anhydrous sugars. Uryu, Ito, and Matsuzaki (1979) also reported the polymerization of 3,5-anhydro sugars viz. 3,5-anhydro-1,2-*O*-isopropylideneα-D-xylofuranose.

3. Methods of preparation

There are four methods of preparation of synthetic polysaccharides. They are as follows:

1. Polymerization of the vinyl sugar monomers to obtain poly(vinylsaccharide)s.
2. Cationic polymerization of anhydro sugars to obtain synthetic polysaccharides.
3. Enzymatic or enzyme- mediated (chemo- enzymatic) polymerization methods to obtain polymers containing sugars.
4. Grafting of sugars onto functionalized polymeric backbone by polymer analogous reactions.
5. Each of the methods is described in brief.

3.1. Polymerizations of the vinyl sugar monomers to obtain poly(vinylsaccharide)s

Cationic polymerization methods have been employed to polymerize the vinyl ether derivatives of saccharides. An example of this is the polymerization of 6-*O*-vinyl ether of 1,2:3,4 -di-*O*-isopropylidene-D-galactopyranose (Beereboom, 1983; Whistler et al., 1962) and the corresponding 6-*O*-vinyl ether of 1,2:5,6 di-*O*-isopropylidene glucofuranose (Black, Dewar, & Rutherford, 1962). The above monomers were prepared by bubbling acetylene gas into a mixture containing the corresponding diisopropylidene derivatives of the sugars viz. glucose and galcactose, and potassium hydroxide. The polymerizations of the vinyl ether derivatives of these sugars were carried out using boron trifluoride-etherate catalyst in hydrocarbon solvent. The removal of the isopropylidene protecting groups was effected with 80% formic acid.

The most widely used method of synthesis of poly (vinylsaccharide)s was based on free radical polymerizations of the vinyl sugars. A sugar is attached to a polymeric backbone through various optional linkages such as ether (Furuike, Nishi, Tokura, & Nishimura, 1995; Nishimura et al., 1991; Nishimura et al., 1990) amide (Fraser & Grubbs, 1995; Kobayashi et al., 1986; Nishimura et al., 1994a,b), urea (Klein, 1989, 1990a,b) or ester (Chen, Dordick, & Rethwisch, 1995) linkages. The sugar and the polymer can also be separated by a spacer (Fig. 6) (Mandeville & Garigapati, 1997; Nishimura et al., 1990; Tokiwa et al., 2000), e.g. an alkyl spacer.

Free radical polymerizations have been carried out in aqueous as well as non-aqueous media. Earlier reports involved polymerizations of the vinyl sugars using the radical initiator viz. AIBN in non-aqueous media (Carpino et al., 1976; Emmerling & Pfannemuller, 1983; Kimura & Hirai, 1962; Ouchi, Sakamoto, Jokei, & Chikashita, 1984; Rios & Bertorello, 1997) (Fig. 7), or benzoyl peroxide also in non-aqueous media (Bird et al., 1960; Rios & Bertorello, 1997).

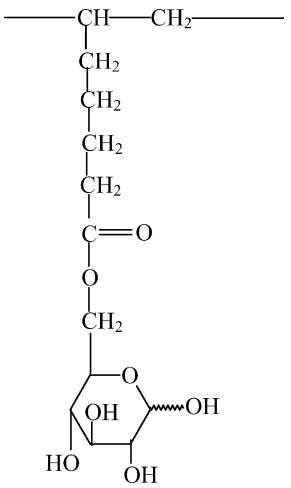

Fig. 6. Poly(vinyl alcohol) with pendant glucose separated by adipic acid spacer.

Use of benzoyl peroxide gave polymers with higher percentages of sugars as compared to AIBN (Rios & Bertorello, 1997). In one case di-*t*-butyl nitroxide based alkoxyamine was used as an initiator in nonaqueous medium with dicumyl peroxide as the accelerator (Ohno, Izu, Yamamoto, Miyamoto, & Fukuda, 1999). Tertiary butyl peroxide was also used for polymerization of poly(vinylsaccharide)s (Moriguchi, 1994). More recently most of the polymerizations of vinyl saccharides have been carried out in aqueous systems using ammonium persulfate or potassium persulfate and *N*, *N*, *N′*, *N′* tetra ethylene diamine (TEMED) (Grande, Baskaran, & Chaikof, 2000; Lee et al., 1999; Nishimura et al., 1991; Zhou, Kurth, Hsieh, & Krochta, 1999). Ammonium peroxidisulfate was used as a radical catalyst for emulsion polymerization of 3-*O*-methacryloyl 1,2:5,6 di-*O*-isopropylidene-D-glucofuranose (Klein et al., 1985). Redox initiators viz $(NH_4)_2\ S_2O_8$/ $Na_2S_2O_8$ were used in aqueous medium for polymerizations of poly(vinylsaccharide)s (Klein, 1987, 1989). Vinyl sugar monomers bearing various functional groups were synthesized and these monomers were either homopolymerized or copolymerized with other polymerizable vinyl monomers

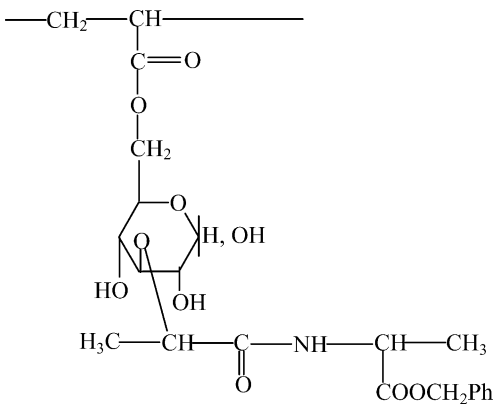

Fig. 7. Poly{1-{3-*O*-[1-(benzyloxycarbonylethylaminocarbonyl)ethyl]-6-*O*-D-glucopyranosylcarbonyl}ethylene}.

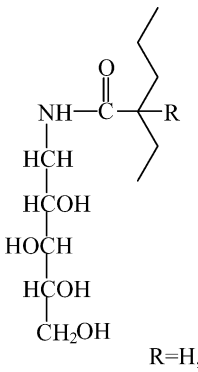

Fig. 8. Poly(1-acrylamido/1-methacrylamido-1-deoxy-glucitol).

to obtain poly(vinylsaccharide)s. Atom transfer radical polymerization of sugar containing radically polymerizable monomers (e.g. acetonide-protected D-glucofuranose methacrylate) in presence of a bromine-containing carbohydate initiator, a ligand and CuBr (Bon & Haddleton, 1999; Ohno, Tsujii, & Fukuda, 1998). High-energy radiation was used for polymerization of 1-acrylamido and 1-methacrylamido-1-deoxy-glucitol (Whistler et al., 1961). Decomposition of peroxide or azo type catalysts and redox catalyst systems were also tried out (Fig. 8).

