RASĀYAN *J. Chem.*
Vol. 17 | No. 2 |317-324| April - June | 2024
ISSN: 0974-1496 | e-ISSN: 0976-0083 | CODEN: RJCABP
http://www.rasayanjournal.com
http://www.rasayanjournal.co.in

STUDY OF AMIDES AND POLYAMIDES SYNTHESIZED FROM BIODEGRADABLE CARBOXYLIC ACIDS

Siddhi S. Panchal[1], Dilip V. Vasava[1,✉] and Rishikesh Joshi[2]
[1]Department of Chemistry, School of Sciences, Gujarat University, Ahmedabad-380009, (Gujarat) India
[2]Department of Biochemistry and Forensic Sciences, School of Sciences, Gujarat University, Ahmedabad-380009, (Gujarat) India
✉Corresponding Author: dilipvasava20@gmail.com

ABSTRACT
A series of seven novel amorphous amides and polyamides were synthesized from four biodegradable carboxylic acids by direct polycondensation with aliphatic diamines using Yamazaki-Higashi phosphorylation. Aliphatic carboxylic acids like acrylic acid, lactic acid, and adipic acid whereas aromatic carboxylic acid like terephthalic acid were reacted with ethylenediamine and diamino-propane respectively. The monocarboxylic acids yielded amides, whereas the dicarboxylic acids formed polyamides. The obtained products were characterized by FT-IR, ^{1}H NMR, LCMS, SEM, TGA, and DSC along with microbial biodegradation. The TGA thermogram comparison studies show a decrease in thermal degradation with an increase in the aliphatic chain. Also, the introduction of an aromatic ring decreases degradability. Glass transition of aliphatic polyamide at 140 °C has negligible melting endotherm. Also, the samples were structurally degraded after 15 days of biological treatment which was confirmed via FT-IR.
Keywords: Direct Polycondensation, Biodegradable Acids, Aliphatic Diamines, Thermal Degradation, Biodegradation.
RASĀYAN *J. Chem.*, Vol. 17, No. 2, 2024

INTRODUCTION

Among all the families of polymers, polyamides are second to none. Both natural and synthetic polyamides have their importance.[1] Essential macromolecules like proteins and peptides present in flora and fauna constitute natural polyamides, whereas synthetic polyamides can be coveted with desired characteristics like strength, durability, degradability, stability, biocompatibility to show great potential for countless efficient applications.[2] Biomedical applications of synthetic polyamides as in-vivo biomaterials comprise drug delivery vehicles,[3] gene carriers,[4] microbiologically active substrates,[5] cell repair scaffolds as well as for applications in 3D printing of medical components like dental structures and orthopedic joints, intravenous stents, and other long-term implantations with induced nano-dimensions.[6]

These potent characteristics of polyamides have driven us to develop synthetic pathways for new functional polyamides,[7] which can be efficiently equipped as structural arms in designing star-shaped polymers having biomedical applications.[8] Polyamides can be synthesized via two methods: ring-opening polymerization and step-growth direct polycondensation.[9]

Yamazaki–Higashi phosphorylation is one of the direct polycondensation methods where diacids are condensed with diamines with condensing agents, like triphenyl phosphite (TPP) and pyridine (Py); solubility promoters, like lithium chloride (LiCl) and/or calcium chloride ($CaCl_2$), to form polyamides by avoiding the use of moisture-sensitive acid chlorides.[10]

Biodegradation of synthetic polymers primarily involves their depolymerization by microbial culture assistance.[11] Under mild conditions, the microorganism colonizes and releases extracellular enzymes to structurally break down the polymer into fragments of oligomers, dimers, and even monomers.[12] Intracellular metabolization of these fragments results in the formation of molecules like CO_2, NH_2, and H_2O.[13]

In this work, we have designed and synthesized three amides and four polyamides, equipping the Yamazaki–Higashi phosphorylation method. The chemical structures, masses, and properties, such as solubility, and surface morphology have also been studied.

http://doi.org/10.31788/RJC.2024.1728742

EXPERIMENTAL

Material and Methods

Acrylic acid (Sigma Aldrich, USA), glycine (Sigma Aldrich, USA), lactic acid (Merck, USA), adipic acid (Finar by Actylis, Gujarat, India), terephthalic acid (GLR Innovations, New Delhi, India), ethylene diamine (GLR Innovations, New Delhi, India), 1,3-diamino propane (GLR Innovations, New Delhi, India) were used as received. Calcium chloride ($CaCl_2$), lithium chloride (LiCl), triphenyl phosphite (TPP), and pyridine (Py) were bought from Tokyo Chemical Industry Co., Ltd. (TCI), Japan. N-methyl-2-pyrrolidone (NMP) and methanol (MeOH) were bought from Finar by Actylis, Gujarat, India. All solvents were distilled before use.

