Star-shaped lactic acid based systems and their thermosetting resins; synthesis, characterization, potential opportunities and drawbacks

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List of abbreviations:

LA: lactic acid
PLA: poly lactic acid
S-LA: star-shaped LA based resins
ROP: ring opening polymerization
EF: end-functionalization
NMR: Nuclear Magnetic Resonance
DMA: dynamic mechanical analysis

37 TGA: thermogravimetry analysis
38 MW: molecular weight
39 PLGA: poly lactic-co-glycolic acid
40 PGA: poly glycolic acid
41 PEG: poly ethylene glycol
42 PENTA: pentaerythritol
43 IT: itaconic acid
44 MAAH: methacrylic anhydride
45 MAA: methacrylic acid
46 TEG: tetra (ethylene glycol)
47 THMP: 1,1,1-tri(hydroxy methyl)propane
48 DPE: dipentaerythritol
49 TAN: Total Acid Number
50 FT-IR: Fourier transform infrared spectroscopy
51 USDA: U.S. Department of Agriculture
52 E: modulus of elasticity
53 UTS: ultimate tensile strength
54 HRR: heat release rate
55 FDA: Food and Drug Administration
56

57 **Abstract**

58 Shortcomings of the conventional PLA synthesis methods have encouraged researchers to
59 investigate on alternative methods for PLA synthesis. Utilization of chain extenders is an
60 effective way to achieve high MW polymers. The concept of using star-shaped resins as the
61 reinforced matrices for biocomposites or in biomedical applications is gaining more and more
62 attention day by day. Star-shaped lactic acid based resins are a class of branched resins with a
63 multifunctional core molecule and lactic acid branches. In order to increase the reactivity of
64 branches, the star-shaped resin oligomers can get end-functionalized which yields in a
65 crosslinkable product. Changing the architecture of a polymer from a linear to a multiarm or
66 hyperbranched one, would change its chemical, diffusional and physical-mechanical properties.
67 This review paper presents the current state and recent advances in the synthesis,
68 characterization, properties and applications of the star-shaped resins made from lactic acid and
69 multi-hydroxyl core molecules with a focus on the role of the morphology of the polymer on the

properties of resins. Rheological, physiochemical and thermomechanical properties of to date synthesized star-shaped resins are compared and discussed. Special emphasis would be made on potential opportunities, probable applications and also gaps and drawbacks concerning these systems. This review aims to provide useful information to help future development of efficient, highly engineered bioresins which can be especially designed for a certain application.

Keywords

Star-shaped; Lactic acid; Thermosetting resins; Applications; Limitations

1. Introduction

Different studies have been published on the synthesis of resins from lactic acid (LA) or lactide and branching point molecules. In order to increase the MW of PLA and induce branching points in the structure, different techniques have been employed, including free-radical branching in the presence of epoxides [1], beam irradiation [2], copolymerization with cyclic monomers having hydroxyl groups in the cycle [3] or use of polyfunctional chain extenders. Generally, the star-shaped resins are synthesized via a two-step strategy: polycondensation of LA with the core molecule followed by end-functionalization of the branches. So far, star-shaped LA based resins (S-LA) were synthesized employing core molecules such as ethylene glycol, xylitol, glycerol, pentaerythritol for different applications. The rationales for employing a core molecule in the structure of star-shaped polymers are that it increases the MW of the oligomers, lowers the viscosity and enhances processability of the resin; this technique is also provides a better extended network resulting in better thermomechanical properties of the cured resin. In addition, the core molecule will provide reactive sites which can be further used

for the addition of a special functionality, e.g. a flame retardant agent, a drug carrier, an anti-microbial agent, etc. It is also possible to manipulate the biocomposites' properties by changing the nature and the portion of the block units of copolymers of LA and the core molecule. This manipulation could be in terms of changing the hydrophilicity or designing and altering the voids' sizes of the polymer network. For example, by employing longer oligomers, it is possible to increase the size of the voids in the network and by using hydrophilic monomers, the hydrophilicity of the product can be tailored. Manipulation of both void's size and hydrophilicity will provide the unique opportunity for designing a polymeric matrix for certain component release or a desired drug delivery with a substantial control over release rate.

Different methods have been introduced for synthesizing and characterizing the S-LA. The differences between the S-LA properties, resulted from employing of different core molecules, different lengths of the LA (or co-polymers) monomers in branches, utilization of different end-functionalization (EF) agents, employing different curing techniques as well as using different curing initiators. Choosing a combination of these sets results in a unique product with specific characteristics which could be suitable for a certain purpose. The concept of using star-shaped resins as the reinforced matrices for biocomposites or in biomedical applications is gaining more and more attention day by day. The increasing number of publications during the recent years, concerning the synthesis and characterization of star-shaped resins for different applications, including biocomposites [4-7], coating [8], biomedical [9, 10], drug delivery [11-13], tissue engineering [14], smart packaging, functionalized polymers [15, 16] and so on, reflects the growing importance of these new resins. To date, there is no comprehensive study exists on the different synthesis methods and characteristics of the synthesized S-LA.

This review paper presents the recent advances in the synthesis, characterization, properties and applications of S-LA and their thermosetting systems using a multi-hydroxyl clustering core molecule. The synthesis, chemical and thermomechanical properties of S-LAs are assessed. Special emphasis would be made on potential opportunities, probable applications and also drawbacks concerning the use of the multi-hydroxyl core molecules in the structure of the S-LA. Finally, the limitations and technological gaps of these systems are highlighted. This paper will not address other branched LA based polymers, including dendrimers, hyperbranched, grafted or comb-like polymers; and also, synthetic fiber reinforcements for bio composites are out of the scope of this paper. In addition, studies on fiber treatment for composite productions are excluded from this review article.

This review paper consisted of four different sections. In the first part, the synthesis of the S-LAs are explored. Different synthesis methods of PLA are discussed and currently applied multi-hydroxyl monomers as the core molecule for S-LAs are introduced. The role of EF and attributed methods of end-functionalizing of the branches as well as different methods for curing of the resins are emphasized. In the second part, the characterization of the S-LAs are discussed, including chemical characterization, general properties and thermomechanical properties. In chemical characterization, titration, nuclear magnetic resonance (NMR) and Fourier transform infrared spectroscopy (FT-IR) of S-LAs are discussed briefly. Special emphasis are made on rheological properties and curing kinetics of the star-shaped resins. The general properties section presents the current knowledge on water absorption properties, the biobased contents and the morphological properties of the S-LAs. Finally, the thermomechanical properties of the cured resins are discussed based on the reported results of dynamic mechanical analysis (DMA), flexural, tensile and charpy testing as well as the thermogravimetry analysis (TGA). The third

part will discuss different applications of these systems, including biocomposites, drug delivery, biomedical and tissue engineering. In the fourth part, the limitations and future of these systems are discussed.

2. Introduction to PLA synthesis methods

Lactic acid (2-hydroxy propionic acid) exists as the two stereo isomers of L-LA and D-LA, and can be produced via bacterial fermentation of carbohydrates or chemical synthesis. The LA produced by the chemical route is an optically inactive racemic mixture (50/50 L-D) while fermentation-derived LA exists almost exclusively as L-LA [17]. Due to major limitations of chemical synthesis, the fermentation pathway is often preferred [18, 19]. Poly lactic acid (PLA), an aliphatic polyester made up of LA monomers, is a biodegradable and compostable thermoplastic which has extensive applications in biomedical fields, including bone fixation, drug delivery and tissue engineering. The applications of PLA are not limited to biomedical field and it has potential for use in a wide range of applications, including food applications, packaging, structural composites, furnishings, etc. [19, 20].

Synthesis of PLA from LA can follow two different routes of polymerization, including condensation polymerization of LA and polymerization through lactide formation [19]. The condensation polymerization route includes direct condensation-polymerization of LA and azeotropic dehydration condensation of LA. In direct condensation-polymerization, esterification of monomers happens with the aid of solvents and the consequent water is removed progressively at high temperatures and partial vacuum. The molecular weight of the condensation derived polymer would be low, which results in poor mechanical properties [19, 21]. In azeotropic dehydration-condensation method, the azeotropic solution and catalysts are

employed to produce a high molecular weight PLA. The azeotropic solution helps to reduce the distillation pressure and enables the separation of the PLA from the solvent. In general, polycondensation methods require a good control over the reaction for achieving a PLA with desired MW, and water, as a byproduct of the condensation, must be efficiently removed from the solution for achieving a high MW PLA [22]. In the lactide formation pathway or ring opening polymerization (ROP), first LA is dimerized to lactide. Adding a proper catalyst at elevated temperatures under vacuum, the PLA is synthesized with relatively high MW. Reaction time, temperature, purity of lactide and type of the employed catalysts are of the key parameters in ROP method [23]. The ROP of LA is a complicated and expensive method for production of high MW PLA and condensation methods result in low MW PLA [24].