There are various methods to obtain these vinyl sugar monomers so that they can be linked to the polymer through various linkages. These are listed below:

1. Incorporation of acrylic ester onto a sugar moiety and homopolymerizing or copolymerizing it with an acrylate using a radical catalyst (Patil et al., 1991). This acryloylation can be done either chemically or enzymatically (Fig. 9).
2. Converting the sugar into a sugar oxime and homopolymerizing it without the protection of hydroxyl groups (Zhou et al., 1997) (Fig. 10).
3. Condensation of an alkyl isocyanate with a sugar amine followed by its free radical polymerization to obtain a poly(vinylsaccharide) with a urea linkage (Zhou et al., 1999) (Fig. 11).
4. Oxidation of sugars to their corresponding lactones, which in turn are reacted with *p*-vinyl benzyl amine and polymerization of the adducts by free radical means (Kobayashi et al., 1985) (Fig. 12).
5. Conversion of sugars to their corresponding glycosyl amines, followed by their conversion to *N*-acryloyl derivatives, followed by their polymerization by radical polymerization methods. (Kallin et al., 1989) (Fig. 13).
6. Bulk polymerization of isopropylidene protected vinyl sugars (Wulff, Schmidt, & Zhu, 1999) (Fig. 2).

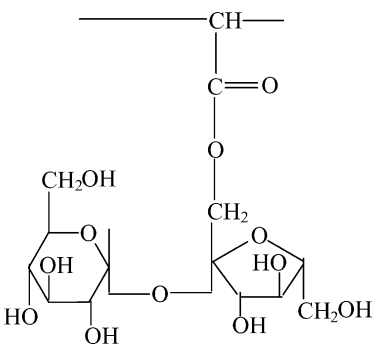

Fig. 9. Poly(sucrose acrylate).

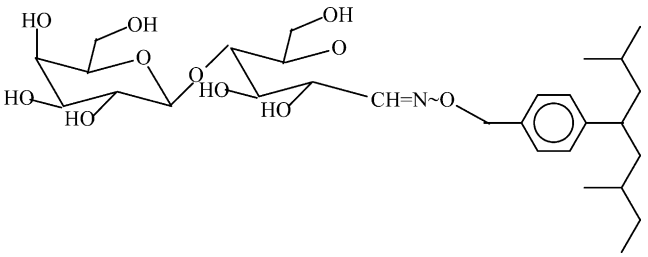

Fig. 10. Homopolymer of D-lactose *O*-(*p*-vinylbenzyl) oxime.

Olefin metathesis reaction, although not a general method of synthesis of poly(vinylsaccharide)s, has also been employed in some cases to obtain poly(vinylsaccharide)s (Fraser and Grubbs (1995) and Mortell, Weatherman, and Kiessling (1996)) (Fig. 14).

3.2. Polymerization of anhydro sugars

Cationic polymerization methods in carbohydrate chemistry have been more commonly employed for the ring-opening polymerization of an anhydro sugars. The polymerizations are initiated by carbonium ions. The advantage of this method lies in the acquisition of a highly stereoregular polymer with high molecular weight. Such polymerization reactions require extreme purity of the monomers and solvents, and reactions are sensitive to even traces of nucleophilic impurities in the reaction mixture. This has limited the use of these polymers for bulk applications. However this method is definitely useful for obtaining polysaccharides with high stereoregularity (Uryu, Hagino, Terui, & Matsuzaki, 1981b) which is a prime requirement in cellular studies. The ring strain and the hydroxyl protecting groups also dictate the polymerizations.

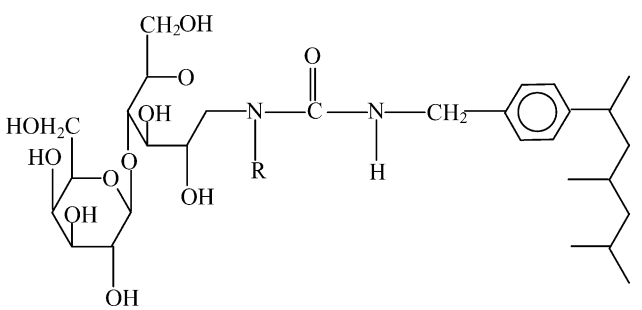

Fig. 11. Polystyrene linked to lactose via urea linkage.

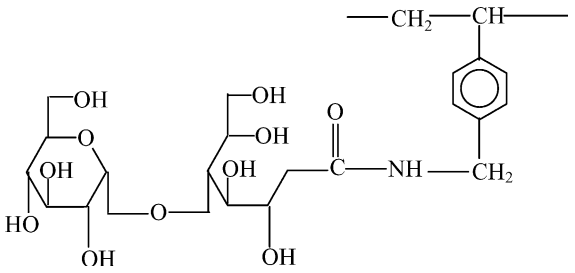

Fig. 12. Maltose linked to polystyrene via amide linkage.

3.2.1. 1,6-Anhydro sugar polymerizations

Bredereck and Hutten (1963) were the first to successfully polymerize the perbenzyl ethers and peracetates of levoglucosan cationically, using organic halides and silver perchlorates as catalysts, to obtain non-stereoregular polymers. The effects of different Lewis acid catalysts on the polymerization of levoglucosan in 1,4-dioxane were studied (Korshak, Golova, Sergeev, & Merlis, 1961). They obtained branched products with mixed anomeric configuration. They obtained less viscous and crystalline products by carrying out the reactions in toluene at 50 °C in presence of boron trifluoride–etherate catalyst. Lowering of reaction temperatures resulted in polymers with higher viscosities. Ruckel and Schuerch (1966a,b, 1967) carried out a series of experiments to determine the optimum conditions, solvents and catalysts required for obtaining stereoregular polymers and they reported that the best results were obtained using phosphorous pentafluoride as the catalyst at a temperature of −78 °C in dichloromethane solvent. Number of triether derivatives of levoglucosan do support polymerizations to obtain stereoregular polymers of high molecular weights (Schuerch, 1981), whereas triester derivatives failed to effect polymerization, particularly below 0 °C. Only the trinitrate derivative polymerized at 0 °C (Zachoval & Schuerch, 1969). The polymerizibility of 1,6-anhydro-2,3,4-tri-*O*-benzyl-glucopyranose was tested in dichloromethane solvent at −60 to −78 °C using different Lewis acids such as boron trifluoride and its etherate, phosphorous pentafluoride, titanium tetrachloride, antimony pentachloride and antimony pentafluoride, and different initiators such as (triphenylmethyl) antimony hexachloride, 2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl hexafluorophosphate, pentamethylbenzyl hexafluorophosphate, acetyl hexafluorophosphate and triethyl oxonium salts with various anions,

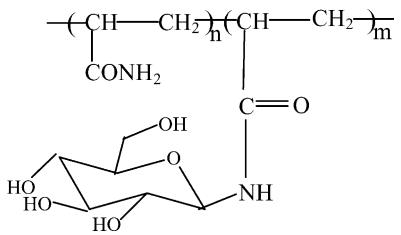

Fig. 13. Copolymer of *N*-acryloyl-4-*O*-(β-D-galactopyranosy)-β-D-glucopyranosylamine with acrylamide.

