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Sugar-linked biodegradable polymers: Regio-specific ester bonds of glucose hydroxyls in their reaction with maleic anhydride functionalized polystyrene and elucidation of the polymer structures formed

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Abstract

In the development of sugar-linked synthetic polymers as biodegradable polymers, it is imperative to know the variety of polymer structures formed by the reaction of a multi-functional sugar molecule with the functionalized synthetic polymer on which the sugar is to be anchored. Enzymes produced by the microorganisms causing the polymer to biodegrade can be sensitive to the particular type of sugar hydroxyl utilized (such as anomeric, primary, or secondary hydroxyl group) for getting anchored to the polymer. In this paper, we present synthesis of regio-specific ester derivatives of glucose with anhydride, functionalized polymers, i.e., ester formation specifically with the anomeric, primary or secondary hydroxyls of glucose. Characterization of these different esters groups was done using FTIR spectroscopy; each ester peak was further deconvoluted to yield its different components. For this purpose, we studied the reactions of D-glucose, 6-*O*-trityl glucose, methyl glucoside, 1,2-5,6-diisopropylidene-D-glucose, and 1,2,3,4-tetraacetyl-D-glucose with maleic anhydride functionalized polystyrene (PSMAH). In this study, the primary hydroxyl of glucose was found to be even more reactive than the anomeric hydroxyl. The peaks at ~1716, ~1725, and 1729–1737 cm^{-1} were assigned to the ester carbonyl of the anomeric, primary, and secondary hydroxyls of glucose (C2, C3, and C4), respectively. An attempt was made to quantify the extent to which the different polymer structures are formed in a particular reaction by taking ratios of non-variable reference peaks (polystyrene peak at 1493 cm^{-1}) and variable peaks caused by the reaction (the residual anhydride carbonyl at 1780 cm^{-1}).

Keywords: Biodegradable polymers; Sugar-linked polystyrene; Regio-specific; Functionalized synthetic polymer; Glucose

1. Introduction

In one of our recent studies (Galgali, Puntambekar, Gokhale, & Varma, 2004; Galgali, Varma, Puntambekar, & Gokhale, 2002), we reported our results on the biodegradation of carbohydrate-linked polystyrenes, prepared by reacting poly(styrene maleic anhydride) (PSMAH) with unprotected sugars by polymer analogous reactions. The most striking observation of this study was that incorporation of even minute quantities of sugar brought about substantial enhancement in the rates of biodegradation of these polymers. Since the grafting percentages were very low (typically less than 3% by weight, determined by the phenol-sulfuric acid assay), the NMRs of these polymers appeared as very weak signals that which were not useful for chemical characterization purposes. In this context, FTIR spectroscopy proved to be a useful tool to characterize these polymers. The FTIR spectra show changes in the absorption bands in the region 3650–2500 cm^{-1} due to hydrogen-bonded hydroxyl groups and H-bonding involved in case of carboxylic acids (Wang, Zhu, Wang,

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& Zhang, 1999; Zhbankov, 1966). The reduction in the intensity of the carbonyl stretching bond of the anhydride group, with occurrence of a new broad band at ~1730 cm^{-1} suggests opening of some of the anhydride rings with the formation of acid and ester groups. The FTIR spectrum of glucose-linked PSMAH did not give any information regarding which of the glucose hydroxyl groups has been esterified and to what extent. Knowledge of this information is extremely important in order to evaluate the diversity of the polymer structures produced by the reaction of glucose and its derivatives with functionalized polymers. If the reactivity of the individual hydroxyl groups of glucose can be controlled, then it also presents us an opportunity to study the specificity of enzymes for that particular type of ester linkage (i.e., ester with anomeric, or primary or secondary hydroxyl). In order to elucidate the reactivity of the different glucose hydroxyls, different glucose derivatives with specific hydroxyls protected, were grafted onto PSMAH, and were characterized by FTIR spectroscopy. The WAXRD of polystyrene, polystyrene-maleic anhydride copolymer (PSMAH), and glucose-linked PSMAH show differences, which can be related to their structures and morphology.

2. Experimental

2.1. Materials

The glucose derivatives viz. 6-*O*-trityl D-glucose, 1,2-5,6-diisopropylidene-D-glucose and 1,2,3,4-tetraacetyl-D-glucose were synthesized by standard methods (Otto & Schmidt, 1963; Whistler & Bemiller, 1972). 1,2-5,6-Diisopropylidene-D-glucose (diacetone D-glucose) and poly(styrene maleic anhydride) containing 14 weight percent of maleic anhydride were obtained from Aldrich Co. and used as such without further purification and analysis. The general procedure for esterification of poly(styrene maleic anhydride) with different sugars has been reported elsewhere (Galgali et al., 2002). However, all the reactions of the different derivatives were synthesized under identical conditions.

2.2. Instrumental methods

The FTIR of PSMAH and sugar-linked PSMAH were all recorded as films cast from tetrahydrofuran (THF), *N*,*N*′-dimethylformamide (DMF) or chloroform solutions. The spectra were recorded on Perkin Elmer Spectrum 1 instrument at a resolution of 4 cm^{-1} and the numbers of scans were 200. Fourier deconvolution was used for assignment of the different ester carbonyls formed by the reaction of the different hydroxyls of glucose with the maleic anhydride component of PSMAH. The gamma (γ) values (1.5–2.3) and the smoothening points (58–83) used for the deconvolution were within the acceptable limits of the Perkin Elmer Spectrum 1 deconvolution software.

WAXRDs were recorded on a Rigaku Dmax 2500 with 2θ values ranging from 0° to 40°. Quantification of glucose linked to the PSMAH was done by the phenol–sulfuric acid assay (Dubois, Gilles, Hamilton, Rebers, & Smith, 1956).

3. Results and discussion

The FTIR spectrum of PSMAH was recorded, and peak assignments are based on reported spectral assignments of polystyrene and PSMAH (Fig. 1 and Table 1).