General Procedure

A series of amides and polyamides were synthesized via Yamazaki-Higashi phosphorylation by directly poly-condensing monocarboxylic acids: acrylic acid (AcA), lactic acid (LA), and dicarboxylic acids: adipic acid (AdA), terephthalic acid (TA) respectively with two aliphatic diamines: ethylene diamine (EDA) and diamino propane (DAP).

Synthesis of Amides

A calculated amount of AcA (1.0 mmol), and diamine (1.0 mmol) was added to a solution of $CaCl_2$ (0.3 mmol), LiCl (0.2 mmol) in 7.0 mL NMP, 0.5 mL Py and TPP (2.0 mmol). The mixture was stirred for 10 hr at 110°C under an inert atmosphere. After room temperature is reached, the resulting reaction mixture was dumped in a solution of distilled H_2O: MeOH (1:1). Acrylic acid-ethylene diamine (AcA-EDA) (1a) in the form of white precipitates is produced on constant stirring. After washing thoroughly with distilled water, the precipitates were collected by vacuum filter. This procedure was repeated two times before drying the product at 110°C under vacuum for 24 hr. (Fig.-1) Similarly, two different amides: lactic acid-ethylene diamine (LA-EDA) (2a) and lactic acid-diamino propene (LA-DAP) (2b) were synthesized by reacting LA with two diamines (EDA and DAP) respectively via this procedure. (Fig.-2)

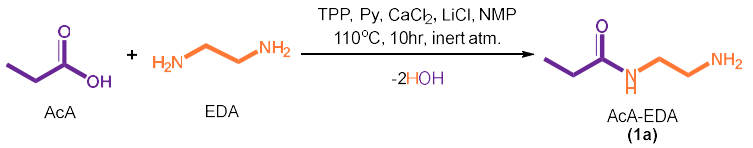

Fig.-1: Scheme for Acrylic Acid-Ethylene Diamine

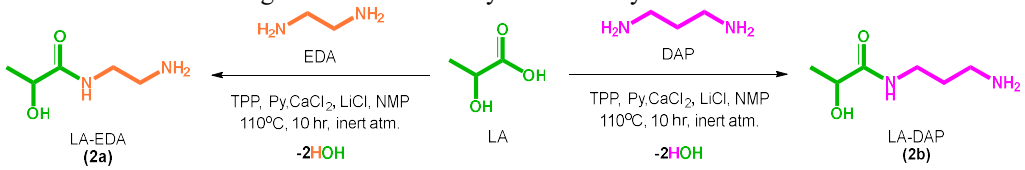

Fig.-2: Scheme for Lactic Acid-Ethylene Diamine and Lactic Acid-Diamino Propene

Synthesis of Polyamides

A calculated amount of dicarboxylic acids (1.0 mmol), and diamine (2.0 mmol) was added to a solution of $CaCl_2$ (0.3 mmol), LiCl (0.2 mmol) in 7.0 mL NMP, 0.5 mL Py and TPP (2.0 mmol). The mixture was stirred for 15 hr at 110°C under an inert atmosphere. After room temperature was reached, the resulting polymer mixture was dumped in a solution of distilled H_2O: MeOH (2:3). Polyamide in the form of white precipitates was produced on constant stirring. After washing thoroughly with distilled H_2O, the precipitates were collected by vacuum filter and repeat procedure two times before drying the product at 110°C under vacuum for 24 hr (Fig.-3).

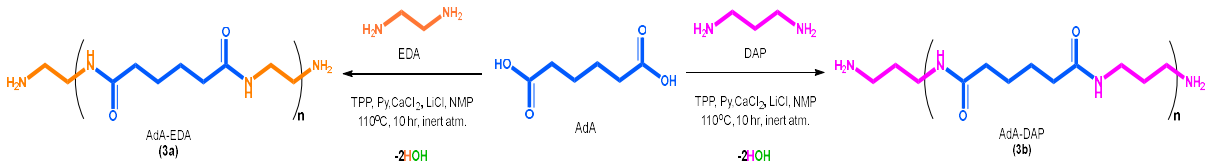

Fig.-3: Scheme for Adipic Acid-Ethylene Diamine and Adipic Acid-Diamino Propene

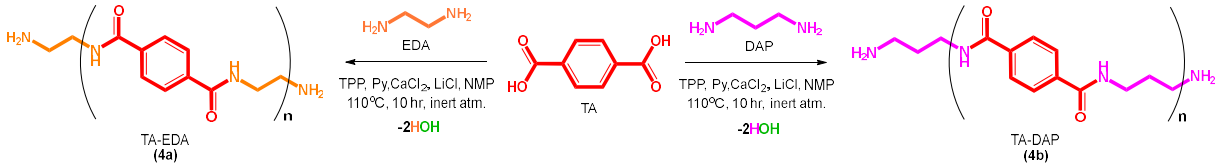

Fig.-4: Scheme for Terephthalic Acid-Ethylene Diamine and Terephthalic Acid-Diamino Propene

Four different polyamides: adipic acid-ethylene diamine (AdA-EDA) (3a), adipic acid-diamino propene (AdA-DAP) (3b), terephthalic acid-ethylene diamine (TA-EDA) (4a) and terephthalic acid-diamino propene (TA-DAP) (4b) were synthesized by reacting both the diacids (AdA and TA) with two diamines (EDA and DAP) respectively via this procedure (Fig.-4).