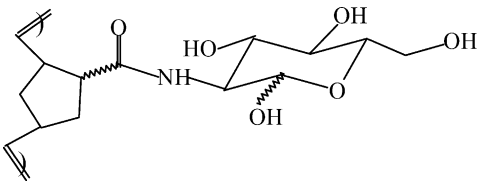

Fig. 14. Poly 2-((±)-exo-5-norbornene-2-carboxamido)-2-deoxy-D-glucopyranose.

and it was found that phosphorus pentafluoride catalysed polymerizations with low catalyst: monomer ratios, i.e. less than 1 mol%, gave polymers with highest molecular weights with highest specific rotations (Schuerch, 1981).

3.2.2. 1,5-Anhydro sugar polymerizations

The polymerization of 1,5-anhydro-2,3-*O*-benzylidene-β-D-ribofuranose was tried out at 0–40 °C was carried out in presence of various Lewis acid catalysts such as phosphorous pentafluoride, boron trifluoride etherate and stannic chloride to obtain polymers with molecular weights of 2000–20,000 with mainly α-furanose and α-pyranose units. The (1 → 4) β-ribopyranans with molecular weights between 26, 000 and 32,500 were obtained using antimony pentachloride as the catalyst.

3.2.3. 1,4-Anhydro sugar polymerizations

The polymerization of the 1,4-anhydro sugars has been less extensively studied as compared to 1,6-anhydro sugar polymerizations. The polymerization of 1,4-anhydro-2,3,6-tri-*O*-methyl-β-D-galactopyranose and 1,4-anhydro-2,3-di-*O*-methyl-α-L-arabinopyranose were the first of the 1,4-anhydro sugar series and were synthesized by Korshak et al. (1961). Generally the polymerizations were carried out at a concentration of 10% (g/ml) in dichloroethane solvent or aromatic hydrocarbons. The common catalysts used were phosphorous pentafluoride or boron trifluoride etherate at a concentration of 1–5 mol%. The polymerizations were carried out at temperatures of −78 to −97 °C for long periods of time to obtain conversions of 50–90%. Polymerizations of 1,4-anhydro-2,3,6-tri-*O*-benzyl-α-D-glucopyranose reported by Micheel et al. (1974) with 15–20 mol% of phosphorous pentafluoride gave molecular weights of 21,000–41,000. The polymerization of this monomer using antimony pentafluoride was not fruitful and boron trifluoride etherate totally failed.

3.2.4. 1,3-Anhydro sugar polymerizations

1,3-anhydro-2,4,6-tri-*O*-benzyl-β-D-glucopyranose has been polymerized using various catalysts like phosphorous pentafluoride, boron trifluoride etherate, triethyloxonium hexafluorophosphate, antimony pentachloride and silicon tetrachloride. Of these, phosphorous pentafluoride gave the best results with yields of 60–70%. Polymerizations with basic catalysts failed (Schuerch, 1981).

3.2.5. 1,2-Anhydro sugar polymerizations

Attempts were made in Haq and Whelan (1956), to polymerize a 1,2-anhydro sugar, viz. 1,2-anhydro-3,4,6-tri-*O*-acetyl-α-D-glucopyranose by thermal methods but it resulted into formation of only oligomers. Polymerization of 1,2-anhydro sugars with ether protecting groups, viz., 1,2-anhydro-3,4,6-tri-*O*-benzyl-β-D-mannopyranose, has been carried out in presence of iodine, methyl borate, phosphorous pentafluoride and triethyloxonium hexafluorophosphate, and produce polymers of mixture of α- and β- anomeric linkages (Yamaguchi & Schuerch, 1980).

3.3. Enzymatic and enzyme mediated polymerizations (chemo-enzymatic methods)

Enzymes are highly stereoselective catalysts, which have been effectively used in the synthesis of sugar based polymers, or in specific poly(vinylsaccharide)s (Dordick, Rethwisch, & Patil, 1991; Kobayashi & Kamiya, 1996), wherein no protection of the hydroxyl groups of the sugar was required. Sucrose contains eight hydroxyl groups, which are all capable of undergoing esterification reactions. However polycondensation of sucrose was affected with diacids using enzyme catalysts to obtain linear polymers, where only two hydroxyls of sucrose were functional (Patil et al., 1991; Patil, Rethwisch, & Dordick, 1991). The advantages associated with enzymatic reactions are that they can be carried out both in aqueous and non-aqueous media, and as they are selective, protection and deprotection of the sugars can be avoided. There are certain limitations involving enzyme-catalyzed reactions. Most known enzymes catalyze only selective reactions to produce specific sugar derivatives. Therefore, currently only a limited variety of vinyl sugar derivatives can be synthesized by this method. Examples of vinyl sugars that can be synthesized enzymatically are sucrose1-acrylate (Patil et al., 1991a,b), methyl 6-acryloyl-β-galactoside (Martin et al., 1992). The other limitation encountered with enzyme catalyzed reactions is its very slow rate, thereby making use of such reactions less feasible. This problem can be taken care of by using chemo-enzymatic methods of synthesis wherein the vinyl sugar is synthesized in a single step without protection of the sugar hydroxyls using enzymes and then polymerized by chemical means (Chen, Dordick and Rethwisch, 1995; Nishimura et al., 1990; Patil et al., 1991a,b). The chemo-enzymatic method capitalizes both, on the enhanced regio-selectivity over chemical methods and on the speed of conventional chemical methods of polymerizations (Patil et al., 1991a,b). Sucrose acrylate was synthesized by enzymatic catalysis using an enzyme proleather (a protease from Bacillus. Sp) (Patil, Dordick, & Rethwisch, 1991). The sucrose acrylate was polymerized using potassium persulfate/(H_2O_2) to obtain poly(sucrose acrylate). The chemo- enzymatic method was also useful for the synthesis of a glycopolymer viz. Poly(acryl(aminophenyl)) backbone chain with enzymatically synthesized oligosaccharide (Kobayashi, Goto, Kobayashi, & Akaike, 1994a; Kobayashi et al., 1994b). Tokiwa et al. (2000) reported esterification of glucose with adipic acid enzymatically and later on effected its polymerization by conventional methods to obtain biodegradable polymers. α-D-galactose was acryloylated with vinyl acrylate enzymatically and later polymerized chemically. Martin et al. (1992) reported variety of monosaccharides with vinyl acrylate in pyridine to obtain 6-acryloyl esters and later on polymerized them in DMF solvent with AIBN as the initiator to give poly(acrylate) products.