In addition to the C=C stretching frequencies of aromatic compounds present in the spectrum of polystyrene, the FTIR spectrum of PSMAH shows bands at 1780 and 1857 cm^{-1} due to the symmetric and asymmetric carbonyl stretching frequencies of the anhydride group and also a band at 1220 cm^{-1} which is attributed to a five membered cyclic anhydride (Bellamy, 1975).

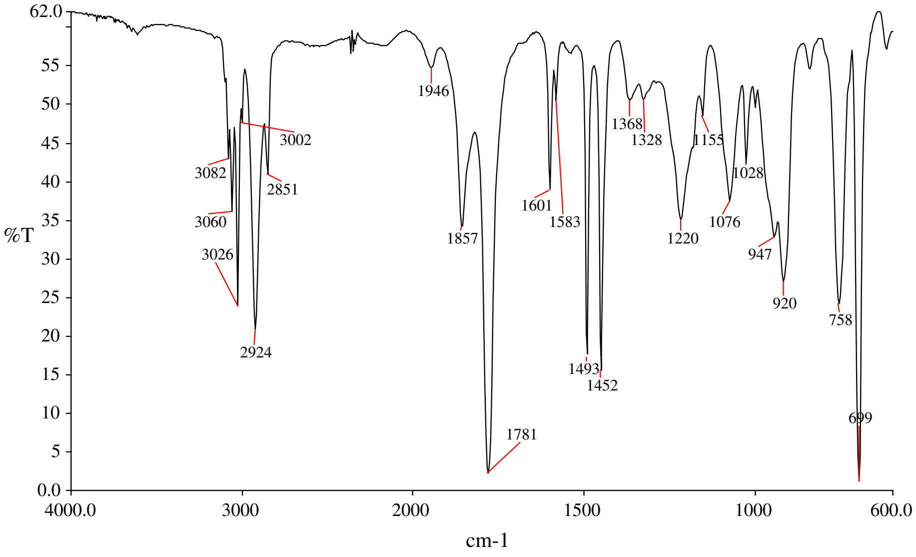

Fig. 1. FTIR spectrum of unmodified PSMAH.

Table 1
Peak assignments for PSMAH used in our study

Peak at (cm^{-1})	Assignment	Reference
3060 and 3026	Aromatic C—H stretching	Mark and Bikales (1987)
2923 and 2852	Aliphatic C—H stretching	Mark and Bikales (1987)
1857	Asymmetric >C=O frequency of the anhydride	Bellamy (1975)
1780	Symmetric >C=O frequency of the anhydride	Bellamy (1975)
1601, 1493, and 1453	In plane bond-stretching phenyl ring	Mark and Bikales (1987)
1076	B_1 ring vibration in mono-substituted benzenes	Painter and Koenig (1977)
756	Out of plane H	Mark and Bikales (1987)
700	Out of plane phenyl ring	Mark and Bikales (1987)

The FTIR spectra of the sugar linked PSMAH polymers show reduction in the intensities of the anhydride carbonyl bands at 1780 and 1857 cm^{-1} with appearance of a new carbonyl band at ~1730 cm^{-1} assigned to ester and carboxylic acid carbonyl. This variable peak at 1780 cm^{-1} was chosen for comparison with the reference peak of polystyrene (1493 cm^{-1}), which does not vary, with the progress of the reaction. Hydrolysis of PSMAH, i.e., the opening of the anhydride group would result in formation of a diacid. The FTIR spectrum of the hydrolyzed product would show a band in the carbonyl region. To find the exact position of this carbonyl an FTIR spectrum of hydrolyzed PSMAH was recorded (Fig. 2), along with the deconvoluted spectrum (Fig. 3). This confirms the position of the acid carbonyl group at ~1711 cm^{-1} which is consistent with the reported value (Bruch, Mäder, Bauers, Loontjens, & Mülhaupt, 2000; Yan & Zhu, 1999).

On reaction of PSMAH with an alcohol (in this case a sugar), the anhydride opens up into an ester and an acid. The carbonyl band (overlapping ester and carboxylic acid) appeared at ~1730 cm^{-1}.

Fig. 4 shows the FTIR spectrum of D-glucose linked PSMAH. The FTIR spectrum shows reduction in the intensity of the 1780 cm^{-1} anhydride carbonyl and appearance of a new peak at ~1730 cm^{-1}. The latter peak is formed by the merging of the ester and carboxylic acid carbonyls, as shown in our earlier work (Galgali et al., 2002). The ester carbonyl bond was deconvoluted to find out the different ester groups formed by the reaction of anomeric, primary and secondary hydroxyls. The deconvoluted carbonyl spectrum showed six peaks – at 1709, 1715, 1724, 1731, 1737, and 1747 cm^{-1} (see Fig. 5).

The peak assignments of the different ester groups in case of glucose-linked PSMAH could be made only after studying the deconvoluted carbonyl regions of the different glucose derivatives linked to PSMAH and the hydrolyzed product of PSMAH. The spectra of these derivatives are shown below, along with the respective deconvoluted spectra.

Fig. 6 shows the FTIR spectrum of methyl glucoside linked PSMAH. The FTIR spectrum shows changes similar to that of the glucose-linked counterpart. However, the deconvolution of the carbonyl region (Fig. 7) shows five peaks, in contrast to six peaks in case of glucose-linked PSMAH. The peaks at 1710 and 1747 cm^{-1} can be ascribed to the acid carbonyl (formed by partial hydrolysis of MAH, as described earlier). The other three peaks at 1737, 1731, and 1724 cm^{-1} are the three different ester groups formed in the reaction. Comparing this deconvolution with that of the glucose reaction (Fig. 5), we find