2.1 Synthesis of the PLA by chain extension

In direct polymerization (also called solution poly-condensation or melt polycondensation), LA is condensate polymerized to yield a low MW brittle glassy polymer. Presence of water, the high viscosity of the polymer melt, the presence of impurities, low concentration of reactive groups and occurrence of the unwanted “back biting” reactions which result in lactide formation are of reasons for achieving a low MW polymer [21, 25]. Therefore, this polymer is not suitable for any application without further utilization of the external coupling agents which are employed to increase the MW of the polymer [21]. Azeotropic condensation-polymerization is also sensitive to the presence of impurities of the supplied LA. The impurities endcap the polymer and limit the chain growth and have a large effect on the MW of the final polymer. In addition, in azeotropic condensation-polymerization, various diacids, diols or hydroxyl acids interfere with polymerization step and affect the purity of the produced polymer. Residual catalysts in the products would be another drawback of this method [21].

From the other hand, the yield and efficiency of ROP method heavily depend on the type of the employed catalyst and the employed polymerization mechanism. Cationic [26], anionic [27] and coordination-insertion [21] are the three mechanisms of catalytic reactions in ROP, which are sensitive, complex and expensive [28]. Tin compound catalysts, e.g. tin (II) bis-2-ethylhexanoic acid (referred to as tin octoate or stannous octoate) are the most common catalysts used in the ROP method [29]. It is shown that the rate of chain growth varies greatly depending on the presence of lactide impurities and also by formation of crystalline phase during polymerization. It is believed that the presence of impurities does not significantly affect the rate of polymerization, but it dramatically reduces the final MW of the polymer. However, carboxylic impurities have an inhibitory effect on the rate of polymerization as well, which could be due to deactivation of the catalyst by forming a complex. Substantial sensitivity of the ROP method to impurities, indicates that a rigorous purification of lactide is required beforehand in those processes which impose substantial costs to the process [21, 30].

Shortcomings of the direct condensation methods and complexity of ROP, encouraged researchers to investigate on alternative methods for PLA synthesis. Utilization of chain extenders is an effective way to achieve high MW polymers. Generally, chain extenders are multifunctional low MW chemicals which are attached to the low MW oligomer and link it into a polymer with higher MW. The most common chain extenders for polyesters which contain –OH and –COOH groups include diisocyanates, diepoxides, bisoxazolines, dianhydrides and bisketeneacetals [21, 30].

Figure 1, PLA synthesis methods.

2.2 Synthesis of star-shaped resins; currently applied monomers as the core molecule

Currently, polymers are designed for a certain application. In order to add special physical properties, it is sometimes desirable to change the architecture of the polymer from linear to a star-shaped polymer [15]. Changing the architecture of a polymer to achieve a multiarm or hyperbranched one would change its morphological and physical-mechanical properties [31]. Different methods for achieving star-shaped polymers have been introduced, including employ of multifunctional linking agents or multifunctional initiators [15, 32-36]. However, a few studies have been devoted to syntheses of star-shaped polyesters. The early star-shaped polyesters have been synthesized by the reaction of multifunctional hydroxyl compounds and octoate using an ROP approach [37, 38]. Currently, different polyol molecules with various hydroxyl groups have been employed as the core molecule in S-LA. In the next part of this review article, the recent methods for synthesis of different star-shaped resins using these polyols are explored.

Core molecules with two hydroxyl groups: Poly lactic-co-glycolic acid (PLGA) is a copolymer of PLA and poly glycolic acid (PGA), (see fig 2-5) which has been used to fabricate

220 devices for drug delivery and tissue engineering applications for decades [39, 40]. Physical
221 properties of PLGA are dependent on multiple factors, including the MW of the polymer, the
222 ratio of lactide to glycolide (see fig 2-4) in the structure, time of exposure to water and the
223 surface shape [41]. Polymers can be synthesized using ethylene glycol (see fig 2-3) and lactic
224 acid as either random or block copolymers. PLGA/PEG block copolymers have been synthesized
225 as diblock oligomers of PLGA-PEG [42] or triblock oligomers of PLGA-PEG-PLGA [43] and
226 PEG-PLGA-PEG [44]. Generally, PLGA copolymers are synthesized by ring-opening
227 copolymerization of d,l-lactide and glycolide and common catalysts used include tin(II)2-
228 ethylhexanoate, tin(II)alkoxides, or aluminum isopropoxide. The copolymerization happens by
229 ester linkage of successive monomeric units of glycolic or lactic acid, which yields a linear,
230 aliphatic polyester [45, 46]. Tetra(ethylene glycol), TEG, has also been used as the chain
231 extender and telechelic polylactides having two CH-OH end groups were obtained. The ratio of
232 LA to TEG was set to 20:1 mole and dry chlorobenzene was added under an atmosphere of dry
233 nitrogen. The reactants were heated to 120°C and after 5 min, Bi(OAc)₃ was added – with a ratio
234 of 0.02 mole to mole of TEG [47]. Biela et al. employed diethylene glycol (see fig 2-2) as
235 another chain extender with two hydroxyl groups and synthesized hydroxyl group terminated R-
236 (PLA-OH)₂ according to the procedure employing Sn(Oct)₂ as co-initiator. Sealed glass ampules
237 using a standard high vacuum technique were employed for polymerization at 120°C [48].
238 Butanediol (see fig 2-1) is also used as the chain extender in synthesis of the S-LA. The
239 oligomers were polymerized via ROP method from d,l-lactide at 160°C for 3 h. In the presence
240 of 0.02 mole % Sn(II)octoate as an initiator, the appropriate amount of the extender to LA
241 molecules were added in which the ratio of the LA monomer to butanediol was varied between
242 100:12.5 to 100:5 [49].

Core molecules with three hydroxyl groups:

Bakare et al. synthesized an S-LA with glycerol (see fig 2-6) core molecules. The resin was synthesized in two stages: direct condensation reaction of LA with glycerol and EF of the oligomers with MAAH. Resins with different LA chain lengths of 3, 7 and 10 were synthesized using 9, 21 and 30 moles of LA per glycerol mole. Condensation reactions performed in the presence of toluene reflux from an azeotropic distillation apparatus (50 g toluene per LA mole) as an auxiliary solvent for water removal containing 0.1 wt% of the catalyst, methanesulfonic acid. The temperature was set to 145°C for two hours, increased to 165°C for another two hours and to 195°C for one more hour. For EF, in the presence of 0.1 wt% of hydroquinone as the stabilizer, 3.3 mole MAAH per mole of glycerol was added under a nitrogen atmosphere. The resin was purified from the remained water/toluene and the produced MAA by a rotary evaporator at 13 mbar at 60°C for 2 hours [4]. In a more recent study, tri(hydroxymethyl)benzene (see fig 2-7), has been used as the core molecule using a tin octanoate catalyst, for producing S-LA oligomers with 10 lactide monomer units arms. Polymerization reaction was performed at 125°C for 8 h under nitrogen atmosphere. The precipitation in cold methanol was employed for separation of the polymers from the reactants [50]. 1,1,1-tri(hydroxymethyl)propane (THMP) (see fig 2-8) has also been used as the core molecule where a three-armed S-LA with three CH-OH end groups was formed. The ratio of lactide to THMP was 20:1 mole to mole and dry chlorobenzene was added under an atmosphere of dry nitrogen. The reactants were heated to 150°C for homogenization before cooling to 120°C and after 5 min, Bi(OAc)₃ was added with a ratio of 0.02 mole to mole of THMP [47, 48]. In another similar study, the same core molecule, THMP, was used with tin(II) octoate [Sn(Oct)₂] as initiator in which lactide was polymerized with Sn(Oct)₂ with the polyol, at 120°C [16].

