Industrial Crops & Products 111 (2018) 529–535

Contents lists available at ScienceDirect

Industrial Crops & Products

journal homepage: www.elsevier.com/locate/indcrop

Research paper

# One-pot solvent-free synthesis and characterisation of hydroxypropylated polyflavonoid compounds

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ARTICLE INFO

*Keywords:*
Flavonoid
Proanthocyanidin
Condensed tannin
Etherification
Poly(lactic acid)
Melt spinning

ABSTRACT

An efficient, one-pot solvent-free synthesis using mild base catalysis has been developed to prepare hydroxyalkylated flavonoid and polyflavonoid compounds. Based on reaction conditions developed with catechin, condensed tannins have been reacted with propylene oxide to give a range of hydroxypropyl substitutions and chain extended compounds. The resulting etherified flavonoid and polyflavonoid products were characterised to reveal the degree of substitutions and non-specificity of hydroxypropylation. Analysis showed the products to have decreased thermal stability with degradation onset between 100 and 200 °C. Hydroxypropylated catechin products have glass transitions (−20 to 80 °C) which decrease with greater substitution, whereas chain-extended hydroxypropylated polyflavonoids show sub-ambient gelation and melt behaviours. An initial application of the hydroxypropylated polyflavonoids was demonstrated by compounding with poly(lactic acid) to produce high tannin content melt-spun fibres. These results demonstrate the facile synthesis of hydroxypropylated flavonoids as a sustainable bio-based feedstock for various material applications.

## 1. Introduction

Condensed tannins, also termed proanthocyanidins, are polyphenolic oligomers and polymers of the flavan-3-ol monomer possessing various hydroxylation patterns of the flavanyl unit (Fig. 1). They are commonly found in the leaf, wood, bark, and fruit of plants and exhibit high chemical and biological activities including antioxidant, antimicrobial, and UV absorption properties (De Bruyne et al., 1999). The chemical and biological properties are dictated by multiple hydroxyl patterns of the flavanyl unit which have been exploited in applications such as leather tanning, wood adhesives, and nutraceuticals with emerging uses in personal care and pharmaceuticals (Pizzi, 2006; Reuter et al., 2010; Ververidis et al., 2007). However, these polyphenolic materials are hydrophilic, vitrifiable, and lack defined macromolecular properties such as melt or flow which can be limiting factors for new applications. Any enhancement in lipophilicity and processing properties may broaden the potential of tannins and extend their utility beyond current uses (Grigsby et al., 2014; Grigsby et al., 2015).

Various chemical modifications of the flavonoid hydroxyl groups have been reported to improve the lipophilic solubility and impart melt flow behaviour (García et al., 2016b). Esterification of flavonoids has been extensively reported and can be achieved by direct acylation using acyl chlorides and anhydrides or by transesterification (Bridson et al., 2013; Grigsby et al., 2013; Nomura et al., 2004; Urano et al., 1991). Etherification is another potential modification relevant to flavonoids achievable by base-promoted $S_N2$ type Williamson ether synthesis and demonstrated using alkyl halides to partially functionalise hydroxyl groups of quercetin, chrysin, and tannin (Mitchell et al., 1998; Wurm and Rehn, 1985; Zheng et al., 2003). Etherification has also been achieved using propylene carbonate, however the carbonate functionality may further react in chain coupling reactions (Duval and Avérous, 2016). Epoxide ring opening reactions are an alternative, efficient route to preparing ethers under neutral, basic, or acidic conditions (Herzberger et al., 2016). Initial work in this field was performed using lignin, which has similarities to polyflavonoids, being a forestry derived resource with multiple hydroxyl functionality. Changes in the thermal and mechanical properties of lignin were achieved by hydroxyalkylation with various alkylene oxides (Lora and Glasser, 2002; Sen et al., 2015). Hydroxypropylation of lignin improves non-polar solubility and decreases the glass transition temperature by disrupting hydrogen bonding (Glasser et al., 1984). As a result, these modified lignins have found applications for example in polyurethane foams to improve stability at elevated temperature (Lora and Glasser, 2002). Similarly, flavonoid modification with epoxides has also been reported including quercetin alkylation (Courbat and Valenza, 1973) and tannin

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https://doi.org/10.1016/j.indcrop.2017.11.028
Received 10 August 2017; Received in revised form 9 November 2017; Accepted 12 November 2017

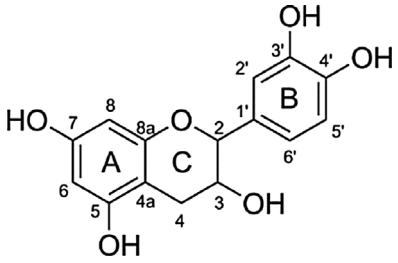


**Fig. 1.** Structure of catechin; an example flavan repeat unit common in condensed tannins.

alkoxylation in anhydrous or aqueous alkali media (Arbenz and Avérous, 2015; García et al., 2016a; García et al.,2013). Like lignin, these derivatives were shown to have reduced glass transition temperatures and have been employed as polyols in polyurethane synthesis (García et al., 2015; García et al.,2014).