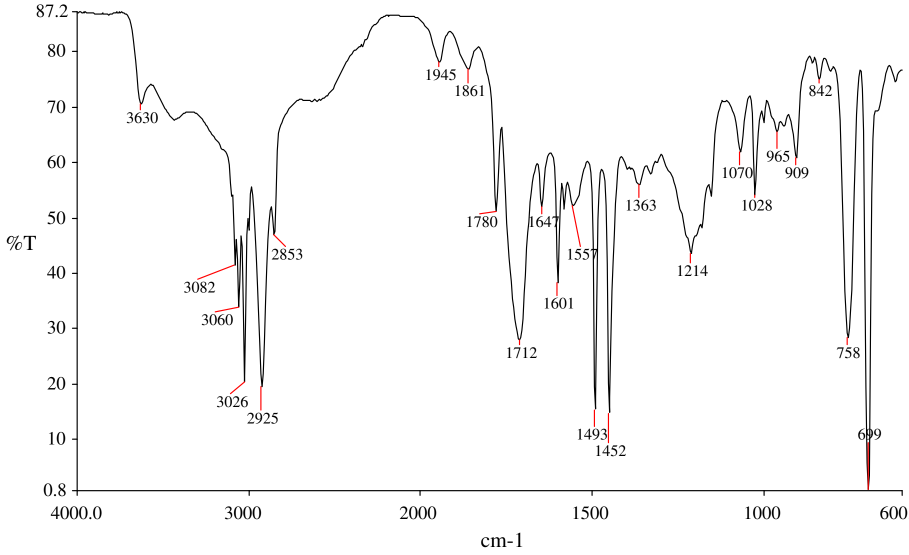

Fig. 2. FTIR spectrum of hydrolyzed product of PSMAH.

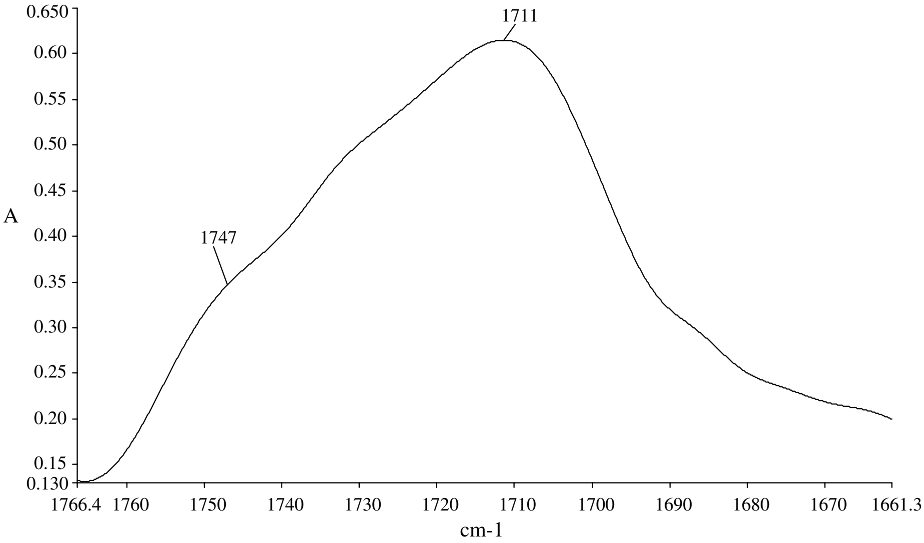

Fig. 3. Deconvoluted carbonyl region of the hydrolyzed product of PSMAH.

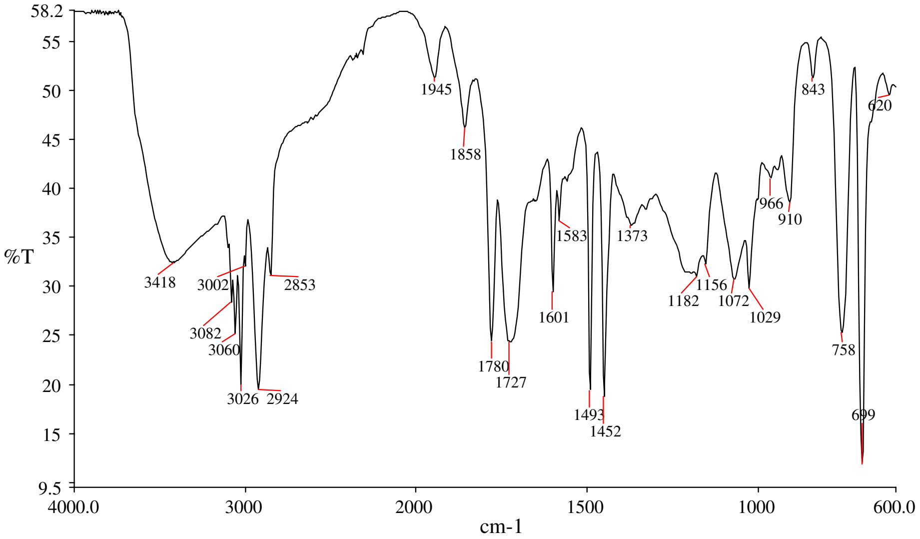

Fig. 4. FTIR spectrum of glucose linked PSMAH.

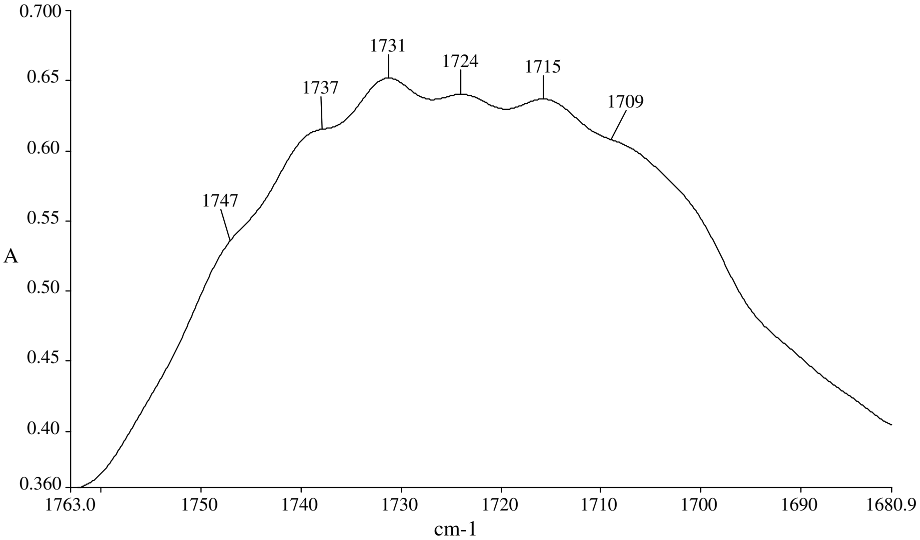

Fig. 5. Deconvolution of the carbonyl band of glucose-linked PSMAH.