Core molecules with four hydroxyl groups: Kim et al. showed the possibility of the preparation of higher MW S-LA with pentaerythritol (PENTA) (see fig 2-9) as the core molecule. The initiator was octoate and the resulted resin showed a lower intrinsic viscosity compared to those of the linear ones, which confirms the lower viscosity of the star-shaped architecture [37, 51]. Åkesson et al. synthesized a crosslinkable thermoset resin from LA and PENTA core molecules. The resin was synthesized via direct condensation reaction of LA with PENTA and itaconic acid (IT) followed by EF of the oligomers with MAAH. At 120°C, the catalyst, 0.05 wt% of tin octoate, was added, and the reaction temperature was set to 180°C. The total polymerization time was 15 h and the resulted product was a yellowish, transparent, rigid, brittle resin. It is assumed that IT was only reacted with one branch of PENTA. For EF at 100-110°C, first, 0.1 wt% of hydroquinone was added as the stabilizer and then, 15 wt% of MAAH was added dropwise. The reaction continued at 120°C for 3 h under nitrogen purge [8]. In another study, Biela et al. synthesized four hydroxyl groups terminated R-(PLA-OH)₄ employing di(trimethylolpropane) (see fig 2-10) as the core molecule according to the procedure employing Sn(Oct)₂ as the co-initiator- which is previously explained [48].

Core molecules with five hydroxyl groups: In a recent study, the utilization of xylitol (see fig 2-11) molecule was examined and evaluated as the core molecule in an S-LA resin. The resin was synthesized via direct condensation reaction of LA with xylitol, in the presence of toluene reflux from an azeotropic distillation apparatus. 50 g toluene per mole of LA was initially added as an auxiliary solvent for water removal containing 0.1 wt% of the catalyst, methanesulfonic acid. The reaction temperature was set to 145°C for two hours and then increased to 165°C for 7 hours. The branches were then end-functionalized at 90°C with methacrylic anhydride (5.5 mole MA per mole of LA) in the presence of 1 wt% hydroquinone. Finally, under partial vacuum, the

residual toluene and the released methacrylic acid were removed - ~10 mbar, 1 h at 60 °C and two hours at 90 °C [52].

Core molecules with more hydroxyl groups: Biela et al. reported the synthesis of S-LA with higher hydroxyl groups -6 and 13- arms. The dipentaerythritol (DPE) (see fig 2-13) core molecules were used to produce 6 arms S-LA with $\text{Sn}(\text{Oct})_2$ coinitiator with the same technique at 120°C. The same technique was employed for synthesizing 13 arms S-LA with poly(3-ethyl-3-hydroxymethyloxetane) (see fig 2-14) as the core molecule [53]. Perry and Shaver also synthesized and characterized a S-LA, using cyclic hexa(hydroxymethyl)benzene core molecule (see fig 2-12) and a tin octanoate catalyst with 10 lactide monomer units in arms. Polymerization reaction was performed at 125°C for 8 h under nitrogen atmosphere [50].

Figure 2. Currently applied monomers as the core molecule in S-LA resins. 1:Butanediol, 2:diethylene glycol, 3:ethylene glycol, 4:glycolide, 5:glycolic acid, 6:glycerol, 7:tri(hydroxymethyl)benzene, 8:1,1,1-tri(hydroxymethyl)propane, 9:pentaerythritol, 10:di(trimethylolpropane), 11:xylitol, 12:hexa(hydroxymethyl)benzene, 13:dipentaerythritol, 14:poly(3-ethyl-3-hydroxymethyloxetane).

2.3 End functionalization of oligomers

The star-shaped oligomers resulted from the condensation reaction of LA with a multifunctional hydroxyl core molecule, would have reactive groups (either the terminal LA's hydroxyl groups or the core molecules' unreacted hydroxyls) but yet, the groups are not reactive enough for a satisfactory cross-linking [8, 52]. In order to produce a thermoset, capable of efficient crosslinking, branches must be further functionalized- or end capped- with an EF agent. The role of EF is to improve the reactivity of branches, generally by adding carbon-carbon double bonds. The stoichiometric amount of the EF agent will be calculated from the theoretical molecular weight of the synthesized oligomer and the functionality of the co-initiator [49]. Common EF agents presented in the literature are MAA [7] (see fig 3-2), MAAH [4, 52, 54-56] (see fig 3-1) or IT [7] (see fig 3-3). The two olefinic bonds of the MAAH, bestow a higher reactivity to the molecule and make it more desired for EF purpose, compared to other EF agents. Usually, a stabilizer agent, e.g. hydroquinone, is used to protect the olefinic carbon-bonds during the EF reactions and avoid subsequent cross-linking reactions and gelation. Generally, EF reactions are sensitive to high temperatures, which induce gelation inside the reactor; therefor, a good control over the temperature is required.

Figure 3, End functionalization agents. 1: methacrylic anhydride (MAAH), 2: methacrylic acid (MAA), 3: itaconic acid (IT), 4: crotonic acid.

2.4 Thermal curing of the resins

Curing involves the irreversible transformation of low molecular weight oligomers of a resin into a solid network [57]. The liquid resin is usually composed of several ingredients with three or more reactive groups per molecule that can react by an external action, such as heating or UV irradiation which results in a tridimensional cross-linked structure [58]. Generally, thermal curing of resins consists of two different stages: the heating period and curing reaction phase. During the heating period, the heat is transferred by conduction through the resin which is heated up to a temperature at which the cure reactions start. In the curing reaction phase, the heat evolved from the overall cure reaction zone at a constant temperature which can be described by an Arrhenius equation [57]. Often, in the S-LAs, a free-radical polymerization method is employed for curing in which the reaction starts by the assistance of a radical initiator. The common studied initiators for free radical polymerization are benzoyl peroxide [4, 19, 59], 2,5-bis(tert-butylperoxy)-2,5-dimethylhexane [14], 2-butanone peroxide [49], cobalt naphthenate

[15], *tert*-butyl peroxybenzoate [8], N,N-dimethylaniline [5] and *tert*-butyl peroxybenzoate [7, 56]. Different factors are involved in free radical curing reactions, including the nature of the initiator, initiator-to-resin ratio, applied heat regimes, retention times and cooling strategies. Often, 1-2 wt% of the initiator is utilized for the thermal curing. Using excess amount of the curing agent or applying high temperatures for curing may result in higher exotherms, faster gelation and more shrinkage due to excessive thermal zoning [52, 60]. Figure 4 presents the reaction Scheme for the synthesis steps and the curing reaction.

Figure 4. Reaction Scheme for the two-step synthesis of the S-LA and the thermosetting network

3. Characterization of the S-LA systems

3.1 Chemical characterization

Titration: The condensation retention time is a crucial factor in poly-condensation step. From one hand, insufficient retention time in the reactor results in unreacted reactants and from the other hand, excessive reaction time results in transesterification reactions, which gradually degrades the structure of the oligomers [52]. The progress of the condensation reaction can be evaluated by determination of the *Total Acid Number* (TAN) for residual acidic constituents (carboxyl groups) during the poly-condensation step. According to the ASTM D974-12, the TAN is defined as the quantity of KOH (in mg), required for the titration of 1 g of the sample which is dissolved in a specified solvent system. The samples are diluted in predefined solvent systems, capable of dissolving the S-LA, and then, titrated with a base in the presence of an

indicator, e.g. phenolphthalein 1% [61]. The currently used solvent systems for the TAN determination are 1:1 v/v xylene/isopropyl alcohol solutions [4, 52, 61], acetone [62] and a mixture of toluene and isopropyl alcohol (based on the ASTM D664 and D974-12). The ratio of the *reacted* to *initial* available carboxylic groups, indicates the degree of completion of the condensation reaction.