3.4. Polymer analogous reactions

Although much has been reported on poly(vinylsaccharide)s, there have been relatively few reports on synthesis of poly(vinylsaccharide)s by polymer analogous reaction, to obtain linear polymers. In this connection, the contributions of Beate Pfannemuller need special mention. His earlier work was based on grafting monosaccharide segments onto natural polymers like amylose to obtain comb like polymers. He later extended this strategy to grafting of sugars onto synthetic polymers. The method of grafting sugars onto synthetic backbones has not been investigated intensively due to perceived difficulties in grafting large monomeric molecules quantitatively onto polymers. However, this method has obvious advantages and the present investigators are of the opinion that this methodology has much to offer in terms of tailored polymer properties. Sugars with protected as well as unprotected groups can also be grafted onto the polymer (Galgali & Varma, 2001; Galgali et al., 2002; Varma et al., 2002). Mild conditions should be chosen in order to avoid formation of cross-linked products. Another advantage is the ease in controlling the number of sugars being grafted as well as their randomness for low degrees of grafting on the polymer chain. Dramatic improvement in rates of biodegradation of biodegradation of these polymers were reported by these workers, and has caught the attention of researchers worldwide. In spite of these advantages, some difficulties have been encountered in compositional analysis (Klein, 1987).

Pfannemueller (1978) reported the grafting of glucose and maltoligomers onto linear polymers like poly (ethylene glycol) having carboxymethyl end groups, poly(acrylic acid) etc via hydrazone linkages (Andresz, Richter, & Pfannemueller, 1978). Mono-, di- and oligosaccharides were also linked via amide bonds to synthetic and natural polymers carrying $-COOH$ or $-NH_2$ groups, e.g. poly(acrylic acid), poly(vinyl amine) and polysaccharide derivatives like chitosan. The number and the length of the saccharide branches were varied to obtain polymers exhibiting polyelectrolyte behaviour (Emmerling & Pfannemueller, 1983). A 1981 Japanese patent describes emulsion grafting of glucose onto styrene butadiene rubber

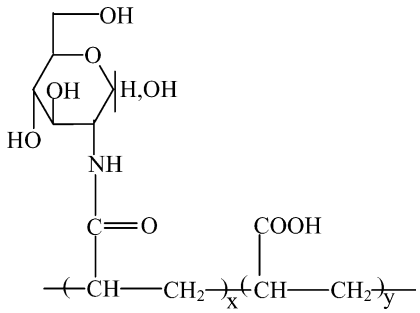

Fig. 15. Poly(acryl amide) with pendant glucosamine/galactosamine.

but they obtained a crosslinked product (Showa, 1981). Galactose was covalently linked to 2-hydroxyethylmethacrylate-ethylene methacrylate copolymer (Jiri, Karel, & Jan, 1978; Karel, Jiri, & Jan, 1980). This polymer was used as a stationary phase material for column chromatography of proteins.

A 1985 Japanese patent describes grafting of α-bromo-3,4,6,-tri-*O*-acetyl-D-glucosamine hydrobromide. The deacetylated product (Koyama, Yoshida, & Kurita, 1986) was bactericidal and useful in the treatment of steel (Keisuke, Yoshiyuki, & Masaaki, 1985a,b). Usmani and Salyer (1983) reported grafting of sucrose onto poly(vinyl alcohol) by polymer analogous reactions, which was not supported by any spectral data. However a repetition of the same work by Bahulekar et al. (1998a,b) in the same year disproved the above findings giving spectral evidences. Bahulekar et al. (1998a,b) reported synthesis of poly(vinylsaccharide)s by polymer analogous reactions. Glucosamine hydrochloride and galactosamine hydrochloride were reacted with poly(acryloyl chloride) to obtain linear polyacrylamides with pendant sugar residues (Fig. 15).

Sucrose was grafted onto butadiene acrylic acid copolymers and poly butadiene carboxylate (Alvarez, Strumia, & Bertorello, 1988). The acid chloride derivatives of the polymer were reacted with sucrose in dry DMF using triethyl amine as the catalyst. The esterified polymers were then either reacted with toluene diisocyanate to obtain polyurethanes. The polymers were characterized by IR, PMR. In one of the recent articles (Gruber & Knaus, 2000) polymer surfaces were modified with carbohydrate derivatives by polymer analogous methods (Fig. 16).

Partially substituted sucrose esters with 4-azido benzoyl chloride along with swelled polypropylene films were taken in acetone and irradiated by UV radiation. The surface of

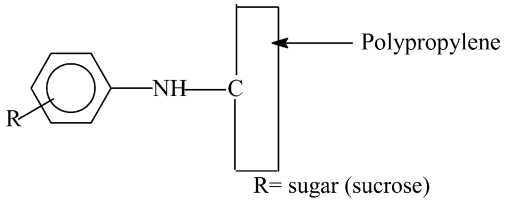

Fig. 16. Polypropylene surfaces modified by carbohydrate residues.

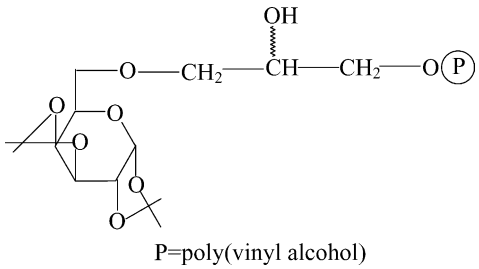

Fig. 17. Polyvinylether of 1,2: 3,4-diisopropylidene galactose.

poly(vinyl chloride) was modified by polymer analogous reactions (Rios & Betorello, 1997). The polymer film was suspended in acetone containing the initiators, viz benzophenone and 2,2′- azoisobutyronitrile and sucrose acrylate. The grafting was initiated using ultraviolet radiation. The modification was done in order to improve the interfacial phenomenon between the microorganism and the PVC surface. Kraska and Mester (1978), reported the base catalyzed adsorption of poly(vinyl alcohol) in DMSO (with traces of KOH) with reducing carbohydrates to obtain pseudopolysaccharides through a chemically and enzymatically inert ether linkage(Figs.17–19).

