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REVIEW ARTICLE

Synthesis and Biodegradability of Polyaspartic Acid: A Critical Review

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Poly(aspartic acid) (PAA) being biodegradable is suitable for various industrial medical and agricultural applications to replace many non-biodegradable polymers in use. Poly(aspartic acid) can be synthesized by different methods with and without catalyst in different forms such as polysuccinimide, either hydrolyzed to acid or salt. The polymer of (aspartic acid) is present in different forms such as α,β *and* L, D *isomers. The conformational analysis of poly(aspartic acid) was done by various analytical methods. Different combinations of these two isomer present in different percentage can be detected by various methods such as Hoffman degradation, IR, and NMR spectroscopic analysis. From the standard test for biodegradability, it was shown that the polymer is fully biodegradable. In this review, synthesis and characterization of homo and copolymer derivatives of PAA, along with the application and biodegradability in comparison with the other polymer in use, is discussed briefly.*

Keywords biodegradation, poly(aspartic acid), polysuccinimide, synthesis, thermal, polycondensation

Introduction

Water-soluble poly(carboxylic acid) such as acrylic acid and their derivatives, though efficiently used as detergent builders, dispersants are rarely collected and composted which exert adverse effect on the environment (1). Starch and lignin based dispersants though biodegradable are not as efficient as their polyacrylate counterpart. In order to increase the environmental acceptability of poly(carboxylic acid) and its derivatives non-biodegradable water-soluble poly(carboxylic acid) can be replaced by biodegradable poly(amino acid). In general several kinds of reagents, inorganic acid such as sulfuric acid

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and hydrochloric acid can be used to dissolve calcium salt, in scaling of water cooling and heating system with deposition of calcium salt; which is one of important industrial problems due to its inverse solubility at higher temperature. These reagents are used because of its high solubility at low pHs, and can provide H^+ ion in aqueous solution. But inherent toxicity and a high level of reactivity, which can cause corrosion in metallic process equipment and piping system due to strongly acidic solution, make its use impractical and undesirable in many applications. Alternative calcium chelating agents (2–5) such as citrate EDTA and other poly(amino acid) were used which degrade slowly in environment and their strong chelating power has raised concerned about their role in heavy metal mobilization in ground water (6, 7). Poly(aspartic acid) is a good dispersant, nontoxic, biodegradable, can be used as an anti-scalent for many mineral salt with good chelating power for calcium mineral salt and also used as a corrosion inhibitor for steel (8, 9).

Interest for synthesizing biodegradable and biocompatible polymers such as poly(α-amino acid), poly(α-hydroxy acid) for biomedical and pharmaceutical application is increasing (10, 11). Poly(amino-acids) are naturally occurring compounds. Synthetic polymers based on it can be nontoxic biodegradable and biocompatible. Poly(aspartic acid) is one among them, which can also be used in medicine, cosmetis, fabric and metal absorbent materials (12–14). In comparison to the non-biodegradable high molecular weight, polyacrylate based materials, which are the major products used in the super absorbent field, biodegradable poly(aspartic acid) (PAA) based super absorbent, produced from relatively low molecular weight PAA provide higher absorbency (15). PAA can also be used to protect the plants' nutrients by mixing with fertilizer to form a temporary microscopic layer around the roots of the plant (16). Biodegradable and biocompatible polymer can be used for tissue engineering, regeneration and as drug carrier (17–21). Polymer as a drug carrier can be divided into degradable and nondegradable type based on their destination; at present it is safe to treat any macromolecular drug carrier as nondegradable (22). Biodegradable polymeric drug carriers are derivatives of poly(amino acid) and polysaccharides. Drug targeting moieties or biologically active compounds can be attached to the carrier polymer by various ways such as covalent bond or covalent conjugation via ester, amide, urethane hydrazones, and thioether disulfide (23). The behavior of the polymer usually changes when a drug or targeting moiety is attached to the polymer. Poly(ethylene glycol) (PEG) is biocompatible and it has been chosen as a drug carrier, which is soluble in water and common organic solvents (24, 25) and retain the biological and enzymatic activity even after being coupled by enzymes, proteins and many drugs (26, 27). Poly(α-hydroxy acids) such as poly(glycolic acid) and poly(lactic acid) (PLA) and their copolymer can be used as biomaterials (17–21), but one of the shortcomings of these polymers is that there is no pendant functional group on the backbone. Among synthetic poly(amino acids, the trifunctional amino acids such as aspartic acid, glutamic acid and lysine are of great significance because they have pendant group on the backbone chain. Homo and co-polymer derivatives of amino acid polymers with a wide range of properties from hydrophilic to hydrophobic, neutral to ionic and linear to random coil can be synthesized by modification of the above polymers with the introduction of various alkyl group as co-ester or amides, which is feasible due to an amide bond involving a side chain group (28). The side chain can be used for covalently bonding of either biological active agents or drugs. One of the major drawbacks of all available poly(amino acids) as biomaterials is the potential immunogenicity of random copolymers of more than two different amino acids (29). The polymer like PLA and