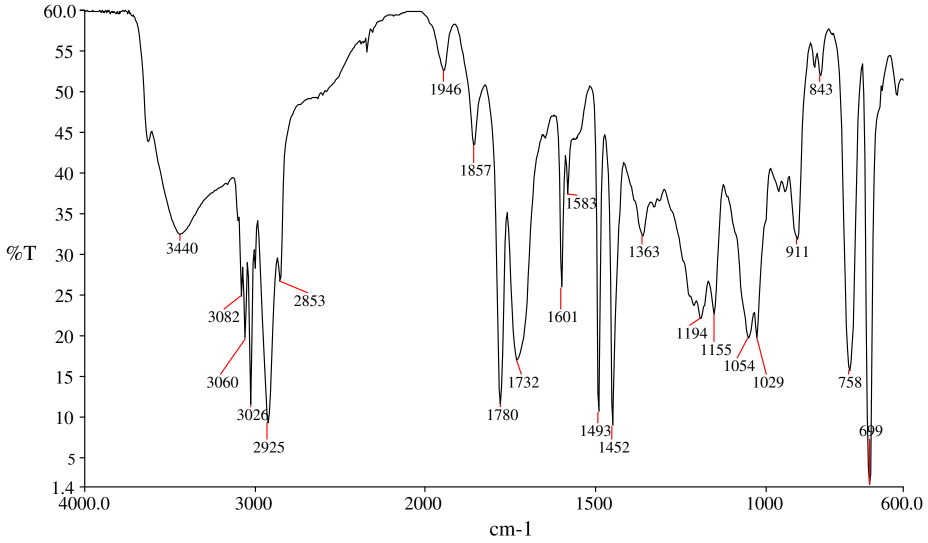

Fig. 6. FTIR spectrum of methyl glucoside linked PSMAH.

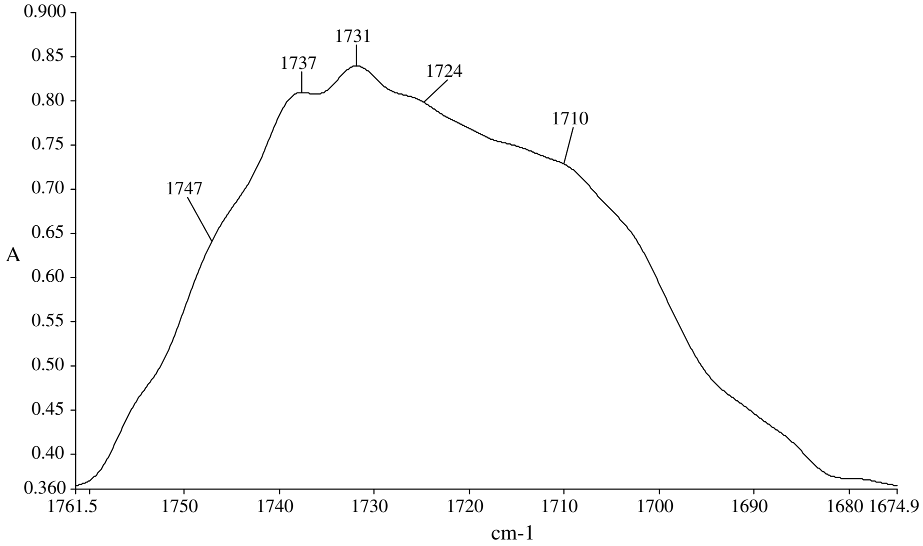

Fig. 7. Deconvolution of carbonyl band of methyl glucoside-linked to poly(styrene maleic anhydride).

that the peak at 1715 cm^{-1} is missing in Fig. 7. This shows that the peak at ~1715 is the ester carbonyl formed by the reaction of the anomeric hydroxyl of glucose with the maleic anhydride component of PSMAH (since the anomeric hydroxyl group is absent in case of methyl glucoside).

Fig. 8 shows the FTIR spectrum of diacetone D-glucose linked to PSMAH. The spectrum shows reduction in the intensity of the anhydride band at 1780 and 1857 cm^{-1} and appearance a new carbonyl band at 1735 cm^{-1} as compared to PSMAH. A peak also appears at 1373 cm^{-1}, which is a characteristic of gem dimethyl group present in diacetone-D-glucose (Kobayashi & Sumitomo, 1980; Silverstein & Webster, 1998). The deconvolution of the carbonyl band shows splitting of the peak into two peaks, one at 1736 cm^{-1} (ester carbonyl) and 1711 cm^{-1} (carboxylic acid) (Fig. 9). Diacetone-D-glucose has only one free hydroxyl group, which is secondary in nature. Hence the peak at 1736 cm^{-1} can be attributed to the ester carbonyl formed by the reaction of the secondary hydroxyl of the glucose molecule with the anhydride moiety.

Fig. 10 shows the FTIR spectrum of 6-*O*-trityl-D-glucose linked to poly(styrene maleic anhydride). The FTIR spectrum shows reduction in the intensity of the anhydride carbonyl at 1780 and 1857 cm^{-1} and appearance of a new peak at 1720 cm^{-1} due to the ester and the carboxylic acid carbonyls.