They are useful in the solid phase syntheses of glycosides, as potential carriers of drugs and they also serve as a useful probe in the study of protein–carbohydrate interactions. 6-*O*-epoxy propyl derivative of D-galactose-6-*O*-allyl ether was used for this study. Hemocompatibility of polymer surfaces was improved by grafting of monomers (α-amino acids, peptides and amino sugars like glucamine and D-glucosamine) onto polymers (poly(ether urethanes), poly(ethylene glycol), poly(tetrahydrofuran), poly (vinyl alcohol and dextran) (Bamford, Lamee, Al-Middleton, Paprothy, & Carr, 1990). Pellethane-poly D-glucamine graft was found to be the most inert material towards platelets. Maltamine, which is a mixture of α-D-glucopyranosyl-(1,6)-2-amino-2-deoxy-D-sorbitol and α-D-glycopyroanosyl(1,6)-2- amino-2-deoxy-D-mannitol was bound to chloroethylated poly(g-Me L-glutamate) and this membrane resolved optically active substances (Nakagawa et al., 1994). A prepolymer prepared from 2-ethyl-2-butyl-1, 3-propane diol and hexamethylene diisocyanate was copolymerized with ethyl galactomannan oligomers (Mueller, Peter, & Kurt, 1991). Isoamylene and maleic anhydride were polymerized with $Me_3COOCMe_3$ and mixed

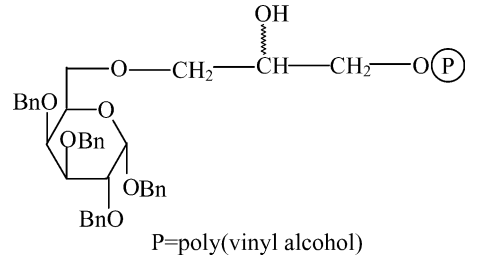

Fig. 18. Polyvinylether of benzyl galactoside.

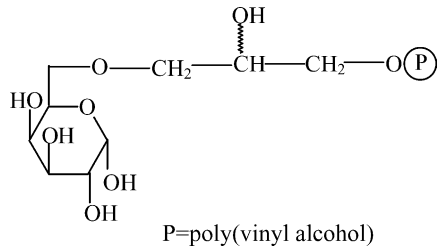

Fig. 19. Polyvinylether of galactose sugar.

with D-sorbitol, which showed good dispersibility and Fe-chelating ability (Moriguchi, 1994). Sugars were bound to polymer supports as thiosemicarbazones and they served as means for immobilization of enzymes (Tweeddale, Batley, & Redmond, 1994). Glucose and N-acetyl glucosamine hydrazones were reacted with isothiocyanate substituted polystyrene. 3-azido styrene and *N-p*-vinyl benzyl-(*O*-B-D-galactopyransoyl (1 → 4)-D-gluconamide were polymerized and the resulting polymer was applied on a PVC dish and irradiated using ultraviolet radiation to obtain PVC fixed with sugar, which prevented adhesion of blood platelets on the dish (Yura, Goto, Tanaka, & Saskurai, 1997). Solvent evaporation technique was also used to prepare nano particles with carbohydrate chains on their surface (Maruyama, Ishihara, Adachi, & Akaike, 1994).

4. Methods of characterization

Elemental analysis has been extensively used in the of analysis of poly(vinylsaccharide)s. In case of copolymers containing N, the nitrogen percentage becomes useful in determining the composition of the copolymer (Ouchi, Sakamoto, Jokei, & Chikashita, 1984).

Optical rotation measurements have been used to determine the stereo-regularity of the anhydro sugar homopolymers. They are accurate with a variation of $\pm 1-2\%$ on different preparations (Schuerch, 1981).

Circular dichroism (c.d.) spectra have been used for determining the configurations at the carbon atoms of the synthetic polysaccharides. As an illustration, both D-glucan and D-galactan exhibited almost identical c.d. bands, but since D-mannan has a different configuration at the C-2 position, the negative sign present in D-glucan and D-galactan is changed to positive sign in D-mannan (Schuerch, 1981).

Intrinsic viscosities of the polymers have been used to calculate the molecular weights of the poly(vinyl sacchahide)s. However intrinsic viscosity does not necessarily give the number average molecular weight. Membrane osmometry in both aqueous and DMSO solvents have been used to determine number average molecular weights for linear and branched D-glucans (Ito & Schuerch, 1979; Uryu & Schuerch, 1971). Light scattering measurements have been used to determine the intrinsic viscosities of the poly(vinylsaccharide)s in 0.1 M sodium sulfate aqueous solution and related to their absolute molecular weights (Klein & Blummenberg, 1988). Sedimentation velocity measurement has been employed to determine the molecular weight distribution in case of tribenzyl ethers of (1 → 6)-α-D-gluco-, manno-, and galacto-pyranans (Bluhm & Sarko, 1973). Light scattering measurements were also used for determination of molecular weight and hence degree of polymerization (Klein et al., 1985). Since most of the work on poly(vinylsaccharides) was based on polymerization reactions involving vinylsaccharides, the viscosities of the polymer were recorded. The intrinsic viscosity was found to be comparatively small for poly(methacryloyl glucose) (Klein et al., 1985). Gel permeation chromatography was used for determination of molecular weights and polydispersities of the resultant poly(vinylsaccharide)s (Zhou et al., 1999).

Infrared spectroscopy is the most widely used method for anlaysis of poly (vinyl saccharide). Since most of the work in this area involved polymerization of the vinyl sugars, the disappearance of C=C bond was used as a means for determining the completion of polymerization. In almost all cases IR were done using KBr. The IR was used only for qualitative analysis. Reports on synthesis of poly(vinylsaccharide)s before 1960 did not include analysis by IR spectroscopy. IR spectroscopy was used to monitor the grafting of sucrose acrylate on PVC surface (Rios & Bertorello, 1997). The relative decrease in the band at 616 and 669 cm^{-1} due to −C−Cl and appearance of new bands at 1720 and 3450 cm^{-1} due to ester bond formation and hydroxyl groups of the sugar.