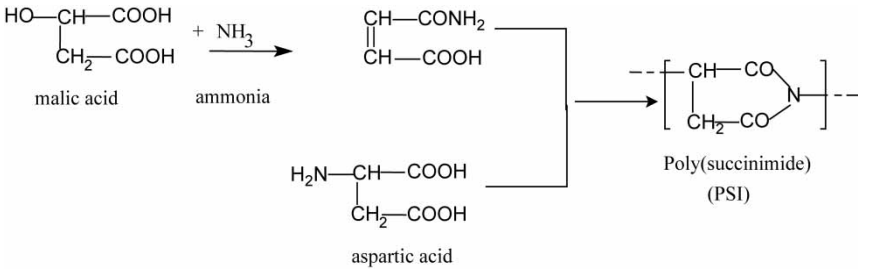
PEG can be used as a drug carrier by copolymerizing with a polymer having a functional side chain. Water-soluble carbonate derivatives of PEG based on copolymer of L-lysine and bis(succinimidyl) were synthesized (30, 31). The preparation of poly (PEG-Lysin) with multiple functional pendant groups, and the attachment of antibiotics (31), doxorubicin (32) and cis-hydroxy-L-proline onto it, and their biological activities were reported (33–35). Poly(lactic-co-lysine) copolymer was synthesized, and a biologically active RGD peptide was attached on the pendant amino functional group (36, 37). Block copolymers of (polyethylene oxide) PEO-PAA and PEG-PAA were conjugated to the hydrophobic anticancer drug, adriamycin (ADR), to pendant carboxylic group of PAA. The stable micelle system, with drug binding inner core permitting administration of a high concentration of this compound (38–40) was reported, which is otherwise toxic. Synthesis of polymerizable dendrimers consisting of one methacrylic function combined with an alkylene spacer and several condensed l-aspartic acid was carried out by a convergent approach (41). Dendrimers are polymer with three distinct structural features, a central core, surface functionalities and branching units that link these two. The dendrimers containing peptide bonds, defined as peptide dendrimers, are radial or wedge like branched macromolecules. The multimeric nature, unambiguous composition and ease of production, make this type of dendrimer well suited to various biotechnological and biochemical applications. Applications include use as biomedical diagnostic reagents, protein mimetic, anticancer and antiviral agents, vaccines, and drug and gene delivery vehicles. Synthesis of peptide dendrimer covers a large range of chemistry from conventional solid phase peptide synthesis in organic solvent to the regiospecific amide or nonamide bonds in aqueous solutions. Strategies for preparing peptide dendrimer can be divided into two categories. The first one is divergent strategy, a direct approach by which the dendrimer is built stepwise in a continuous operation on solid support and diverges outward, and the second one is convergent strategy, an indirect modular approach by which peptidyl surface functional groups and the branching unit are prepared separately, purified and then linked together. Both the strategies have some advantages and limitations (42). Niggemann et al. (41) synthesized highly functionalized monomers by condensation of N-methacryloyl amino undecanoic acid with free amino groups of L-aspartic acid dimethyl ester, α,β-bis-(L-dimethoxyaspartyl)-L-aspartic acid hydrobromide and α,β-bis-(L-aspartyl-α,β-bis-(L-dimethoxyaspartyl)-L-aspartic acid hydrobromide. The free radical homo and copolymerization of the monomers were studied, and the analysis of the resulting polymers was carried out using NMR and IR spectroscopy. The GPC and MALDI-TOF analysis did not provide meaningful results. In the case of styrene as comonomer, the highly functionalized copolymer was obtained. The polymers were characterized by the presence of a high density of ester groups in branched side chains. These polymers are potential carriers for biologically active compounds.

Poly(amino acid), consisting of naturally occurring amino acid, can be synthesized either chemically or biologically. Poly(glutamic acid) is synthesized by the polymerization of N-carboxyglutamic acid anhydride without using microorganisms, i.e., the NCA method (43–45). Use of phosgene or diphosgene for the synthesis of N-carboxyglutamic acid anhydride results in high production cost. In addition, glutamic acid by heating produces pyroglutamic acid, a cyclic unimer, though copolymer based on glutamic acid obtained on thermal polycondensation (46–50), whereas PAA can be synthesized by thermal polycondensation of unsubstituted aspartic acid (ASP) or a product of malic acid or maleic acid and ammonia, followed by hydrolysis (51).