NMR: The Nuclear magnetic resonance (NMR) is a technique frequently used for identifying the chemical structure of the synthesized resins as well as LA chain length in the branches. The ^{13}C NMR data for different S-LA is presented in the literature [4, 8, 11, 12, 38, 49, 52, 61, 63, 64]. Of particular interest is the carbonyl region (160-180 ppm) [5, 52]. For neat S-LA, different types of carbonyl bonds are expected, including a) main-chain carbonyls, b) LA carbonyl groups adjacent to the ($-\text{O}-\text{CH}_2$) branches of the core molecule, and c) carbonyls of the LA end-group for unreacted LA. For the end-functionalized resins, signals in the carbonyl area would be broad, because signals for carbonyls of LA next to the core molecule (or next to the end-capping agent) differ from that of LA in chains. In addition, the end-group agent may add other carbonyl bands. The other class of chemical shifts used for characterization, belongs to a carbon atom adjacent to an oxygen atom which is revealed in the range of 60–75 ppm [65]. These CH groups could be a) in the structure of the core molecule, b) next to the reacted LA carbonyl groups and an oxygen atom, or c) adjacent to the hydroxyl end-group. The other expected groups are methyl groups. The LA methyl groups are detected in the 16–22 ppm range [52]. Hydroxyl functionalized end-group of methyl groups are present in the S-LA, but not present in the EF resins. The probable CH_3 groups of the end-capped agent in the resin structure and the olefinic carbon sites of the end-groups are other characteristic signals of the EF resins. Moreover, the NMR technique can also be used for measuring the chain length of the branches

[5], the percentage of the LA in forms of reacted with the core molecule as well as the percentage of the LA reacted into free oligomers [4, 52].

FT-IR: The FT-IR analysis of the S-LA is often performed for verifying the structure of poly-condensation resins, the EF resins and also the cured samples. Infrared spectroscopy data of the S-LAs' functional groups is presented in the literature [4, 5, 8, 13, 56, 63, 65-68] and summarized in the following Table (table 1). Different groups might appear in the IR spectra of the S-LA, EF resins and the cured samples. Generally (—OH) Stretch spectra is just present in poly-condensation resins as hydroxyl groups will react with an EF agent during the end-capping reactions. The spectra for (—CH— stretch and bend), (—C=O carbonyl stretch) and (—C—O—C— Stretch), generally presented in all samples. The spectra for (—C=C— stretch) and (=CH_2 bending) are just expected in EF resins in which carbon-carbon double bonds are present.

Table 1. Infrared spectroscopy data of the S-LAs' functional groups.

Assignment	Peak position, cm^{-1}
—OH Stretch (free)	3380 [67], 3428 [5], 3491 [63], 3500 [4, 5], 3506 [13], 3508 [56], 3520 [66, 67]
—CH— stretch	2870 [13], 2879 [66], 2900 [4], 2994- 2943 [63], 2947 [13], 2990 [65]
—CH— bend	1382-1454 [63], 2947 [13]
—C=O carbonyl stretch	1705 [67], 1722 (MAAH) [56], 1734 [13], 1749 [56], 1755 [63], 1757 [5], 1758–1763 [66], 1759 [5]
—C=C— stretch	1635 [4], 1638 [56], 1640 [4, 5, 8]
=CH_2 bending	815 [68], 816 [4, 5, 56, 68]
—CH_3	1453, 2999 [13]
—C=O bend	757 [66]
—C—O—C— Stretch	1095–1130 [66], 1170 [13], 1271-1188-1093 [63]
—CH ring of lactide	932–934 [66]

3.2 General properties

Water absorption: The water absorption rates of polymers and composites are of interest, especially when the material is supposed to exposure to relatively humid conditions. The moisture content affects polymers' properties such as electrical insulation resistance, dielectric losses, mechanical strength, appearance, and dimensions. It is believed that the diffusion of water

into polymer matrix is dependent to several factors, including a) the square root of immersion time, b) the type of immersion, c) dimensions and shape of the specimen and d) the inherent properties of the polymer [52, 69]. In composites, the type and characteristics of the reinforced fiber also affect the water uptake. For example, using the same matrix, the flax/basalt composites showed a lower water uptake than the flax composites [6, 70]. The fiber volume fraction of the composite is also believed to be proportional to the water uptake rate of the composite [61, 71]. The *water absorption tests* are generally carried out based on the ASTM D 570-98 in 3 modes: *Long-Term Immersion*, *Two-Hour Boiling Water Immersion* and *Immersion at 50°C*. In Long-Term Immersion, the sample is immersed in a distilled water bath at 23°C and the total water absorption versus time is recorded, in the two-hour-boiling-test, the water absorption is measured after 2 hours of immersion in the boiling distilled water bath and in the Immersion at 50°C mode, water absorption is measured at 50°C at different time intervals. Tests are continued until the samples get substantially saturated (achieved water absorption rates to be $\leq 1\%$ or 5 mg between intervals). The initial slope of the water-absorption versus time curve is proportional to the diffusion constant of water in the matrix [69].

Biobased content: The biobased content or “*Percent biobased*” is a measure of the proportion of the biobased carbon fraction to the total carbon in the product. The ASTM D6866 has set a standard method based on radiocarbon analysis for the calculation of the biobased content included in a resin, which is frequently used for measuring the biobased content of resins [52, 54, 72]. This standard method is also used by the U.S. Department of Agriculture (USDA) BioPreferred program¹ to calculate the biobased content included in a material. Based on this standard, the biobased standard can be calculated using the following formula:

¹ <https://www.biopreferred.gov/BioPreferred/>

$$\text{Biobased content} = \frac{\text{biobased carbon content}}{\text{total carbon content}} \times 100$$

The total carbon content includes both renewable based and petroleum based carbons.

3.3 Thermomechanical properties

In this part, the effect of external forces on the behavior of cured S-LA thermosets and their composites are discussed and the thermomechanical tests currently employed in determining various properties, including elastic modulus, yield stress, ultimate strength, toughness, flexural modulus, storage modulus, flexural modulus and glass transition temperature are highlighted. The mechanical tests currently employed in characterizing thermomechanical properties of S-LA thermosets, including DTMA tests, tension tests, compression tests, bending or flexural tests, hardness tests, fatigue tests, creep tests, thermogravimetry analysis, dynamic scanning calorimetry and impact tests. The type of the employed testing methods on the specimen depends on the service expected for the produced thermoset. However, the more testing applied on a specimen, the more information acquired for the intended S-LA. The mechanical properties of S-LA is very dependent on the molecular weight and the structure of the network. Generally, employ of a star branching point in the S-LA systems, results in lower melting temperatures (T_m), lower glass transition temperatures (T_g) and lower crystallization temperatures (T_c) for polycondensation resins. The lower T_c indicates that the starting points make the material harder to crystallize, while lower T_m indicates that it makes stacking of the polymers more difficult [73]. The following section provides a short description of the current mechanical testing methods and the type of information obtained from these methods.

Tension or tensile tests are the most fundamental tests employed for characterizing mechanical properties of S-LA based matrices. In tensile tests, a specimen is subjected to a controlled tension until failure happens and stress to strain curve is obtained. The modulus of

442 elasticity (Young's modulus), E , is a measure of the stiffness of the sample in the linear region of
443 the curve in which the specimen can return to its exact initial conditions, if the load is removed;
444 the yield strength is the stress applied to the material at which plastic deformation starts to occur;
445 and ultimate tensile strength (UTS) is the maximum load the specimen sustains during the test.
446 Increasing the temperature generally increases the ductility (the extent of plastic deformation
447 before fracture) and the toughness of a material while decreases the yield stress, tensile strength
448 and the modulus of elasticity [74, 75]. It is believed that the tensile properties of the star-shaped
449 structure are different with linear oligomers. The strength can be lower for networks with
450 flexible extension units, or higher for structures with rigid starting points. It is reported that S-LA
451 systems with high crosslinking density demonstrate similar mechanical properties to those of
452 other biodegradable composites, however, longer LA chains will decrease tensile properties [49].
453 Helminen et al. reported lower tensile strength for butanediol-LA systems (despite higher
454 crosslinking density), which was ascribed to the flexible butanediol units used in the linear
455 oligomers [49]. However, it is believed that the tensile strength is a function of crosslinking
456 density and generally, a higher crosslinking density results in higher tensile strength [76]. In
457 compression tests, the specimen is subjected to a compressive load usually by a solid cylindrical
458 object between two well-lubricated flat platens. For the brittle materials, a disk test is applied
459 instead, in which the disk is subjected compression and uniform tensile stresses develop
460 perpendicular to the centerline of the disc [75, 77]. The bending, flexural or transverse beam test
461 measures behavior of brittle materials (usually with a rectangular cross section) by applying
462 vertical load in which tensile stress produced on the convex side of the specimen and
463 compression stress in the concave side. The load is applied on either one point (3 point bending)
464 or two points (four-point bending) and the specimen deflection is measured by the crosshead