Nuclear magnetic resonance spectroscopy, both proton and carbon 13 spectroscopy, have been used widely in the analysis of poly(vinylsaccharide)s synthesized after 1980. Linear structure of the poly (vinyl saccharide) can be confirmed by ^{13}CNMR (absence of peak at $\delta > 80$ ppm indicates absence of branching (Klein, 1989). Sugar region in the ^{13}C NMR is between 40 and100 ppm and in the ^{1}H NMR is between 3.5 and 6.0 δ. Peak at 45 ppm (^{13}C NMR) of poly(1-acrylamido-1-deoxy-D-glucitol) (Klein, 1987) was attributed to branching at the β carbon. Proton NMR spectroscopy was used for determining the grafting of sucrose onto carboxylated butadiene polymer. Where the grafting percentages were high the sugar protons appeared between 3.1 and 4.8 δ and −OH group between 2.4 and 3.0 δ. However where grafting percentages were low the sucrose peaks did not appear. They were then silylated and then characterized by proton NMR spectroscopy to observe methylic protons at 0.0–0.4 δ. Both CMR and PMR had been used to determine the conformation of poly(*N-p*-vinylbenzyl-D-gluconamide) in water and attributed the broadening of the signals to intense stacking of the phenyl groups and little mobility of the main chains in water (Kobayashi, Sumitomo, & Ina, 1983). Proton NMR spectroscopy has been instrumental in determining the copolymer compositions in anhydro sugar polymers (Schuerch, 1981). For example, compositional analysis of

the copolymer consisting of tri-*p*-xylyl derivative of glucan and tri-benzyl derivative of mannan was made by comparing the difference in the chemical shifts of the methyl protons of the tri-*p*-xylyl derivative of glucan homopolymer (Schuerch, 1981). Relative intensities of the peaks corresponding to the α- and the β- anomeric carbon atoms in the CMR spectra are often useful in determining the stereoselectivity in case of anhydro sugar polymers. The assignment of the signals of the anhydro sugar polymers of glucose is made based on a standard linear D-glucan (Colson, Jennings, & Smith, 1974).

Absorption spectroscopy. ultra violet spectroscopy has been used for the determination of the copolymer composition. The value of $\varepsilon_{257} = 2751\ \text{mol}^{-1}\ \text{cm}^{-1}$ in water at room temperature was used for the same (Ouchi et al., 1984). Absorption spectroscopy has also been used to study the binding of methyl orange and magnesium-1-anilo-8-naphthalene sulfonate to poly(*N*-*p*-vinylbenzyl-D-gluconamide) (Kobayashi et al., 1983).Vacuum-ultraviolet, circular dichroism was used for the study of the conformations of dextran and its oligomers. The linear dextran exhibited a band at 165 nm in contrast to a band at 177 nm for non-linear dextran (Stipanovic & Stevens, 1980).

Scanning electron microscopy was used to study the surface characteristics of the polymers (Bahulekar et al., 1998a,b; Rios & Bertorello, 1997). The weathering behavior of PVC grafted with sucrose acrylate was studied with microorganisms in a growing media and SEM was used to monitor the degradation of the polymer along with IR and weight loss measurements.

Multiple internal reflection fluorescence method: this method was used for studying the interfacial recognition of sugar residues of a sugar carrying block polymers by lecithin (Akira, Naoki, Yukari, Makato, & Hiromi, 1999).

Thermal analysis. Form the thermogravimetric curves of poly(glucosamine acrylate) and poly (acrylic acid) it was found that poly(glucosamine acrylate) is thermally more stable than poly (acrylic acid) (Tirkistani, 1997) which was explained on the basis of free amino groups. Differential thermogravimetry was used to determine the initial decomposition temperature and the maximum rate of weight change for PVC and PVC grafted with sucrose acrylate. Both the temperatures were found to lower for PVC grafted with sucrose acrylate as compared to PVC alone (Rios & Bertorello, 1997). Homopolymers of styrene main chain with pendant lactose units were characterized by thermal analysis. The homopolymers showed a two stage degradation related to the lactose moiety and polystyrene main chain and their glass transition temperatures were 133–134 °C (Zhou et al., 1999). The urea linkage increased the glass transition temperatures due to hydrogen bonding. The thermogravimetry showed 25% weight loss between 160 and 310 °C in case of 6-methacryloyl 1,2:3,4 di-*O*-isopropylidene-D-galactopyranose (Caneiro et al., 2001). Its differential thermal analysis showed that the weight loss occurred in two stages suggesting thermo-oxidative decomposition of the sample.

X ray photoelectron spectroscopy has been instrumental in determining the percentage of sugar viz. glucosamine or galactosamine grafted onto poly(acryloyl chloride) using nitrogen percentage values (Bahulekar et al., 1998a,b). The polyacrylamide containing glucose and galactose showed a shoulder for the C1s peak due to presence of acid or ester carbonyl.

Size exclusion chromatography has been used to determine the molecular weight distribution in case of glycopeptide macromers. Unimodal peak indicated narrow molecular weight distribution (Aoi, Tsutsumiuchi, Aoki, & Okada, 1996).

Colorimetric titrations were used to determine the sugar contents in the polymers by modified Park–Johnson colorimetric titration (Nishimura et al., 1991).

Contact angle measurements were used for determination of the hydrophilicity of the polymers. Water contact angle decreased substantially for polymers grafted with sugars (Bahulekar et al., 1998a,b).

Gravimetric and dye absorption measurements were used for determining the percentage of grafting of sugars (Rios & Bertorello, 1997). Crystal violet has a tendency to adsorb on hydrophilic surfaces and this property was used to determine the percentage of sugar grafting.

5. Applications of polymers containing carbohydrates

1. They act as cell surface mimics (Fraser & Grubbs, 1995).

   They are used in lecithin or antibody-binding assays, wherein recognition of pendant sugars on the liposomal surfaces by lecithin or enzyme was studied (Kitano & Ohno, 1994; Kitano, Sohda, & Kosaka, 1995). Copolymers of *N*-acryloyl-4-O-(β-D-galactopyranosyl)-β-D-glucopyranosylamine and acrylamide exhibited strong specific binding to antibodies against antigens in ELISA assays. Hence they act as substitutes for glycolipid and glycoprotein antigens in immunological assays (Kallin et al., 1989). Kosma and Gass (1987) synthesized artificial antigens based upon polyacrylamide copolymer containing 3-deoxy-D-manno-2-octulopyranosylonic acid residues. Allyl β-cellobiosiduronic acid and allyl β-pseudolaminari biosiduronic acid (Chernyak, Antonov, & Kochetkov, 1985) were copolymerized with acrylamide to obtain synthetic antigens. A pseudo polysaccharide that can be useful for binding of monoclonal antibodies by radio-immunoassays and ELISA was developed which contained rhamnose units (Roy & Tropper, 1988). Anhydro sugar polymers have also been used for such studies and concanavalin or lectin were found to react with the terminal α-D-glucopyranosyl and α-D-mannopyranosyl groups (Schuerch, 1981). Since lectin has a valency of four, if two or more of the α-D-glucopyranosyl groups are

present in the polysaccharide, it results in he formation of a network. This characteristic has been exploited to determine the linearity of the synthetic polysaccharides (Goldstein, Poretz, So, & Yang, 1968; Robinson & Goldstein, 1970; So & Goldstein, 1968).