Synthesis of Poly(aspartic acid) and its Derivatives

Homopolymer. Poly(aspartic acid) has been synthesized by thermal polymerization of l-aspartic acid (ASP) or monoammonium malate, resulting in poly(succinimide) (PSI) with relatively low molecular weight followed by hydrolysis. The product of thermal polymerization was washed with water several times until it was neutral and then with methanol and then kept for dialysis for 3–5 days (52). However, it has some irregularities in its structure for example, α and β amide linkages and a mixture of L and D isomer, even if the monomer used for condensation is L or D aspartic acid. The high molecular weight polymer was synthesized by the polycondensation of L-aspartic acid in a large amount of phosphoric acid and solvent under reduced pressure (53). Polycondensation of aspartic acid was carried out either by heating *in vacuo* or removing the water formed by azeotropic distillation. Aspartic acid on heating in tetralin, the first water molecule was lost within 17 h, while the second molecule was obtained only after several days (54). The presence of polycondensation accelerants, preferably phosphoric acid, results in a polymer of superior biodegradability and relatively high molecular weight compared to the other method but have difficulty in isolating the product from the remaining phosphoric acid. Synthesis of homopolymer and copolymer derivatives of poly(aspartic acid) using a catalytic amount of acid in different solvents, such as toluene, mesitylene, DMF, sulfolane or mixture of two of these solvents also results in high yield and polymer with relatively high molecular weight and high biodegradability in comparison with the polymer synthesized without catalyst (55). Polymer synthesized using phosphoric acid as a catalyst reported to be linear and totally biodegradable whereas, thermal polymerization without a catalyst was observed to be a branched one and did not biodegrade completely (55–58). The structure of poly(aspartic acid) has been mainly investigated using spectroscopic methods (56, 60).

The variation in the concentration of various functional groups such as amide protons, dicarboxylic acid end group, succinimide end group, maleimide end group, and diketopeperazine with polycondensation time of thermally synthesized PSI was observed by ^{13}C and ^{1}H NMR. Matsubara et al. (58) studied the reaction mechanism on the basis of end group analysis. The polymer chain is preferentially extended by the condensation of the amino group of monomer and dicarboxylic acid end group of the polymer. Thermal condensation of aspartic acid, results in PSI by conversion of aspartic acid to aspartic anhydride or α and β dipeptide (Scheme 1). The presence of diketopiparzine was reported during the early stage of polycondensation of L-aspartic acid; a small part of 0.4 per monomer units, and then its concentration decreases while polycondensation proceeds (49, 58). The relationship between the polymer structure and its biodegradability and chelating ability was investigated in order to use it (61–63). Takeshi Nakato (63) and



Scheme 1. Flow sheet of synthesis of polyaspartic acid by different starting material.

his coworkers explored the effect of reaction conditions on the molecular weight of poly(succinimide) using o-phosphoric acid as a catalyst. The acid catalyzed bulk polycondensation in a twin-screw extruder as a continuous method and batch process for the large-scale synthesis of PSI and sodium-polyaspartate (PASP-Na) was developed. The effect of biodegradability on the method of synthesis such as acid catalyzed bulk method, continuous and batch process in bulk production was discussed (64).

Copolymer Derivatives: Polyaspartate Hydrogel. A poly(aspartic acid) hydrogel was produced by various methods such as crosslinking reaction with poly(aspartic acid) or its functionalzed and defunctionalized derivatives (15, 65), by γ-irradiation (66), radical polymerization of end functioned macromonomer (67) and thermal curing (68) of a freeze-dried mixture composed of poly(aspartic acid) and a proper amount of PEG diepoxide in water. The effects of the pH, concentration, molecular weight of PAA in the aqueous solution, and dosage of γ-irradiation on the PAA hydrogel preparation were investigated. The study of swelling and biodegradability of the hydrogel revealed the swelling of PASP hydrogel using artificial urine was 27.4 g-water/g hydrogel and biodegradability 50% for 28 days using activated sludge (66). The swelling value of the PAA-hydrogel with lower molecular weight PAA used for hydrogel formation by γ-irradiation was the same as that for the PGA-hydrogel (polyglutamic acid) with higher molecular weight of PGA used in hydrogel formation. Kusuno et al. (67) reported the synthesis of PSI with an end functionalized methacrylate group and with controlled molecular weight hydrogel by acid catalyzed polycondensation of aspartic acid with cyclic anhydride such as phthalic anhydride, succinic anhydride, maleic anhydride, and pyromellitic anhydride followed by the reaction with 2-(methacryloxy) ethyl isocyanate, using radical initiator.