Given the recent reports of alkoxylation of tannins in alkali media together with emerging routes to alkyloxylates based on renewables, this paper provides an alternative facile route for the efficient synthesis of hydroxypropylated polyflavonoid derivatives. A one-pot, solvent-free synthesis of tannin hydroxypropyl derivatives was developed using mild base to avoid the potential for base-catalysed rearrangements (Hashida and Ohara, 2002). Resorcinol and the flavanyl monomer catechin were employed as model compounds to first develop $S_N2$ alkoxide modifications of flavonoid materials. This chemistry was then adapted to similarly modify different polyflavonoid materials in a solvent-free system. The resulting etherified products have been chemically characterised and their processability into an industrial product initially evaluated by melt-spinning with poly(lactic acid) (PLA) for potential use in textile, filter, composite, and health care applications.

## 2. Materials and methods

### 2.1. Materials

Resorcinol (BDH) was purified by refluxing over potassium hydroxide (30 min) followed by distillation and storage over A4 molecular sieve. (+)-Catechin hydrate was obtained from Fluka and dried under vacuum (> 16 h) prior to use. Commercial quebracho tannin (QT, Colatan GT100) was sourced from Unitan (Argentina). Pine bark tannin (PBT) was extracted from fresh *Pinus radiata* bark into hot water (90 °C) and after filtering, was subsequently spray dried. Both tannin materials were dried under vacuum (> 16 h) before use. Laboratory reagent grade propylene oxide (BDH), triethylamine ((TEA) Aldrich) and dibutyltin oxide (Aldrich) were used as received without further purification. Poly(lactic acid) 3001D was obtained from NatureWorks (USA) and dried at 105 °C before use. All other reagents were general purpose grade and used as received.

### 2.2. Synthesis of hydroxypropylated resorcinol and catechin

The general procedure involved adding 0.1–0.2 g catechin (or resorcinol) into a 15 mL Teflon-lined stainless steel pressure reactor, triethylamine (5 % w/w), and 1, 3, 5, 10, or 20 mol equivalents of propylene oxide (PO) to give products labelled C1 to C20, respectively. The reactor was sealed and heated to 110 °C for 24 h, before cooling to room temperature. The product mixture was neutralised with 0.1 mol $L^{-1}$ hydrochloric acid, poured into butanol and washed with saturated sodium bicarbonate, water, and finally saturated sodium chloride before drying with magnesium sulfate and concentrating by rotary evaporation.

**Table 1**
Overview of Processed Tannin/Polymer Blends.

| Blend | Ratio (PLA:PBT) | Processing Temperature (°C) | | Observation |
|---|---|---|---|---|
| | | Rotor | Head | |
| PLA | 100 | 160 | 179 | Good fibre |
| PLA/DBTO | 100 | 155 | 174 | Good fibre |
| PLA/PBT/Gly | 75/25 | 155 | 170 | Good fibre |
| PLA/PBT/Gly | 50/50 | 165 | 180 | Decomposition, no fibre |
| PLA/PBT5 | 75/25 | 155 | 179 | Difficulty drawing fibre |
| PLA/PBT5/DBTO | 75/25 | 150 | 170 | Good fibre |
| PLA/PBT5/60Gly | 75/25 | 155 | 170 | Good fibre |
| PLA/PBT5/75Gly | 50/50 | 155 | 165 | Good fibre |
| PLA/PBT5/60Gly | 25/75 | 150 | 162 | No fibre |

### 2.3. Synthesis of hydroxypropylated polyflavonoids

Being similar to the above, the general synthesis procedure involved adding 1.0 g tannin (PBT or QT) into a Teflon-lined stainless steel pressure reactor (15–100 mL), triethylamine (5 % w/w) and 1, 3, 5, 10, or 20 mol equivalents of PO (*ca.* 24–480 % w/v) to give products labelled PBT1 to 20 and QT1 to 20, respectively. Mole equivalents were based on the average C-15 flavan unit determined for PBT and QT (Bogun, 2007; Pasch et al., 2001). The reactor was sealed and heated to 110 °C for 24 h, before cooling to room temperature. The product mixture was neutralised with 0.1 mol $L^{-1}$ hydrochloric acid and concentrating by rotary evaporation.

### 2.4. Compounding and melt spinning

Polymer blending and melt spinning with PLA was conducted on a Dynisco laboratory mixing extruder (Grigsby and Kadla, 2014). Blends of PLA with 25–75 % hydroxypropylated tannin, 60–75 % glycerol (Gly) or 0.1–0.5 % dibutyltin oxide (DBTO, as transesterification catalyst) were fed into the extruder employing conditions outlined in Table 1. Blended material was processed by first extruding as 4 mm diameter rods before reprocessing and melt spinning as a fibre drawn from a 0.5 mm outlet die. The melt spun fibre was collected onto a spool with minimal tensioning of the fibre.

### 2.5. Characterisation

Solution state NMR spectra were recorded on a Bruker Avance DPX 400 spectrometer with a 5 mm inverse broad band probe (Bruker). Chemical shifts were reported in δ ppm referencing to tetramethylsilane. The molar substitution (MS) was determined by $^1$H NMR spectroscopy using Eq. (1) adapted from Bridson et al. (Bridson et al., 2013),

$$DS = \frac{I_1/n_1}{I_2/n_2} \quad (1)$$

Where: $I_1$ is the ether $CH_3$ integral; $n_1$ is the number of protons corresponding to the ether integral; $I_2$ is the polyphenol unit aromatic integral; and $n_2$ is the number of aromatic protons based on the hydroxylation pattern of the monomeric polyphenol unit (catechin = 5, pine bark tannin = 3.5, quebracho tannin = 4) (Bogun, 2007; Pasch et al., 2001).

Solid state $^{13}$C NMR spectra were obtained on a Bruker Avance DRX 200 instrument with a 7 mm doubly tuned $^1$H/X MAS probe (Bruker).