position. The bending test provides values for the modulus of elasticity in bending (E_f), flexural stress (σ_f), flexural strain (ϵ_f) and the flexural stress-strain response of the material. Usually, the 3-point bending test is applied to polymers and the values like flexural strength and flexural modulus are reported. Flexural strength is defined as the maximum stress in the outermost fiber, the modulus of rupture is defined as the stress at fracture in bending and the flexural modulus is the slope of the stress-deflection curve [78, 79]. Hardness, which is defined as the resistance to permanent indentation, is an indicator of the strength of a material and its resistance to scratching or wear. The resistance to indentation depends on the shape of the indenter and the applied load; therefore, several hardness test methods have been developed to measure the hardness of a material, including Brinell test (using a steel or tungsten-carbide ball indenter [80]), Rockwell test (using a diamond cone or steel ball indenter [81]), Vickers test (using a diamond pyramid indenter), Knoop test (using a diamond pyramid indenter) and Scleroscope and Leeb test (using a diamond-tipped indenter) [75, 81]. Impact tests measure the ability of a specimen to resist high-rate loading and it is used for determining the energy absorbed in fracturing a test specimen at high velocity which is important for estimating the service life of a test piece. Typically, this test is performed by placing a notched specimen in an impact tester (supported at both ends in Charpy test, or at one end in Izod test) and breaking it with a swinging pendulum. In brittle materials, less energy is required for starting a crack, and a little more to propagate it to the shattering climax [75].

Dynamic mechanical, thermal analysis (DMTA) is another technique frequently employed to characterize the viscoelastic properties of polymers, in which a sinusoidal stress is applied to the specimen and the resulting displacement (strain) is measured. Properties such as storage modulus, loss of modulus, lag phase (between stress and strain) and glass transition

temperature can be measured with this technique [82]. The storage modulus, which measures the stored energy, represents the elastic characteristic of a polymer. The storage modulus G' is related to the molecular packing density in the glassy state [56, 57] and higher G' means the better mechanical properties. The G' is decreasing upon elevated temperatures when the polymer chain is in the rubbery plateau region [54] due to the free movements of the polymer chains. The loss modulus, G'' , measures the energy dissipated as the heat and represents the viscous part. Generally, smaller G'' suggests better mechanical properties and the strong tendency for reversibility in the samples [54]. At the glass transition temperature, T_g , the G' decreases dramatically while G'' reaches its maximum. Temperature sweep tests, frequency sweep tests and dynamic stress-strain tests are the most common test modes employed for characterizing the viscoelastic properties of polymers in DTMA studies.

Thermogravimetric analysis (TGA), is a technique currently employed for measuring changes in physical and chemical properties versus temperature (constant heating rate mode) or time (constant temperature or mass loss mode). As the temperature increases, various components of the sample decomposed. Commonly, in TGA, the percentage of weight loss or the rate of weight loss would be presented versus temperature, which are referred to as the thermogravimetric curve and the differential thermogravimetric curve, respectively [83]. For thermosets, TGA can provide information about the thermal stability, loss of volatiles, decomposition rate and oxidation-reduction reactions and it is employed to study of degradation mechanisms and reaction kinetics [84]. The degradation in thermoset systems starts with decomposition of the crosslinked network and follows by the random scission of the linear chains [85].

3.4 Rheological properties and curing kinetics of the star-shaped resins

Viscosity of the resins: Inadequate and poor impregnation of a viscous matrix to fibers is a major problem in composite manufacturing. It makes the production process to be slow and also reduce the mechanical strength of the product [12, 13]. The resistance to flow of a liquid is expressed in terms of the viscosity. The viscosity is of importance for manufacturing processes, maximizing the production efficiency, improving processability as well as for improving the impregnation efficiency of the matrix to the reinforcement fiber for composite production [86]. It is believed that the linear PLA shows a long Newtonian plateau typical of polymers having a linear chain structure (at low to moderate oscillation frequencies <100 rad/sec). For the S-LA systems however, a Non-Newtonian behavior has been reported. Also, the S-LA systems show an intensified shear thinning response (similar to comb-like PLA) compared to the linear PLA [87]. In composite manufacturing industry, low viscosity of thermoset resin is a crucial factor for several processing methods, including vacuum infusion, spray and hand lay-up, filament winding, and pultrusion [8]. The solution and melt rheological properties of linear PLA have been studied intensively in the literature and a proportional relationship between the MW and the viscosity has been reported [87-89]. Comparably lower viscosities of thermosets, suggest better processability and better impregnation in these systems and make thermosets desirable as a matrix for reinforced composite applications. Generally, the lower the viscosity, the better rheological properties and more desired matrix to be used for reinforced composite applications [90]. For a satisfactory composite manufacturing, Li et al., suggests that the resin flow viscosity needs to be below 5 Poise (0.5 Pa s) [91]. It is believed that employing a core molecule in the structure of oligomers can reduce the viscosity of the resins. This reduction can be ascribed to the coiling character of polymers [73]; therefore, as the star-shaped polymers have smaller hydrodynamic volume compared to that of linear polymers with the same molecular weight, the

viscosity will be lower [15, 56]. However, the contradictory observations have also been reported by Nouri et al. in which higher viscosity and elastic modulus was observed for branched PLA structures [87]. The viscosity of the S-LA, generally measured based on stress viscometry technique at different temperature intervals. Increasing the length of the LA branches will increase the MW and the viscosity. Bakare et al. reported the same trend for glycerol S-LA thermosets with different LA chain lengths in which resins with shorter arms proportionally had lower viscosities. The same trend was reported for the xylitol S-LA resins and similarly, up on increasing the temperature, the viscosity of resins substantially dropped down. Low viscosity, even at elevated temperatures (up to curing temperature), is substantially important as low viscosity facilitates the impregnation of the resin into the fiber reinforcement at higher temperatures. There is not a considerable number of studies exist on the effect of star-shaped structures and the following table summarizes the viscosities reported for to date synthesized S-LAs.

Table 2. The effect of the core molecule and the LA chain length on the viscosity of the S-LA.

Core molecule	LA Chain length	End-functionalization	Number of branches	Viscosity at 25°C Pa. s	Viscosity min Pa. s	Ref
Unsaturated polyester	-	none	-	0.3	0.1 at 70°C	[6]
xylitol	3	MAAH	5	2.97	0.06 at 85°C	[52]
pentaerythritol	5	IT-MAAH	4	7000	4 at 80°C	[8]
glycerol	3	MAAH	3	1.09	0.04 at 100°C	[4]
glycerol	7	MAAH	3	80	0.33 at 100°C	[4]
glycerol	10	MAAH	3	900,000	1.05 at 100°C	[4]
pentaerythritol	5	MAAH-Allyl alcohol	4	0.02	0.01 at 70°C	[6]

Curing kinetics: Curing involves the irreversible transformation of low molecular weight oligomers into a solid network. Thermal curing of thermosets consists of the heating period stage and the curing reaction stage. During the heating period, the resin is heated up to a temperature at which the curing reaction starts, while in the curing reaction stage, the heat evolved from the

overall curing mass at a constant temperature [57]. Often, in the S-LA thermosets, curing reaction starts by the assistance of a radical initiator. The tuning of curing parameters, including temperatures, pressures, time, etc. [90] is of importance, especially in thermosets, as it affects the properties of the final product and applying improper conditions for curing, may result in higher exotherms, faster gelation and more shrinkage due to excessive thermal zoning [52, 60]. Understanding of the cure process is substantially important, especially for more complex systems such as industrial formulations, as a variety of additives are interfering in the curing procedure, resulting in a more complex cure kinetics. These factors indicate that an excellent control over curing process is required for production of thermosets with desired properties [70, 71]. The cure process can be evaluated based on two methods: a) monitoring the changes in concentration of the reactive groups and b) by monitoring the changes in the physiomechanical properties of the sample [71]. Cure kinetics correlate heat release rate (HRR) with the temperature (or time) and the resultant degree of cure [90]. The analytical models of cure kinetics have wide applications in numerical simulations of composite manufacturing processes. Phenomenological –also called empirical- modeling approach is commonly employed for the analytical expression of the cure kinetics based on an Arrhenius type equation in which the approximated relationship of the curing parameters of the mathematical model are compared with the experimental data [90]. Several phenomenological models are presented in the literature for modeling the curing kinetics of the thermosetting resins; however, a few studies are performed for the modeling the curing kinetics of the S-LAs [56, 90]. The degree of cure, α , presents the extent of the curing reaction and is proportional to the amount of heat released by bond formation. The degree of cure is defined as:

$$\alpha = \frac{H}{H_u}$$

where H is accumulative reaction heat up to time t , and H_u is the total heat released during curing reaction. H_u is evaluated by

$$H_u = \int_0^{t_{fd}} \left(\frac{dQ}{dt} \right)_d dt$$

where t_{fd} is the total reaction time and $(dQ/dt)_d$ is the instantaneous heat flow during the dynamic scanning. The curing rate which is proportional to the rate of heat generation, is defined as:

$$\frac{d\alpha}{dt} = \frac{1}{H_u} \left(\frac{dH}{dt} \right)$$

Table 3 provides a summary of suggested phenomenological models in the literature.