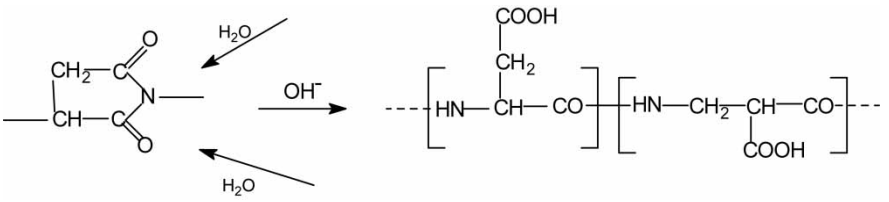
Hydrophobically Associating Poly(Aspartic Acid). Partially modified PSI, such as poly(L-aspartic acid-co-PEG) s was synthesized by melt polycondensation of the prepolymer prepared from N-CBz-L-(asparticacid) anhydride and low molecular weight PEG using acid catalyst which is biodegradable (40). Nakato et al. (69) prepared hydrophobically associating polymers by reaction of PSI with dodecylamine (dodecylamine in DMF). Sodium dodecylamine modified poly(aspartic acid) (DDA-PAA-Na) was easily obtained by the alkali hydrolysis of the corresponding PSI derivative. The MnO_2 dispersing property of DDA-PAA-Na was higher than that of PAA-Na. The intramolecular hydrophobic association caused by introduction of DDA was more than that of PAA. DDA modified PAA had the possibility of being used as a biodegradable dispersant having the comparable biodegradability with PAA-Na. Water-soluble polymers can be synthesized by various methods including copolymerization of water soluble monomer with hydrophobic co-monomer which can show amphiphilicity and attaching hydrophobic moieties such as long alkyl chains to water soluble polymer backbone (69) etc. The study of associating behavior of hydrophobically modified PAA synthesized using octadecylamine (70), as well as dodecylamine (DDA), was carried out by M. Suwa et al. (71). Further characterization using a fluorescence and quasielastic light scattering technique as a function % DDA in the polymer was done. The analysis of the polymer treated with octadecylamine by size exclusion chromatography and dynamic light scattering indicated that the aggregates became compact with the increasing amount of octadecyl chain and the particle size was reduced. Hydrophobic interactions of the alkyl groups stabilize aggregates effectively irrespective of polymer concentration. Recently, Ehtezazi et al. (72) carried a synthesis of a model drug by reaction of PAA and diminazene to understand

the interactive forces between PAA and diminazene. A polymer drug delivery system based on molecular self-assembly into complexes or micellar type complex formation system was studied.

Metal Absorbing Poly(aspartic acid). The future of metal waste cleanup depends to a great extent on the development of novel ion-exchange systems for the selective removal of metals from natural and industrial wastewaters. Isolation and recovery is only a possible option for metal removal, and not "degradation". Since permissible limits for many metals are at the ppm to sub-ppb levels, common methods of bulk removal to bring discharge streams and waste sites into compliance usually fail. For the system to be a success, efficient metal ion-exchangers large capacity and selectivity for target metals of interest are needed. To minimize column length and throughput, poly(l-aspartic acid) biopolymer, and a similar synthetic polymer, poly(acrylic acid), each consisting of about 50 repeating aspartic acid and acrylic acid monomers, respectively, were immobilized onto controlled pore glass (CPG) and evaluated for use as metal ion-exchange materials. Both of the polymers achieve metal complexation primarily through their repeating carboxylate side groups resulting in a similar binding trend for the metals tested (Ca^{2+}, Cd^{2+}, Co^{2+}, Cu^{2+}, $Mg^{2+,}$ Mn^{2+}, Na^{+}, Ni^{2+}, Pb^{2+}), with metal binding capacities ranging from 0.1 to 12 mol metal/g column and 0.1 to 32 mol metal/g column for poly(aspartic acid) and poly(arylic acid), respectively. Cu^{2+} and Pb^{2+} exhibited strong binding to both materials, while the other metals demonstrated only weak or minimal binding (73).

Hydrolysis

Thermal condensation of aspartic acid resulted in poly(succinimide), which on hydrolysis readily converted to poly(aspartic acid). Hydrolysis of PSI can be done either by alkali or acid. Almost complete racimization reported during thermal polycondensation and the hydrolytic opening of the ring may proceed at both carbonyls (74) as can be seen in (Scheme 2). Thus, the resulting polymer contains not only D and L isomer, but also has α and β peptide bonds in the main chain. Poly(succinimide) can be hydrolyzed to α-β poly(aspartic acid) or salt by alkali or alkaline hydroxide. The degree of hydrolysis can be controlled by pH control (59). The ratio of the α and β bond in poly(aspartic acid) can be modified by pH of the medium in which hydrolysis takes place. The lower the pH of the medium, the higher the proportion of α-bond in the product. The ratio of α-β is almost unaffected by ionic strength and temperature. PSI can be converted to poly(aspartic acid) by partial hydrolysis. The symmetry of the succinimide ring is small and it may be assumed from the analogy with 3-alkyl succinanhydrides, that both the α and β bond will appear in the product of hydrolysis. In past the biuret test, paper



Scheme 2. Hydrolysis of polysuccinimide at both carbonyls.

chromatography, IR and many other tests were carried out for the conformation of polypeptide as the predominant thermal product from heating amino acid.