Detection Method

The chemical structures of amides and polyamides were characterized by Fourier transform-infra-red (FT-IR) spectrometry and proton nuclear magnetic resonance (^{1}H NMR) spectroscopy. The FT-IR spectra were performed using Spectrum 2 (Perkin Elmer) spectrometer. ^{1}H NMR (500 MHz) spectra were recorded with a Bruker Advance III (AV 500) spectrometer at 25°C using D_2O and DMSO as solvents. The masses of the products were studied by Liquid chromatography-mass spectroscopy (LCMS) using an Agilent 6545XT AdvanceBio LC/Q-TOF spectrometer with an injection volume of 5µL. Scanning electron microscope (SEM) images for morphological studies were obtained with Carl Zeiss UHR FESEM Model Gemini SEM 500 KMAT in high vacuum with 0.8 nm resolution. Thermogravimetric analysis (TGA) was recorded on the HiRes1000 instrument at a heating rate of 0.01 to 200°C/min under nitrogen. Differential scanning calorimetry (DSC) was measured on a Shimadzu DSC-60 instrument with a 200°C/min heating rate under nitrogen. The glass transition temperature (T_g) of amides and polyamides was obtained via DSC thermogram curves. The biological degradation treatment was done in the culture media having a mixture of DH5α strain of gram-positive *Escherichia coli* (*E. coli*) found in the lower intestine of warm-blooded organisms and gram-negative *Bacillus subtilis* found in the gastrointestinal tract of humans.

RESULTS AND DISCUSSION

Structural Confirmation

The chemical structure of obtained amides and polyamides was characterized by FT-IR and 1H NMR analysis. In FT-IR, the -C=O stretching frequency was observed at 1740 cm^{-1}, whereas secondary -N-H stretching was observed between 3500 to 3085 cm^{-1} and bending vibrations at 1645 to 1500 cm^{-1} (Fig 5) confirming the amide group. The -C-H stretching vibrations of the methyl group of AcA and LA were observed between 2990 to 2850 cm^{-1} for AcA-EDA, LA-EDA, and LA-DAP. The -O-H of LA scarcely shows stretching frequency at 3550 cm^{-1} for LA-EDA and LA-DAP. Also, aromatic -C-H stretching vibrations of TA in TA-EDA and TA-DAP are visible at 3100 cm^{-1}.

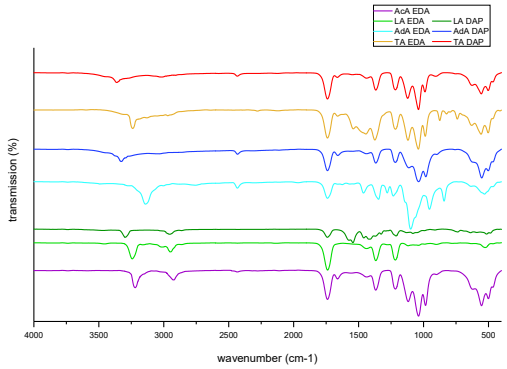

Fig.-5: FT-IR Spectra of Amides and Polyamides

Through ^{1}H-NMR spectrum, the peaks corresponding to the structures given besides were obtained. The signals that occur around 7.29 ppm are associated with the amino protons of the amide group, whereas the peak appearing in a region between 3.46 to 3:84 ppm results from the -C-H protons of the amide group (Fig.-6a and 6b). The very sharp intensive peak of solvents at 3.35 ppm corresponds to the exchanged

protons of deuterium water (D_2O) and 2.50 to 2.53 ppm represents dimethyl sulfoxide (DMSO). The signals at 2.79 and 2.99 ppm correspond to terminal primary amine of EDA and DAP respectively in AdA-EDA, TA-EDA, and AdA-DAP, TA-DAP. Also, the signals at 2.51 ppm represent the aliphatic hydroxyl of LA-EDA and LA-DAP.