The deconvoluted FTIR spectrum of 6-*O*-trityl-D-glucose linked PSMAH (Fig. 11) shows splitting of the carbonyl band into five peaks at 1711, 1719, 1729, 1737, and 1747 cm^{-1}. From the above discussion, it is clear that the peaks at 1711 and 1747 cm^{-1} are due to the carboxylic component of the polymer, whereas, the 1719 cm^{-1} peak is due to the ester carbonyl of the anomeric hydroxyl of

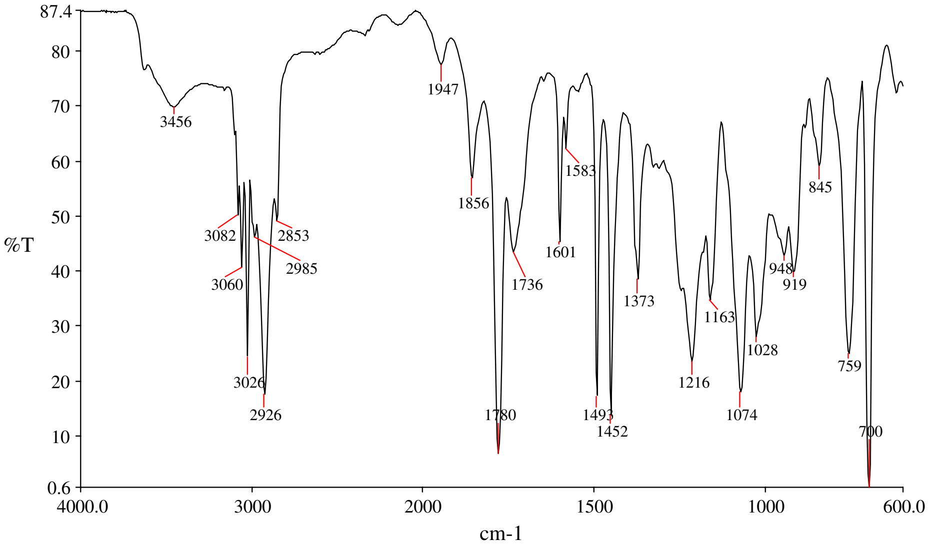

Fig. 8. FTIR spectrum of 1,2-5,6-diisopropylidene-(diacetone)-D-glucose-linked PSMAH.

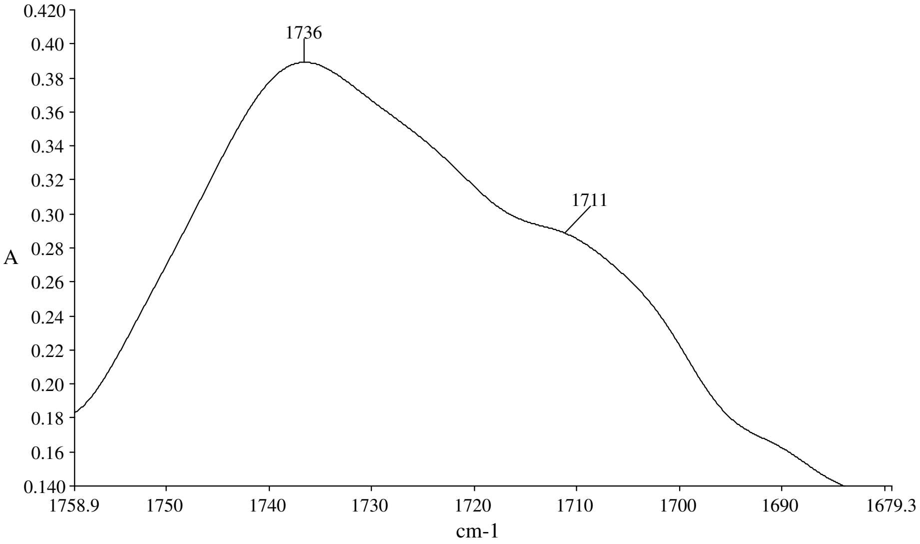

Fig. 9. Deconvoluted carbonyl band of diacetone-D-glucose-linked PSMAH.

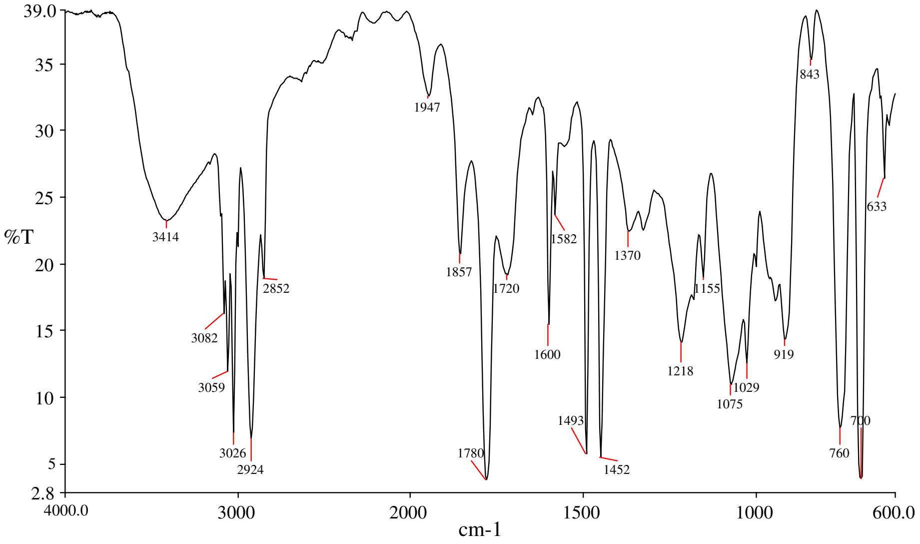

Fig. 10. FTIR spectrum of 6-*O*-trityl-D-glucose-linked PSMAH.