Characterization of Poly(aspartic acid)

Infrared Analysis

Infrared spectra were used to distinguish between poly(aspartic acid) and diketopiperazine. Infrared absorption spectra showed that the entire thermal condensation product from different materials such as ammonia and malic acid or fumaric acid or maleic acid had the polyimide structure. The confirmation of the structure of poly(aspartic acid) came from the study of the sodium salt. Alkaline treatment can convert polyimide structure to a polypeptide structure. Characteristic absorption bands of the resulting peptide type poly(aspartic acid) were reported to be $3300\,cm^{-1}$, $3080\,cm^{-1}$ for NH stretching, $1710\,cm^{-1}$ for CO carboxyl group, $1650\,cm^{-1}$ corresponding aspartic acid and $1550\,cm^{-1}$succinimide type bond (75) respectively.

Molecular Weight

M. Tomida et al. obtained high molecular weight PSI by azeotropic removal of water using toluene, mesitylene, sulfolane and a mixture of these as a reaction solvent. PSI with weight average molecular weight M_w of 64,000 was synthesized using L-aspartic acid and a catalytic amount of o-phosphoric acid in a mixture of solvent mesitylene and sulfolane with the ratio of 7/3 by polycondensation. In mesitylene as solvent, PSI with weight average molecular weight M_w of about 24,000, was obtained whereas, in sulfolane the yield was higher than that for mesitylene but M_w was about 19,000, no polymer formed using toluene (53). A high molecular weight PSI with weight average molecular weight M_w of 64,000 was obtained under nitrogen atmosphere in the mixture of mesitylene and sulfolane. A copolymer of PSI and ω-amino acid such as: (a) 4-amino butylic acid, (b) 6-amino caproic acid, (c) 11-amino decanoic acid with M_w 21,000 for (a) and M_w with the increasing order of (a) > (b) > (c) was obtained (55). A DDA-PAA copolymer synthesized with weight average molecular weight 20,000 was determined and reported (69). The reaction of PSI with a molecular weight of 12,000-14,000 and hydrazine in DMF resulted in the copolymer polyaspartylhydrazide (Pahy) with the molecular weight M_w of 22,000 as determined by light scattering (65). A polymer of (aspartic acid-co-PEG) with pendant functional group protected was synthesized with M_w 31,000 (40). Vlasak (76) and his coworkers determined constants and exponents of the Mark Houwink equation:

$$[\eta] = K\ M^a$$

They found that fractionation of poly(succinimide) in a DMF solvent is considerably more advantageous than a fractionation of water-soluble substituted polyaspartamides derived from poly(succinimide). Poly(succinimide) ($M_w = 28{,}000$) was fractionated and viscosities were measured in 0.1M LiCl solutions in DMF. Without the addition of LiCl, the concentration dependence of reduced specific viscosity displayed a curvature same as that for polyelectrolytes at low ionic strength. It was found, due to COOH end groups or additional COOH group arising in the hydrolysis of some imide groups, the sum of which was found to be at the most 0.9 mol% estimated by titration in water after reaction with ethanolamine. A distinct polyelectrolyte behavior of the polymer in

the measurements of viscosity exhibited in DMF was attributed to the polymer with such low –COOH group content.

Weight average molecular weight for 2-6 fractions of poly(succinimide) was determined by light scattering, by measuring the intrinsic viscosity in DMF + 0.1M LiCl from the plot of log $[\eta]$ vs. log M_w, the constant K and a were determined (76).

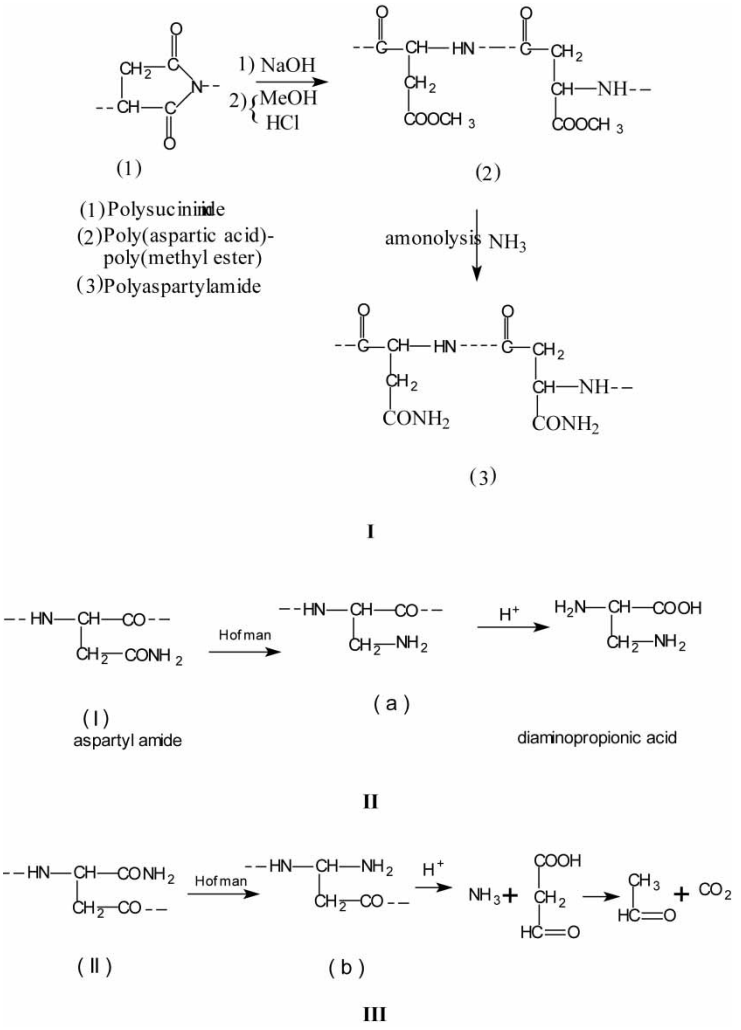
$$K = 1.32 \times 10^{-2}; \quad a = 0.76$$