2. Chromatographic supports for affinity chromatography and for the isolation of proteins with specificity for different sugar residues (Kobayashi et al., 1985; Roy & Tropper, 1988).
3. Matrices for cell culture (Kobayashi, Sumitomo, Kobayashi, & Akaike, 1988; Kobayashi et al., 1986).
4. A polymer with pendant sugar residues was conjugated with various enzymes with enhanced stability (Wang et al., 1992).
5. Appended sialic acid residues serving as invitro inhibitors of agglutination of the chicken erythrocytes by the influenza virus (Callstrom, Bednarski, & Gruber, 1992; Spaltenstein & Whitesides, 1991).
6. Surface grafted lactose, galactose, and *N*-acetyl glucosamine have been used to obtain high levels of liver cell adhesion to polymers (Hubbell, 1994).
7. Polystyrene plates were coated with polyacrylamide with pendant glucose and galactose, which showed adhesion of rat hepatocytes in primary culture (Bahulekar et al., 1998a,b).
8. They act as artificial glycoconjugates (Nishimura et al., 1990, 1991).
9. They are used in drug delivery systems, dental medicine, bioimplants, contact lenses and tissue engineering (Caneiro et al., 2001).
10. They have pharmacological and biomedical applications (Kobayashi et al., 1985).
11. Polymer bound oligosaccharides are used as intermediates in synthesis of oligosaccharides (Kobayashi et al., 1985; Kobayashi & Sumitomo, 1980a,b).
12. Monosaccharide containing poly(vinylsaccharide)s have strong affinity for organic solutes in water (Kobayashi et al., 1985).
13. They are used in preparation and use of specialty polymers, which are endowed with specific functions of sugars (Kobayashi & Sumitomo, 1980a,b).
14. Chiral templates derived from sugars are useful for asymmetric synthesis and optical resolution of organic molecules (Kobayashi and Sumitomo, 1980a,b). Molecularly imprinted polymers prepared from sugar acrylates have been used as chiral stationary phases for the resolution of the D- and L-isomers of CBz- Asp in polar organic eluents (Liu & Dordick, 1999).
15. Hydrophilicity of sugar was applied to the design of a reverse osmosis membrane and a selectively permeable membrane (Kobayashi & Sumitomo, 1980a,b).
16. Potassium *N*-(*p*-vinyl benzyl)-6-D-glucasamid-1-ate copolymerized with acrylamide inhibited the activity of β-glucuronidase through a model reaction with *p*-nitrophenyl β-glucuronide (Hashimoto, Oshawa, & Imai, 1999a; Hashimoto, Oshawa, & Saito, 1999b).
17. Silcone rubbers (polysiloxanes) possess highly hydrophobic surfaces, which is a drawback for biomedical applications such as surgical implants of contact lenses. Polysiloxanes containing glucose, sucrose and other carbohydrate derivatives have been reported which give better wettability and biocompability (Gerd & Stadler, 1991; Mossl, Gruber, & Greber, 1993; Volker & Stadler, 1998).
18. Polypropylene surfaces were grafted with azido substituted sucrose to increase its wettability (Gruber & Knaus, 2000).
19. Polystyrene plates were coated with polyacrylamide with pendant glucose and galactose to increase the surface wettability (Bahulekar et al., 1998a,b).
20. Used in synthetic fibres of the nylon type from 1,6-diamino sugars and dibasic acids (Bird et al., 1960).
21. Used in optically active polysaccharides (Bird et al., 1960).
22. Poly(*p*-vinyl phenol) with grafted α-bromo-3,4,6-tri-*O*-acetyl-D-glucosamine was bactericidal was useful in treatment of steel (Keisuke et al., 1985).
23. They act as polyelectroytes in absence of salt (Emmerling & Pfannemueller, 1983).
24. *N*-(2-hydroxypropyl)methacrylamide copolymers linked by fucosylamine/galactosyl amine with adriamycin drug was oligopeptide spacers are used in cell specific targeting to promote conjugate targeting to L1210 cells and heptatocytes (Duncan et al., 1989).
25. Polyurethane foams especially rigid foams which are prepared by using sucrose as the crosslinking agent are useful as resin binders for foundry use, solid urethane plastics and foam coatings (Faulkner, 1977; Kunz, 1993).
26. Behavior of an amphiphilic chloromethyl styrene polymer containing pendant glucose units behaved as a polysoap in water. Methyl orange was strongly bound to the hydrophobic regions of the polymer in water (Kobayashi & Sumitomo, 1980a,b).
27. Polymers formed by homopolymerization of unsaturated sugars and their copolymerization with comonomers like unsaturated carboxylic acids, esters, acrylic compounds, vinyl heterocycles, styrenes or maleic acid compounds are useful as thickeners which are also biocompatible (Buchholz et al., 1995).
28. An inter polymer formed by reactive blending of a synthetic polymer (maleic anhydride–styrene copolymer) having functional groups with starch was suitable for molding various articles (Vaidya & Bhattacharaya, 1993).
29. Copolymers of glucose or sucrose with comonomers like acrylic acid, sodium methallyl sulfonate, sodium 2-methacryloyl oxyethyl sulfate or vinyl phosphonic acid were useful as sequestering agents for Ca, Fe and other ions, as additives in textile desizing, bleaching, dyeing or printing, as dispersing agents for pigments in paper coating compositions, as additives in leather manufacture for improving chrome tanning, softness, brightness, etc. (Krause & Klimmek, 1984).