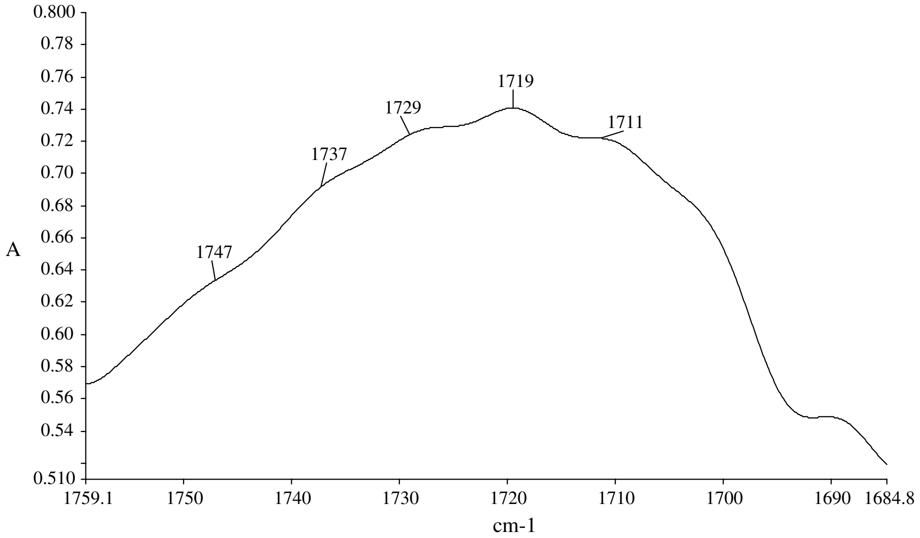

Fig. 11. Deconvoluted carbonyl of 6-*O*-trityl-D-glucose-linked PSMAH.

the glucose molecule and the peaks at 1729 and 1737 cm^{-1} are due to the ester carbonyls of the secondary hydroxyls of the sugar.

Table 2
Tabulation of 2*θ* values and *d* values for the peaks, along with ratios of the two peaks and the full-width at half maximum (FWHM)

Sample	2*θ* Value	Ratio of peak 1 to 2	*d* Value	FWMH
PSMAH	09.6	1.048	9.2	2.7
	18.9		4.7	3.8
(PSMAH–glucose, 1.15 wt%)	11.5	0.945	7.7	3.1
	18.6		4.8	3.8
(PSMAH–glucose, 0.92 wt%)	10.9	1.073	8.1	2.8
	19.2		4.6	3.6
PSMAH–6-*O*-trityl-D-glucose	11.4	0.95	7.8	2.9
	19.4		4.6	4.2
PSMAH–methyl glucoside	10.7	0.80	8.2	3.7
	18.8		4.7	3.9

Referring back to Fig. 5 (deconvolution of the carbonyl band of glucose-linked PSMAH showing six peaks), we can now make, by elimination, assignment of the ~1724 cm^{-1} peak as that being the ester peak of the primary hydroxyl group. This was further confirmed from Fig. 11, showing that the deconvoluted carbonyl of 6-*O*-trityl-D-glucose linked PSMAH has no peak at ~1724 cm^{-1} (since the trityl group selectively reacts with the primary hydroxyl). Thus, we have been able to assign all the different ester peak positions.

An attempt was made to quantify the extent to which the different polymer structures are formed in a particular reaction by use of ratios of non-variable IR reference peaks (polystyrene peak at 1493 cm^{-1}) and variable peaks caused by the reaction (the residual anhydride carbonyl at 1780 cm^{-1}). The ratios are tabulated in Table 2.

The WAXRD patterns of the sugar-linked PSMAH polymers are shown in Fig. 12 and the values are tabulated

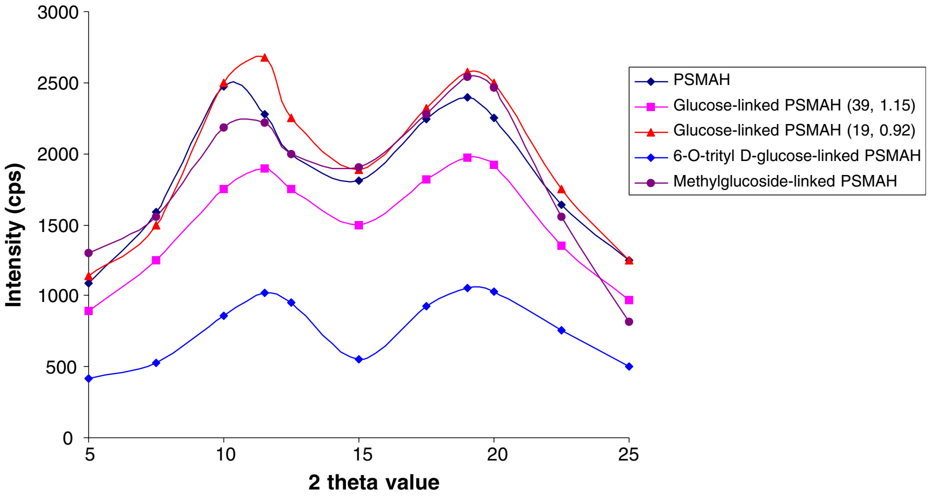

Fig. 12. Overlapped WAXRD spectra of PSMAH and various sugar linked PSMAH derivatives.

in Table 2. It is clearly seen that the structure of the starting polymer PSMAH is not greatly disturbed by anchoring small quantities (~1% by weight) of sugar molecules. The greatest line broadening (higher full-width at half maximum (FWHM)) is for the trityl derivative of glucose linked PSMAH, which is expected due to the three bulky methyl groups causing greater structural changes in the PSMAH polymer chain.

In Table 3, the lower the value of the ratio 1780 cm^{-1}/1493 cm^{-1}, the greater the extent of reaction, since the 1780 cm^{-1} peak represents the unreacted part of the anhydride carbonyl. Assuming that for steric reasons only one hydroxyl of the glucose or glucose derivative can react with PSMAH, we see in Table 2 that the glucose hydroxyl has 60% "secondary hydroxyl character" (three secondary hydroxyls, one primary, one anomeric), whereas the methyl glucoside hydroxyl has 75% "secondary hydroxyl character" (three secondary hydroxyls, one primary hydroxyl) and the 1,2-5,6-diisopropylidene-D-glucose has 100% "secondary hydroxyl character". The ratios obtained are indicative of the different extents to which the reaction products would have these linkages. The different reaction products produced in each reaction are shown in Figs. 13–16.