Analysis of α-β Linkages. The fraction of α-β peptide bond or approximate amount of α-β linkages in poly(aspartic acid) have been determined and reported by many methods like Hoffman degradation, NMR spectroscopy, potentiometric titration, and circular dichroism (77).

Hoffman Degradation. The presence of α,β-linkages in poly(aspartic acid) was determined by Hoffman degradation. J. Kovacs et al. (54) hydrolyzed PSI to the sodium salt of PAA, which was then directly converted to poly(aspartic acid poly(methyl ester) (PAA-PME) using a methanol-hydrochloric acid solution. The methoxyl content of the PAA-PME indicated about 90% of esterification of carboxyl groups. The polyamide resulted from direct amonolysis of polyaspartyl amide. The α-aspartyl amide residue (I) gave intermediate (a) by Hofman degradation, and α,β-diaminopropionic acid on subsequent acid hydrolysis. Similarly, a β-aspartyl amide residue (II) gave acetaldehyde on hydrolysis via the intermediate (b) in (Scheme 3). Acetaldehyde present in the acidic hydrolyzate of the degraded poly(aspartic acid) polyamide was separated as the 2,4-dinitrophenylhydrazone, and any α,β-diaminopropionic acid isolated as the flavianate. Considering the loss during experimentation, the corrected amount of acetaldehyde, that is 2,4-dinitrophenylhydrazone obtained from degraded polyamide preparation, showed that 33% of the aspartic acid was present in the form of β-peptide bonds. Similarly, from the weight of α,β-diaminopropionic acid diflavianate indicated 25% of the aspartyl residue had α-peptide bonds. The ratio of the α-, and β-aspartyl residues in poly(aspartic acid) was found to be about 1 : 1.3, assuming no intramolecular transpeptidation took place during the esterification, amidation, or Hoffman degradation. The remaining 42% of aspartyl residue was further assumed to be similarly bound, that is the ratio of about 1 : 1.3.

NMR Analysis. NMR is the powerful tool for characterization of the polymer structure. The proton NMR spectrum of PSl recorded by using a AC 200 Mz Bruker FT.NMR spectrometer, by dissolving 20 mg of sample in 0.3 ml of DMSO-d_6 is given in Figure 1. Thermal poly(aspartic acid) contains both α and β bonds and their ratio can be modified by the pH of the medium in which hydrolysis takes place The fraction of α-β bonds in the product was determined by NMR spectroscopy. The lower the pH, the higher the α- bond in the product. The ratio of α and β bonds were reported to be almost unaffected by ionic strength and temperature. The molecular mass of the original polysuccinimide had no effect on the ratio of α and β bond.

Pivoca et al. (60) detected the presence of α and β bonds in the peptide chain by means of NMR spectra of aqueous solutions of polyaspartate at various pHs. The other method for proving the α, β bonds by means of NMR spectra of polyaspartate is a through complex formation with metal ions. The complex is formed through the COOH group. It is known that the interaction of the metal ions with poly(α-amino acids) can be followed by means of NMR spectra. From the study of ^{13}C NMR spectrum of



Scheme 3. Hoffman's degradation I). Polysuccinimide converted first to salt of PAA by 1) NaOH and then reaction with 2) MeOH and HCl resulted in α,β-(PAA-PME), direct amonolysis then converted PAA- PME to poly (aspartic acid amide) II). Residue of α-aspartyl amide by Hoffman's degradation through (a) resulted in α,β-diaminopropionic acid on acid hydrolysis. III). β-Aspartyl amide residue gave acetaldehyde via (b) in degradation outline of the manuscript.

thermally synthesized polyaspartate in the presence of various amounts of Co (II) at pH 7.0, it was shown that the CH (β) line in the NMR spectrum is broadened and shifted more than the CH (α) line, and CH_2 (α) line more than the CH_2 (β) line. This is because in the case of α bond, the COOH group is next to the CH_2 group, whereas in case of β bond, it is next to the CH group (60). Matsuyama et al. (78) calculated the ratio of α, β amide unit by integrating the separated methine signals in the ^{1}H-NMR spectrum recorded in the lower pD region.