30. Monosaccharide and oligosaccharide derivatives polymerized with ethylenically unsaturated monomers containing maleic acid salts gave polymers, which had chelating ability towards $CaCO_3$ and biodegradability, and was used as an adjuvant in dyeing of cotton (Yamaguchi, Fugii, & Tsuboi, 1994).
31. Cyclodextrin vinyl diester polymerized with styrene and isoprene are useful as surfactants, thickeners, contacts (Vetter, 1994).
32. Chloromethylated polysulfone membrane treated with amino sugars was used as slow release biomembrane and dialysis membrane (Nakagawa, Higushi, Nin, Tanaka, & Sawada, 1993).
33. Membranes prepared by binding maltamine to chloroethylated poly (g-Me L-gluctamate) are useful for resolution of optically active substance (Nakagawa et al., 1994).
34. Maltose and maltotriose containing polystyrenes had the ability to specifically interact with concanavalin (Kobayashi et al., 1985).
35. Isoamylene and maleic anhydride polymerized with $Me_3COO\,CMe_3$ and mixed with D-sorbitol were useful as water treating agents, scale inhibitors, detergents and the have Fe-chelating ability (Moriguchi, 1994).
36. Copolyemrs of styrene, methyl methacrylate or acrylonitrile with small amounts of vinyl sugars (with sulfate groups) had heparin like activity (Wulff, Bellmann, Schmidt, & Zhu, 1998).
37. Partial deprotection of poly(1,2:5,6 di-*O*-isopropylidene α-D-glucofuanose) was carried out in order to get good coating and imaging properties (Havard et al., 1999).
38. Sucrose methacrylates were polymerized to obtain hydrogels, which were further reacted with succinic anhydride and maleic anhydride to obtain adsorbers for bilirubin (Gruber & Knaus, 2000).
39. 6,1′,6′-tri-*O*-(*p*-vinyl benzyl) sucrose was copolymerized with styrene or methyl methacrylate in presence of a crosslinking agent to obtain biodegradable polymers (Khan, 1976).
40. Sucrose diacids were cross-linked with diepoxide crosslinking agents to obtain sucrogels (Faulkner, 1977). Sucrogel was also prepared by transesterification processes (Carraher et al., 1981). Sucrose was also reacted with organostannane dihalides to form cross-linked network. These gels are useful for separation of heavy metal ions (Alvarez et al., 1991). Sucrogel (Gruber & Greber, 1991) have applications in drug delivery systems. The sugar hydroxyls were derivatized by trimethyl silyl groups and they were incorporated into hydrophilic silicon rubbers which were useful for medical purposes (Gruber & Knaus, 2000).
41. Synthetic linear D-glucan was used as a tool to elucidate the role of the determinants present in dextran which are responsible for the antigenic properties in dextran and it was found that three to seven units of (1 → 6)-α-D-glucopyranose were the antigenic determinants of dextran (Kabat, 1954, 1957, 1960).
42. Sucrose has been extensively used in the manufacture of urethane foams (Faulkner, 1977) and in particular rigid polyurethanes. Sucrose has great advantage due to its relatively low cost and excellent physical properties of the resulting polymers. Generally sugar having a functionality of 2,3 hydroxy groups are used for manufacture of flexible foams coatings, adhesives and elastomers whereas sugars having a functionality of 4,5 hydroxyl groups are used in the manufacture of rigid polyurethane foams. Others uses include solid urethane plastics and foam coatings.

6. Other potential applications of polymers containing carbohydrates

1. They are potentially processible and biodegradable polymers (Carneiro et al., 2001).
2. They are potential biocompatible polymers e.g.. (Chen, Dordick, & Rethwisch, 1995; Patil et al., 1991). Poly(methyl 6-acryloyl-β-galactoside-hema) copolymer swelled in water and contained 98% water and could hold nearly 50-fold its weight in water. Such materials have potential use as biocompatible hydrogels for biomedical and membrane applications (Martin et al., 1992).
3. Crosslinked poly(vinylsaccharide)s form hydrogels which can act as superabsorbers (Patil et al., 1991; Wulff, Schmidt, & Venhoff, 1996; Zhou et al., 1999). Polymers like poly(α-methyl galactoside 6-acrylate) hydrogels have this potential (Chen, Dordick, & Rethwisch, 1995; Patil et al., 1991).
4. Drug delivery systems (Zhou et al., 1999).
5. Chromatographic supports for isolation of proteins with specificity for different sugar residues (Zhou et al., 1999).
6. They can be used as stabilizers in dispersion polymerizations (Zhou et al., 1999).
7. They can serve as anti-inflammatory agents (Fraser & Grubbs, 1995).
8. They might enhance or trigger desirable biological responses such as for use in cancer immunotherapy (Fraser & Grubbs, 1995).
9. Biomimetic models of glycoconjugates (Nishimura et al., 1994).
10. Therapeutic and diagnostic purposes in biomedical and biochemical fields (Nishimura et al., 1994, 1990).
11. They are useful for elucidation of biological roles of carbohydrates and their pharmacological and physiological applications (Kobayashi & Sumitomo, 1980a,b).
12. Poly(methacryloyl glucose) has the potential to be used as a technical viscosifier for special applications (Klein et al., 1985).
13. Since glucosamine derivatives containing alkyl chains exhibit antimicrobial properties, polymers containing glucosamine derivatives have potential anti- microbial properties (Tirkistani, 1997).

14. Poly(vinylsaccharide)s have the potential to serve as water-soluble non-ionic polymers (Wulff, Schmidt, & Venhoff, 1996).
15. Poly(vinylsaccharide)s also have the potential to be used as thickeners in the tertiary oil recovery (Wulff, Schmidt, & Venhoff, 1996).
16. They also have the potential to be used as stable dextran analogues for the immobilization of enzymes and as gel permeation chromatography materials for the separation of water-soluble substances (Wulff, Schmidt, & Venhoff, 1996).
17. They can be used for surface modification of standard polymers (Wulff, Schmidt, & Venhoff, 1996).
18. Poly(vinylsaccharide)s have the potential to be used ad floccolating agents and also as polymeric detergents (Wulff, Schmidt, & Venhoff, 1996).
19. Polystyrene and polyacrylamide which contain reducing sugar moieties like glucose have been reported to interact with the glucose transporter protein of red blood cells and hence has the potential for fixation of cells via a transporter protein (Kitugawa et al., 2001).
20. A poly(vinylsaccharide) containing glucose and adipic acid produced superoxide in aqueous solution under the influence of nitrobluetetrazolium, hence they have an important role in biological systems such as inactivation of viruses and clevage of DNA (Kitugawa et al., 2001).
21. D-Glucaric derivatives are known to behave as inhibitors of β- glucuronidase and hence poly(vinylsaccharide)s containing D-glucaric acid derivatives are potentially capable of inhibiting the activity of β- glucuronidase. The inhibition of this enzyme would enhance the discharge of toxic xenobiotics (Hashimoto et al., 1999a,b).
22. Sulfated alkyl oligosaccharide)s have exhibited high anti-AIDS virus activity and hence sulfated poly(vinylsaccharide)s have the potential for such activity (Uryu).
23. Sucrogels are potentially useful for oral drug delivery (Gruber & Greber, 1991).

7. Conclusions

It is thus clear that more efforts are needed to synthesize poly(vinylsaccharide)s by avoiding multi-step protection-deprotection procedures, at the same time having the ability to control the incorporation of sugars to give tailor made properties for biodegradability, hydrophilicity, solubility and physical and mechanical properties. Our group is currently working along these lines to synthesize linear poly(vinylsaccharide)s by grafting of monosaccharides and disaccharides onto functional polyolefins without having to use hydroxyl protection group chemistry of the sugar molecule. The advantage of this procedure is that it is a single step process. Initial results have shown some promise and we plan to extend our work to oligosaccharides. Another interesting aspect of the study would be to obtain structure–property relationships by reacting the functionalized polymer with specific hydroxyls of the sugar. These sugar modified polyolefins have been found to have greatly enhanced rates of biodegradation as compared to the original functionalized polyolefins (Galgali, Varma, Gokhale, Puntambekar, & Khire, 2002).

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