Table 3, phenomenological models suggested for curing kinetics of the thermosetting systems.

Model	Equation	Parameters	Dependent parameters	Ref
nth- order rate	$\frac{d\alpha}{dt} = K(1 - \alpha)^n$	K : reaction rate constant $K = K_0 \exp\left(-\frac{\Delta E_A}{RT}\right)$	K_0 : Arrhenius frequency factor ΔE_A : activation energy R : universal gas constant T : absolute temperature	[92]
Autocatalytic	$\frac{d\alpha}{dt} = K\alpha^m(1 - \alpha)^n$	K : reaction rate constant. $K = K_0 \exp\left(-\frac{\Delta E_A}{RT}\right)$ m, n : reaction orders defined by experimental data.	K_0 : Arrhenius frequency factor ΔE_A : activation energy R : universal gas constant T : absolute temperature	[93]
Kamal	$\frac{d\alpha}{dt} = (K_1 + K_2\alpha^m)(1 - \alpha)^n$	K_i : reaction constants. $K_i = K_{i0} \exp\left(-\frac{\Delta E_i}{RT}\right), \quad (i = 1, 2)$ m, n : reaction orders defined by experimental data.	K_{i0} : Arrhenius frequency factors. ΔE_i : activation energy R : universal gas constant T : absolute temperature	[94]
Modified Kamal	$\frac{d\alpha}{dt} = (K_1 + K_2\alpha^m)(\alpha_{max} - \alpha)^n$	K_i : reaction constants. $K_i = K_{i0} \exp\left(-\frac{\Delta E_i}{RT}\right), \quad (i = 1, 2)$ m, n : reaction orders defined by experimental data. α_{max} : maximum degree of cure at a given temperature	K_{i0} : Arrhenius frequency factors. ΔE_i : activation energy R : universal gas constant T : absolute temperature	[90]
Cole	$\frac{d\alpha}{dt} = \frac{K\alpha^m(1 - \alpha)^n}{1 + e^{C(\alpha - (\alpha_{c0} + \alpha_{CT}T))}}$	K : reaction rate constant. $K = K_0 \exp\left(-\frac{\Delta E_A}{RT}\right)$ m, n : reaction orders defined by experimental data. C : diffusion constant. α_{c0} : critical degree of cure at $T=0$ K. α_{CT} : increase in critical resin degree of cure with temperature.	K_0 : Arrhenius frequency factor ΔE_A : activation energy R : universal gas constant T : absolute temperature	[95]

The *nth- order* rate equation is the simplest phenomenological model proposed for predicting the rate of the curing reaction in thermosets. The *nth-order* reaction predicts the maximum curing rate at the beginning of the curing phenomenon and does not account for the

autocatalytic effect [92]. The *autocatalytic* models represent the autocatalytic effect of the curing reactions. This model considers a single rate constant for the reaction and the maximum reaction rate is supposed to take place in the intermediate conversion stage. A more accurate model has been proposed by Kamal and Sourour considering two rate constants for the curing kinetics (known as *Kamal's model*) [93, 94]. However, more parameters in the model have made the model to be more complicated. The limitation of all the mentioned models is that they are just valid when the kinetic of bond formation, is considered to be the only rate controlling step in the curing reactions. The vitrification effect (transforming to a non-crystalline amorphous solid) has been considered in a modified version of Kamal's model in which the fractional conversion has been considered to not exceed the degree of cure associated with vitrification. In the *Cole's model*, another controlling mechanism for the curing is considered in expressing the curing kinetic equation. This diffusion constant term in the equation, explicitly accounts for shifting from the kinetics to the diffusion control [90, 95].

4. Applications

4.1 Biocomposites

Composites are engineered materials with wide range of applications, which are currently produced from petroleum based resins and synthetic fibers. Polymers are of the common matrices which are used for fiber reinforced plastics. The matrix material determines the overall durability of the composites as well as the shape, surface appearance and the environmental tolerance of the final product. The fibrous reinforcement role is to carry the structural loads while provides macroscopic stiffness and strength to the composites [96-98]. Increasing attentions toward sustainable development, concerns about petroleum resources and economic and environmental issues have led to many attempts toward replacing the petroleum based materials

with the renewable substitutes. Developments in emerging biobased thermosets are spectacular from a technological point of view. Use of biobased materials and natural fibers not only contributes to the production of a more environmentally friendly product, but also has advantages such as low weight and low manufacturing costs [99, 100].

Different biobased raw materials have been suggested for the production of composites. Versatile and economical renewable sources make LA a suitable source for production of thermoplast bioplastics [17, 29, 101]. Thermoplasts are a class of polymers with high molecular weight, in which the chains are associated through intermolecular forces. Thermoplasts' structure is weakened rapidly upon temperature increase. In contrast, thermosets form chemical bonds during the curing process and the structure cannot be reformed upon further heating-cooling processes [102, 103]. Limitations in impregnation of the matrix to fibers, make the thermoplast processing to be slow and costly and also reduce the mechanical strength of the produced composites [102, 104]. In addition, PLA's hydrophobic nature makes it incompatible with natural fibers [105-107], thus, hydrophilic fibers cannot be efficiently employed for reinforcing the PLA matrix [29, 104]. From the other hand, thermosets bestow a lower viscosity which results in the better processability and better impregnation of fibers which consequently makes thermosets desirable to be used as the matrix for reinforced composite applications [90, 103]. The other privilege of the thermoset systems over thermoplasts is that thermosets can be tailored for a certain functionality by altering the chemical structure or by changing the crosslinking density [108]. However, there are also several disadvantages associated with the current thermosetting resins, e.g. environmental issues, nonrenewable expensive sources and the poor thermomechanical and impact properties [108].

Inexpensive biobased raw material, better environmental profile, low viscosity and better processability of the matrix along with better thermomechanical properties of the produced biocomposites are of advantages expected for the S-LA composites. So far, composites of S-LA matrix and different reinforcements, including viscose fiber [59], flax fibers [6, 7] and basalt [6] have been produced. Hypothetically, unsaturated branches of the core molecule increase the hydrophilicity of the produced resin and make it more compatible with inexpensive natural fibers which eventually increases the mechanical properties and lower the final costs of the biocomposites. However, sometimes a hyper branched core molecule in the structure of the S-LA thermoset can adversely affect the thermomechanical properties, and also it is plausible that unsaturated groups available in the core molecule of the polymer affect the water absorption capacity of the matrix which results in altering the electrical and physiochemical properties of the product.

4.3 Biomedical

Polymers are currently employed in a wide range of biomedical applications, including drug delivery, tissue engineering, scaffold fabrication and gene delivery. Drug delivery is the method of transporting a pharmaceutical compound in the body to achieve a desired therapeutic effect. Biodegradable polymeric systems have been extensively studied for controlled release formulations and drug-targeting systems in forms of microspheres, films, tablets, or implantation devices, almost for two decades [72]. Wide diversity in the topology and the chemistry, ease of formulation for various devices, excellent bio-compatibility, biodegradability and mechanical strength have introduced a class of FDA approved aliphatic polyesters such as PLA, PGA, and PLGA to be used in controlled release of drugs, especially for cancer therapy [39, 63, 69, 72, 109]. Tissue engineering aims to apply engineering methods to create artificial

substitutes for defective tissues and organs [110, 111]. In tissue engineering, specific cells are isolated from the patient and cultivated on a 3D biomimetic scaffold under controlled conditions. The construct is often implanted in the desired site of the patient's body, allowing the new tissue formation into the scaffold which is degrading over time [110]. The matrix can be served as a substrate for attachment, grow and migration of cells or can be utilized as a drug carrier to activate cellular function in the region [110, 112]. Biodegradable polymers, by providing exogenous matrices suitable for facilitating tissue regeneration, play an important role in most tissue engineering strategies [113].