Fig. 16 shows that we obtain a single reaction product with 1,2-5,6-diisopropylidene-D-glucose, whereas multiple products are produced with the other glucose derivatives (Figs. 13–16). Deprotection of the isopropylidene groups after the reaction with the PSMAH would yield a homogenous glucose reaction product with secondary hydroxyls reacted with PSMAH, which can be studied with polymer degrading microorganisms in the development of biodegradable polymers, as function of this type of specific ester bond.

Similarly, we prepared the glucose derivative with a free primary hydroxyl linked to PSMAH, via the 1,2,3,4-tetraacetyl-D-glucose linked to PSMAH (for FTIR of the

Table 3
Ratio of peak intensities of 1780 and 1493 cm^{-1}

Name of the derivative linked to PSMAH	No. of free hydroxyls	Nature of the free hydroxyl group	Corrected heights		Ratio (1780 cm^{-1}/1493 cm^{-1})
			1780 cm^{-1}	1493 cm^{-1}	
PSMAH	–	–	1.52	0.55	2.76
D-Glucose	5	1: anomeric, 1: primary 3: secondary	0.39	0.568	0.68
Methyl glucoside	4	1: primary 3: secondary	0.59	0.68	0.86
1,2-5,6-Diisopropylidene-D-glucose	1	1: secondary	0.563	0.33	1.71
6-*O*-Trityl-D-glucose	4	1: anomeric 3: secondary	0.7	0.66	1.06
1,2,3,4-Tetraacetyl-D-glucose	1	1: primary	0.425	0.254	1.67

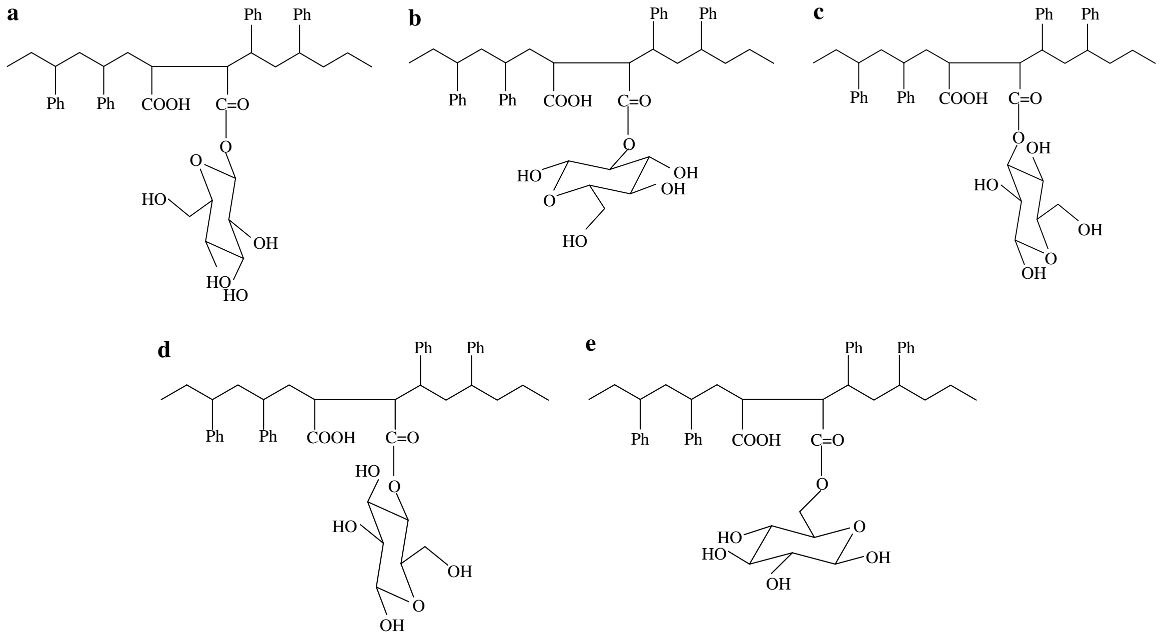

Fig. 13. Polymer structures formed by the attachment of the (a) anomeric hydroxyl (b), (c), (d) secondary hydroxyls and (e) primary hydroxyl in the reaction of glucose with PSMAH.

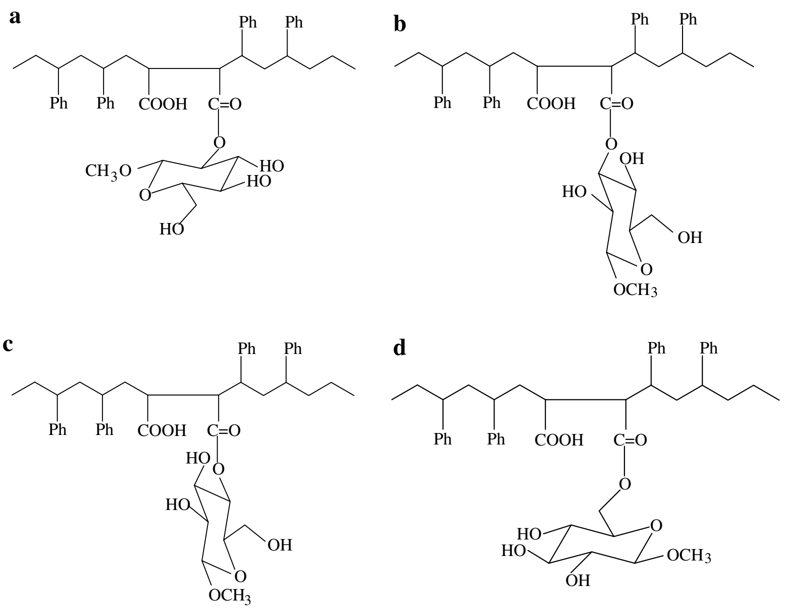

Fig. 14. Polymer structures formed by the attachment of the (a), (b), (c) secondary hydroxyls and (d) primary hydroxyl in the reaction of methyl glucoside with PSMAH.