A methylene signal of ^{13}C-NMR was also used to evaluate the ratio of α and β amide units. Rao et al. (79) studied the tacticity effects for the amide carbonyl signals in the

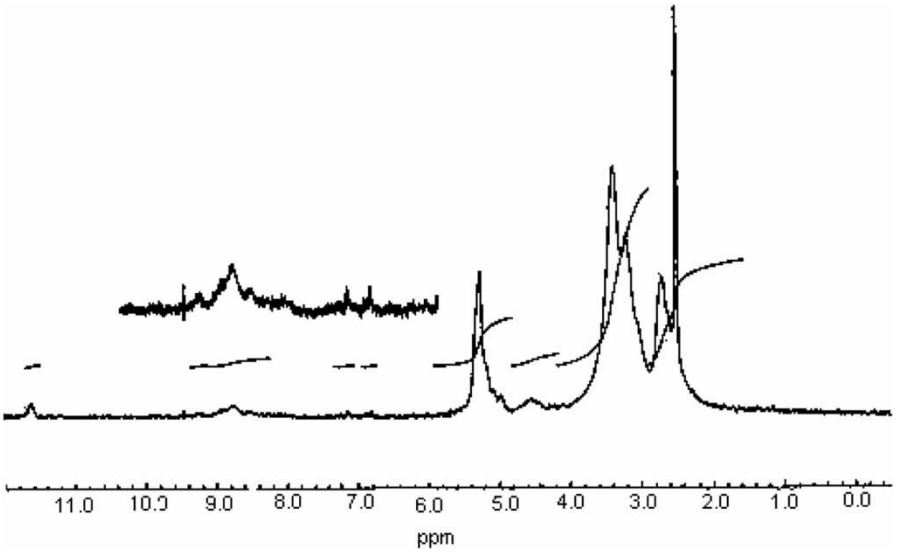


Figure 1. The ^{1}H NMR spectrum of PSl.

^{13}C-NMR spectrum. Both poly(succinimide) and sodium polyaspartate have been analyzed by a variety of one and two-dimensional NMR spectrum. According to the analysis done by ^{1}H-NMR sodium polyaspartate invariably contained 3 : 1 ratio of $\beta : \alpha$ linkages under different synthesis and hydrolysis conditions. On the basis of analysis done by ^{13}C-NMR and ^{1}H-HMBC data, it was concluded that α,β bonds were random. The proton NMR of poly(aspartic acid) was used to detect the residual succinimide level in hydrolysis, down to about 1% (57).

The difference in biodegradability of the polymer prepared by thermal polycondensation of aspartic acid with and without phosphoric acid as catalyst was reported using NMR spectroscopy. The polymer prepared using phosphoric acid as a catalyst, degraded completely whereas the polymer prepared without a catalyst was only 70% biodegradable. This difference in biodegradability was attributed to branching sites on the basis of proton NMR spectra of succinimide taken as a function of a phosphoric acid level (57). Several end groups, irregular structure and byproducts were identified and quantified in end group analysis of polysuccinimide by NMR. The maleimide, succinimide, dicarboxylic acid and fumaric acid end groups were identified, C-termini end group as succinimide and dicarboxylic acid occupy 10% of the monomer units in the polymer. The amino acid end group and maleamic acid end groups were not detected. The branched units were identified as irregular structures in the polymer. It was inferred that the amino end group was probably reduced by deamination, which produces many irregular structure possessing a maleic or fumaric acid unit (58).

Thermal Analysis. The knowledge of glass transition is essential in the selection of the materials for various applications T. Nakato et al. (80) studied the thermal property of poly(succinimide co-amide) as a processable material. In order to improve the thermal property of PSI, the copolymer consisting of succinimide and amide units were obtained, using 1) 4-amino benzoic acid, 2) 4-amino-methyl benzoic acid, 3) 4-amino-phenyl acetic acid and, 4) 4-(4-amino-phenyl) butyric acid. The comparative study of

PSI and its copolymer revealed that, PSI did not exhibit glass transition temperature T_g, and decomposed at 424°C without melting, in contrast, the copolymer had Tg, and a melting temperature T_m. The thermal properties of the copolymer deferred with varying the aromatic amino-carboxylic acid. Thermal analysis of aspartic acid-co-ω amino acid carried by M. Tomida et al. (55) using (a) 4-amino butylic acid, (b) 6-amino caproic acid. and (c) 11-amino decanoic acid for copolymer synthesis reported, glass transition temperature T_g, 92°C for (a), 97°C for (b), and 126°C for (c) and a melting point of 227°C for (b) and 255°C for (c). The degradation temperature of the copolymer of poly(imide-amide) was lower than that for PSI. These thermal properties indicate that poly(imide-amide) can be used as a new thermoplastic material. Synthetic water-soluble, biocompatible polymer such as α-β polyasparthydrazide was produced by the reaction of PSI with hydrazine (PAhy) and crosslinked with ethylene glycol diglycidyl ether (EDGDE) and the physical state of the crosslinked network was evaluated by means of X-ray diffractometry and thermal analysis. The T_g of uncrosslinked (Pahy) and crosslinked (Pahy)-EDGDE at various crosslinking ratios was determined. The glass transition temperature (T_g) increased with a degree of crosslinking and then decreased to an almost constant value at the higher amount of EDGDE in the network (65).