Drug delivery: It is believed that the architecture of the polymer, called topology, often influences the physicochemical properties and effects the microsphere preparation and drug delivery properties [3, 69]. The polymer architectures plays a crucial role in the drug delivery control and in the fabrication of drug delivery systems; however, it is relatively unfamiliar to pharmacists. Different polymer topologies have been studied for drug delivery, which can be categorized in to linear, branched, cross-linked, block, star-shaped and dendrimer topology [69]. Star-shaped polymers are a class of branched polymers with a 3D hyperbranched structure and linear arms, in which branching occurs via controlled polymerization techniques [1, 69]. Compared to linear polymers with the same composition and MW, the star-shaped polymers provide smaller hydrodynamic radius and so, a lower solution viscosity. In the S-LA structure, the employ of higher molecular weights of PEG in the structure of PLA-PEG is possible due to the presence of the core molecule which is an important factor in designing a system with high control over the hydrophilic/hydrophobic balance and core protection [69]. The star-shaped polymers can be synthesized via *arm-first* or *core-first* methods. In the arm-first methods, the linear arms are prepared via a controlled polymerization pathway; then, the chains are reacted

with multifunctional terminating agents. The core-first method which is the dominant employed technique, provides a better control over the process and starts with a multifunctional initiator and the propagation of the arms through a controlled polymerization pathway. Research on S-LA polymers as drug vectors seem rather limited so far; however, different initiators, or core molecules have been studied so far for the drug delivery purposes, including, PEG [38], THMP [16, 48], PENTA [51], di(trimethylolpropane) [48], cholic acid [65] and luminescent ruthenium tris(bipyridine) [2].

Tissue engineering: Successful utilization of biomaterials for tissue engineering is dependent on several factors. The biomaterial must resorb after its service and should provide conditions for sufficient growth rate and effective cell adhesion, while it is -or its degradation materials are- nontoxic, when implanted *in vivo*. The material which is designed for tissue engineering should also meet certain physical properties, including but not limited to having a) high porosity ($\leq 90\%$ for providing enough surface area in a 3D structure), b) minimum diffusional constraints (sufficient to meet the metabolic requirements), c) sufficient space for extracellular matrix regeneration and d) adjustable degradation rate (to match the rate of tissue regeneration *in vivo*) [114, 115]. The microarchitecture of the device is also of importance as it influences the interconnection between the pores for cell proliferation. In addition, as scaffolds are subjected to remain in intimate contact with the cells for prolonged periods, the influence of the polymeric materials on viability, growth, and function of the attached or adjacent cells is of crucial importance [116]. Different biodegradable polymers, including PLA, polylactide, polyglycolide and PLG have been employed for cell transplantation or for various tissue regeneration, including bone, cartilage, liver, and skin [113, 115]. The mechanical strength and the rate of degradation of the PLG is typically adjusted based on the ratio of lactic to glycolide

and polymer's degree of polymerization. Although the polymer blends must be well optimized by refining their properties to be used for tissue engineering, yet, polymer properties are not the only crucial factors in tissue engineering. The interaction of the cells with the surface of the polymer is another crucial factor and polymers that allow surface modification like PLG are particularly promising for tissue engineering purposes [117].

5. Perspectives, opportunities and limitations

5.1 Perspectives and opportunities

Substitution of current petroleum-based platforms with renewable-based technologies would be beneficiary in different ways. First, using the corn-based LA instead of conventional petroleum based monomers, will reduce the dependency of the national thermosetting plastic industry to the petroleum resources. Thus, in the long term, it will enhance the national energy security. Second, compared to petroleum based products, using biobased materials will substantially promote the environmental profile and sustainability of the production chain. In addition, the biodegradability of the products will alleviate carbon footprint and the environmental burdens associated with the final product. Third, using corn-based LA and inexpensive natural fibers as the raw materials, will subsequently promote economic diversification in rural areas. It has been shown that the S-LAs are capable of competing with or even surpassing fossil fuel based resins in terms of cost and eco-friendliness concerns [4, 6, 7, 12, 52].

Modifications for biomedical use: Using a core molecule with adjustable functional groups at the center of the S-LA provides the unique opportunity of designing and controlling over properties of the resin. It is presumed that more hydroxyl groups of the core molecule, provide a better extended network to the final product. The unsaturated hydroxyl groups of the

core molecule ultimately increase the hydrophilicity of the produced resin which make the resin more compatible with hydrophilic systems. The privilege of these thermoset systems over other systems is that these resins can be engineered for a certain functionality by changing the chemical structure or altering the crosslinking density. Moreover, by changing the nature and the portion of the block units of copolymers chain, it is possible to further manipulate the polymers properties. This manipulation could be in terms of changing the hydrophilicity properties as well as designing and manipulation of the void sizes of the polymer network. By employing longer arms which will act as plasticizers, it is possible to increase the size of the voids in the network and by using hydrophilic monomers in copolymers the hydrophilicity of the polymer network can be tailored. Manipulation of both void sizes and the hydrophilicity of voids will provide the unique opportunity for designing a polymeric matrix which is specifically designed for certain chemical component release or a desired drug delivery –based on drugs chemical structure, molecular weight, polarity, etc. with a substantial control over the release rate. In these systems, the polymer network can be tailored based on different parameters, including substitution of LA hydrophobic groups with a more hydrophilic group such as glycolic acid, by changing the ratio of the chain extender to the oligomer units or by changing the cross-linking density of the cured thermoset system. Using short oligomer chains in the network of the polymer leads to a compact network structure results in more resistance on diffusion. In addition, by reducing the ratio of methyl groups to the carbonyl groups in the structure (which results by applying higher ratios of glycolic acid units to lactic ones in the PGLA polymer), more hydrophilic structure is achieved.

Smart packaging applications: The S-LA thermosets provide an adjustable polymeric network, which potentially can be tailored for active packaging of productions. Active packaging (also called intelligent or smart packaging), means having active functions beyond the inert,

passive containment and protection of the product and refers to packaging systems currently employed for foods, pharmaceuticals, and several other types of products [118, 119]. Nowadays, PLA is employed as an active packaging material for antibacterial packaging with the ability of controlled release of antimicrobial or antioxidant compounds. Antioxidant packaging is a well-known, promising technique for increasing food quality and extending food production shelf life [119]. The addition of antioxidants to the polymeric packages has two facets. First, available antioxidants in the polymer formulations protect the ester bonds of the polymer structure from degradation [19, 120, 121]. Second, it helps protecting the food contents by migration of antioxidants from packaging material to the food medium. It is believed that antioxidant compounds can diffuse and migrate from the packaging material to the food product and help maintaining the quality of the food. Previously, antioxidants have been successfully incorporated into different polymeric matrices, including low density polyethylene (LDPE), polyvinyl chloride (PVC) and polypropylene (PP), for various foods [122-124]. The release of antioxidants is a result of the biodegradation of the polymer matrix as well as the diffusion phenomenon. In the diffusion of antioxidants, the migrant diffuses through the polymer matrix toward the interface and then partitioned between the polymer matrix and the food medium until the equilibrium. Therefore, antioxidant release can be presented as a result of diffusion, dissolution and finally, the equilibrium process [124, 125].

Flame retardancy: Many additives have been developed and employed to reduce the risk of fire hazards and to pass safety specifications in polymers. A flame retardant additive reduces the flammability of the product and the smoke generation capability [126, 127]. In the S-LA systems, the flame-retardancy feature can be potentially obtained by adding the phosphorus containing groups (or other flame retardant groups) to the structure of the network. In these

systems, the core molecule provides different reactive sites (hydroxyls) which may be employed for addition of a special functionality. The other sites which may be used to add a functional group, are the chains. In addition, using an EF agent with groups containing a flame retardant component, can add flame retardancy feature to the S-LA thermosets.