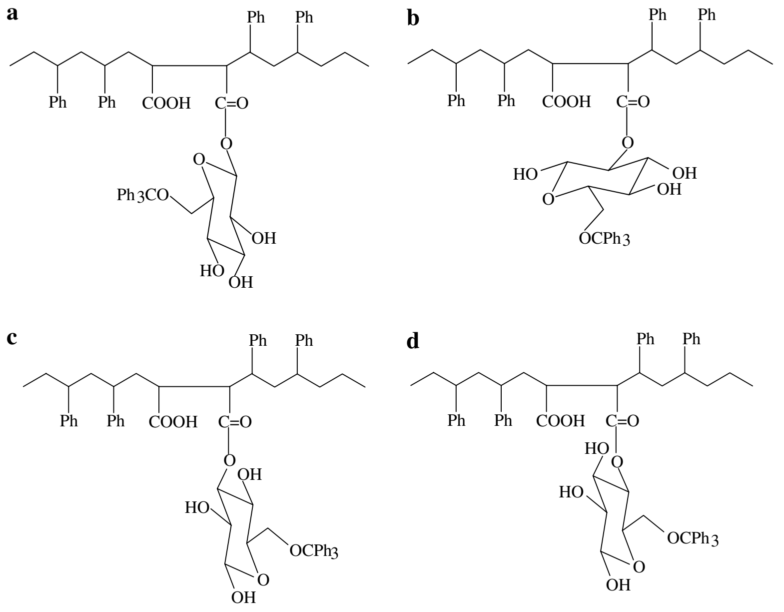

Fig. 15. Polymer structures formed by the attachment of the (a) anomeric hydroxyl (b), (c), (d) secondary hydroxyls in the reaction of 6-*O*-trityl-D-glucose with PSMAH.

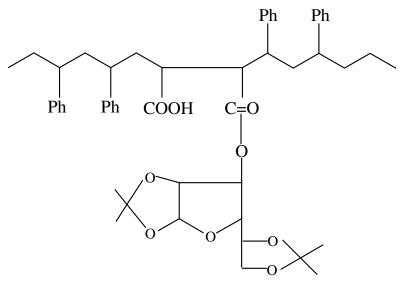

Fig. 16. Polymer structure formed by the attachment of the secondary hydroxyl in the reaction of 1,2-5,6-diisopropylidene-D-glucose with PSMAH.

product see Fig. 17) followed by deacetylation. This reaction product will yield a homogenous glucose reaction product with primary hydroxyl reacted with PSMAH, which can be studied with polymer degrading microorganisms in the development of biodegradable polymers, as function of this type of specific ester bond.

Comparison of the biodegradation kinetics and extent of biodegradation with specific hydroxyl groups would yield key information on the specificity of different enzymes (such as lipases from different sources). Such polymers can

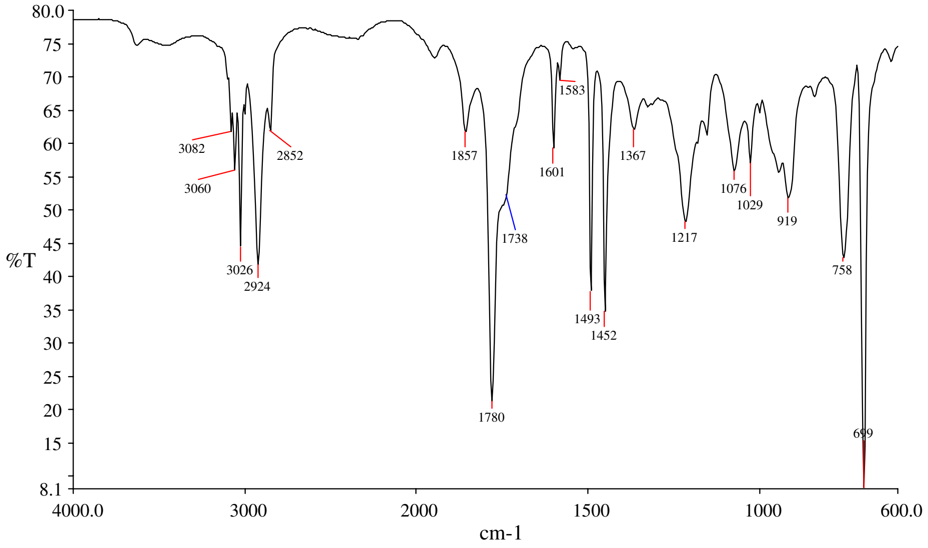

Fig. 17. FTIR spectrum of 1,2,3,4-tetraacetyl-D-glucose linked to PSMAH.

also be used to produce enzymes capable of hydrolysing very specific ester bonds.

4. Conclusion

FTIR Fourier deconvolution technique was helpful in assigning the peak positions of the ester groups formed by the reaction of the different hydroxyl groups of glucose with the maleic anhydride moiety of the PSMAH polymer. The data on relative reactivities of the anomeric, primary and secondary hydroxyls of glucose gave information regarding the extent to which the different polymer structures are formed in the reaction of glucose and its derivatives with PSMAH. This is of particular importance, since structural features can influence chemical and physical properties, in addition to rates of biodegradation. There are several other factors, which can play a role in the relative reactivities, such as the steric hindrance and solubility of the derivative in the solvent. Further, the 1,2-5,6-diisopropylidene-D-glucose derivative exists in the furanose form, whereas all the other derivatives studied are in the pyranose form. Therefore, a larger variety of carbohydrate derivatives and model compounds have to be studied in order to arrive at results throwing light on rates of biodegradation and enzyme specificity for different types of ester linkages.

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