Biodegradability

Natural polymers in the biological system are in a state of flux in which they are continuously being degraded and again replenished by synthesis. Biodegradation is thus the norm in nature. Today, the challenge exists in learning how to mimic some of the remarkable adaptations of the biopolymers with a synthetic one. Biodegradability is one such phenomenon. The environmental degradation of polymers is a complex process, which is influenced by several agencies. There are various factors responsible for degradation, such as solar radiation, atmospheric temperature and its cycles, moisture, wind contaminant, and microorganisms. Chemical structure, molecular weight, morphology, crystallinity, glass transition, hydrophilicity and water uptake, these are the properties of polymer, playing important role in determining the biodegradability of the polymers. Measurement of biodegradability and relating it to the appropriate disposal environment is an essential criterion to be met by biodegradable polymer. ASTM, European and ISO standards have been developed and under development to evaluate biodegradability under different environmental disposal conditions like composting soil, marine wastewater treatment facility, anaerobic digester, etc. Anne Calmaon Decriaud et al. (81) described the standard method for testing the biodegradation of polymer material in their review. In the biomedical area, biodegradation refers to hydrolysis and oxidation that are the primary polymer degradation processes. On the other hand, for materials exposed to fragmentation, biodegradation refers to loss of mechanical properties or chemical modifications through the action of microorganism. Thus, many different degradation modes, either abiotic degradation or biotic degradation, can synergistically combine in natural conditions to degrade polymer, leading to different degrees of degradability and each specific action is difficult to isolate (82–88). The definition of biodegradable polymer is not clear and they are open to a large diversity of interpretations (89–92).

Depending on the state of the material, different test methods like biodegradation liquid test, or standard test method for solid can be applied to test the biodegradability of the polymer. It had been shown that a single measurement of consumed O_2 or produced CO_2 was not enough and must be completed by biomass evaluation and residual organic carbon in order to make the carbon balance. Experimental parameters

like environmental conditions, microbial population and its conditioning, sample concentration and forms that can interfere with the contact between the polymer and the microorganisms, may influence the mineralization rate, differ from one liquid standard test to another. For all these reasons, it was reported that the tests are still far from perfect. There is additional work to be done to make them more reproducible and especially to be sure that the same material gives the same result.

It was found that sodium polyaspartate synthesized in the presence of phosphoric acid, as the catalyst is 100% biodegradable, whereas the same polymer synthesized without a catalyst was only 70% biodegradable. Takashi et al. (61) studied the relationship between the structure and biodegradability of various isomeric forms of poly(aspartic acid) using the OECD 301C method. Distinct tendencies were found both between the number of amide protons and biodegradability and ratio of dicarboxylic acid end group to the dicarboxylic acid end group, plus succinimide end group and biodegradability. It was concluded that the chirality of the aspartic acid unit and the type of amide linkage in poly(aspartic acid) scarcely affected the biodegradability of the polymer. The result of repetitive biodegradability analysis for poly(aspartic acid) suggested 100% biodegradation is possible. It is necessary to find the standard reproducible method to test biodegradability of the polymer giving the same result for the same polymer. Poly(aspartic acid), being a biodegradable polymer, is likely to replace an environmentally hazardous polymer.

Recent Trends

Poly(aspartic acid) has various applications depending on its molecular weight. It can be used as an anti-scalant, dispersant, surfactant, growth enhancer, and fertilizer, and as a absorbent resin, chelating and complexing agent, in cosmetics and in toothpaste for anti-plaque formation. Thermal synthesis of poly(aspartic acid) without a catalyst resulted in a polymer with molecular weight of 10,000–15,000. The use of a catalyst in the synthesis of poly(aspartic acid), starting with amino acid and its derivative, resulted in a polymer with high molecular weight as much as up to 64,000. The catalyst used in the synthesis of homo as well as co-polymer of poly(aspartic acid) was reported to be an acid such as sulfuric acid, hydrochloric acid phosphoric acid and its derivatives. Though poly(aspartic acid) synthesized using these catalysts are reported to be 100% biodegradable, a great amount of solvent is consumed to remove the catalyst from the polymer after synthesis, and still the traces of the acid remaining in the polymer can be hazardous to the environment. The environmentally friendly catalyst or more economic process, which will not cause any hazard to the environment, is today's necessity looking at the increasing applications and demand of poly(aspartic acid) in various fields of life, being a biodegradable polymer. Also, along with biodegradability, a thorough study of the polymer with its many aspects as a possible potential hazard in the use or in the long term use for living beings; it is becoming necessary, for the use of the polymer in various fields. For examples,its use as a drug carrier and super absorbent material or growth enhancer for plants.

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