5.2. Gaps and limitations

In this section, shortcomings and gaps of S-LA systems are discussed. S-LA and their composites have been synthesized and employed for several applications for decades. Employing a core molecule makes the structure of these systems more complex compared to linear thermoplast PLA. Moreover, the combination of different polymerization steps, EF reactions and curing reactions have imposed more complexity to these systems. In addition, numerous applications are considered for these systems, including biomedical applications, adhesives, coatings and biocomposites, and each certain application requires certain characteristics. In order to manipulation of the S-LA for a specific desired property, these systems must be thoroughly characterized. Shortcomings and gaps in the different steps must be well studied. The aim of the following section is to discuss drawbacks associated with different steps of preparation and characterization of these systems. These gaps are classified into two categories: the synthesis and manufacturing concerns and the characterizing issues.

Generally, using a chain extender imposes more complexity to the system which inevitably leads to a comparably poor control over the polymerization. The choice of the core molecule would be one of the most important factors. It can directly effect on the crosslinking density, mechanical properties, thermostability, degradation rate and the hydrophobicity of the system. The ratio of the core molecule to the LA monomers is another important factor which affects the crosslinking density and the final properties of the produced network. Too much core

791 molecule makes the resin brittle and reduces the diffusion rates. The thermostability of the core
792 molecule is of importance, as the synthesis often occurs at high temperatures and molecules with
793 susceptible bonds can be degraded during the synthesis. Steric hindrance, increased by
794 employing the core molecules with multi-hydroxyl branches and may result in an incomplete
795 reaction of branches with the hydroxyl groups which leaves unsaturated sites in the core
796 molecule. Even if the complete reaction of hydroxyl groups ensured, still the length of chains
797 might vary between oligomers which results in unpredictable mechanical and diffusional
798 properties for the batch to batch resins. This is problematic, especially when the resin is expected
799 to be used for the drug delivery and biomedical applications. In addition, the polycondensation
800 synthesis pathway, which is commonly employed for the synthesis of the S-LAs, is an energy
801 extensive step, due to the long reaction times at high temperatures. It also requires large
802 quantities of organic solvents for effective water removal which must be recycled through the
803 azeotropic condensation. This purification and water removal step imposes a substantial
804 environmental load. Thus, there is a need for optimization of the required energy for the
805 synthesis. The energy inputs can be alleviated by optimization of the process and choosing more
806 effective solvents, more efficient catalyst systems or choosing an alternative synthesis method.
807 The EF reaction is the other important synthesis step. Despite the condensation step, the EF
808 reactions occur at moderate temperatures and shorter reaction durations. However, this step
809 requires a crucial control over the temperature as at elevated temperatures, the undesired partial
810 crosslinking happens and the risk of gelation is increased. In this step, in order to avoid unwanted
811 crosslinking, an inhibitor agent often used for protecting the olefinic carbon bonds. The origin of
812 the EF agents, the presence of releasing products during the reaction, e.g. MAA, the progress of
813 EF reactions and the degradation products are of other concerns, especially when the cured resin

is intended to service *in-vivo* in biomedical applications. The optimization of the EF reactions would be a tackle as applying insufficient reaction times and temperatures result in poor crosslinking density and subsequently inferior mechanical properties of the product, and applying excess reaction times and elevated temperatures increase the risk of gelation. Therefore, successful substitution of the nonrenewable EF agents with nontoxic renewable ones is of interest. The rheological properties of these systems are the other hotspot. The rheological properties of the S-LA systems have not been studied intensively in the literature. Although employing a core molecule in the structure of oligomers is believed to reduce the viscosity of the resins [15, 56], yet, resulted viscosities are still far from the desired viscosity for manufacturing processes. It is believed that a proportional relationship exists between the MW and the viscosity of these systems [87-89]. Employing core molecules with fewer hydroxyl groups, reduction in the LA chain length of branches and an efficient functionalization of the remaining hydroxyl groups can further reduce the viscosity of resins. The curing procedure is also of importance and must be well optimized as it can affect the properties of the final product. Applying improper curing techniques result in undesired mechanical strength on the matrix [128]. Different factors are involved in the free radical curing reactions which are often employed for curing of the S-LA systems, including the nature of the initiator, *initiator: resin* ratio, applied heat regimes, retention times and cooling strategies. Using excess curing agent or applying high temperatures for the curing may result in higher exotherms, faster gelation and more shrinkage due to excessive thermal zoning [52, 60].

There are also shortcomings exist in the characterization methods of these systems. Currently, the titration method is employed for monitoring the progress of the polycondensation step which is based on TAN measurements titration of available acidic groups. The samples are

diluted in the predefined solvent systems, capable of dissolving the S-LA, and then titrated with KOH. However, these solvent systems have been optimized for petroleum based materials and might not be capable of efficient dissolving of the high MW oligomers of the S-LA which results in unrealistic high conversion degrees. In addition, comparably more complex structure of these systems makes the interpretation of the FT-IR and NMR analysis to be hard. Therefore, too many peaks often can be found in the spectrums, especially in the carbonyl area of the EF resins, which can obscure the results and make them very hard to interpret. In addition, these techniques provide no solid information about the degree of completion of the polycondensation and EF reactions.

6. Conclusions

The need for designing polymers for a certain application and the shortcomings associated with the conventional synthesis methods, encouraged researchers to explore for the alternative PLA synthesis routes. Utilization of chain extenders is a promising way to achieve a high MW polymer capable of being engineered for a certain functionality. It is well known that changing the architecture of the linear PLA would change its properties. The concept of using star-shaped resins for biocomposites or in biomedical applications is gaining more and more attention day by day. The polymer architecture is a crucial factor for the drug delivery control; however, it is relatively unfamiliar to pharmacists. Employing a multifunctional core molecule at the center of the S-LA systems, provides the unique opportunity of designing and controlling over release properties of the resin. Adjustable structure of these aliphatic polyesters, provides the chance for altering the chemistry, ease of formulation, excellent bio-compatibility and biodegradability and makes them a suitable candidate for the controlled release of drugs, especially in cancer therapy. In addition, altering the linear structure of the PLA, often results in lower viscosity, better

extended network and better thermomechanical properties. Comparably lower viscosities of the S-LA thermosets, results in better processability and better impregnation of the matrix to the reinforcing fibers which is beneficiary for the composite applications. It is believed that often unreacted hydroxyl groups of the core molecule increase the hydrophilicity of the matrix and make it more compatible with hydrophilic natural fibers which results in the better mechanical properties of the biocomposites. However, in some cases, worse mechanical properties may result depending on the type of the employed core molecule. It is also plausible that unsaturated groups increase the water absorption capacity which results in altering the electrical and physiochemical properties of the matrix.

Developments in the emerging S-LA systems are spectacular from a technological point of view. However, these systems still suffer from different limitations and technological gaps and have a long way to go. These limitations can be categorized into the synthesis deficiencies and the characterization gaps. Firstly, employ of a core molecule makes the structure of these systems relatively more complex and reduce the control over the polymerization step. Association of multi-step reactions, including different polymerization steps, EF reactions and curing reactions also impose more complexity to these systems. The steric hindrance, increased by employ of the core molecule, may result in an incomplete reaction which leaves unsaturated hydroxyl groups in the network. Even if the complete reaction ensured, still the risk of inconsistent product remains as the length of chains cannot be efficiently controlled. The former results in the unpredictable mechanical and diffusion properties of the batch to batch product. The properties of the S-LA is dependent on several factors, including the molecular weight, the architecture of the network, rigidity of the core molecule, length of branches, crosslinking density and the degree of conversion. These interrelated factors, make the optimization and

characterization to be complicated and hard. In addition, the type of the employed testing methods depends on the expected service for the product. The tuning of the curing parameters is also a challenge, especially for more complex systems such as industrial formulations. Applying improper curing method results in inferior mechanical properties, higher exotherms, faster gelation and more shrinkage in the cured resins. In addition, the polycondensation synthesis is known as an energy extensive step. Large quantities of organic solvents required also impose substantial environmental load. This is a very exciting period in the development of biocompatible polymers, in particular, biobased S-LA resins. Although these state of the art, adjustable S-LA systems look very interesting and promising for various applications, yet their usage is limited. Therefore, future use of these systems requires systematic optimization and invention of better characterization methods.

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