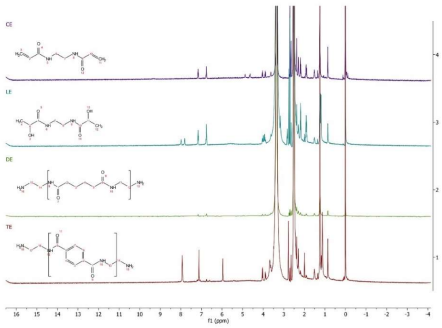

Fig.-6a: NMR Spectra of Amides and Polyamides having EDA

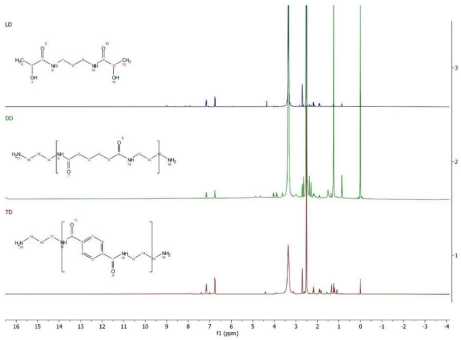

Fig.-6b: NMR Spectra of Amides and Polyamides having DAP

Mass

The LCMS analysis of the synthesized amides and polyamides gave information about the giant fragments of polymeric products. (Fig.-7) The base peak can be detected at m/z = 240.988, 240.988, 240.988, 507.272, 507.271, 338.342 and 485.289 for AcA-EDA, LA-EDA, LA-DAP, AdA-EDA, AdA-DAP, TA-EDA and TA-DAP respectively. The presence of a strong fragment ion peak at m/z = 44 is usually indicative of amide. The significantly bigger fragments in the form of amines having aliphatic chains as well as carboxylic acid chains were also seen which provided evidence of the defragmentation with simultaneous rearrangement of fragments and their reassembly. Unreasonable losses of m/z = 17, 18, 30, or 44 correspond to OH, NH_2, H_2O, CH_2NH_2, or CO_2 respectively.

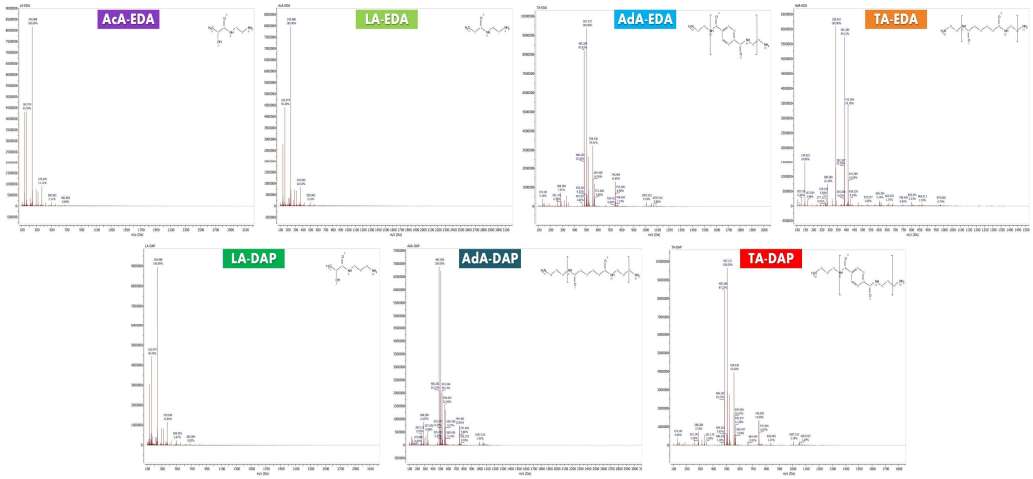

Fig.-7: LCMS Spectra of Amides and Polyamides

Solubility

The solubility of these hydrophobic amides and polyamides was determined by dissolving 1 mg of sample in 5 mL of solvent (10 wt%) at room temperature (Fig.-8). Both the amides and polyamides have good solubility in polar protic solvents like MeOH and polar aprotic solvents such as NMP, DMSO, and N, N-dimethyl formamide (DMF) in comparison to non-polar solvents like chloroform ($CHCl_3$) and dichloromethane (DCM).

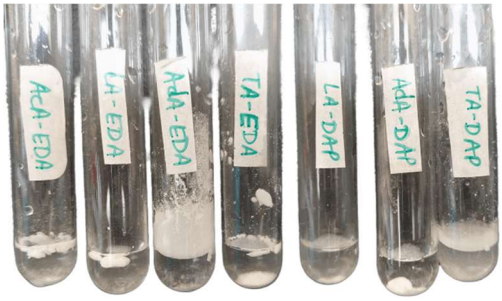

Fig.-8: Insoluble Products in Water Showing Hydrophobicity

Moreover, the solubility increases with an increase in the carbon skeleton of the diamines used in polycondensation, as summarized in Table-1.

Table-1: Solubility of Amides and Polyamides

Solvents (decreasing polarity)	AcA-EDA	LA-EDA	AdA-EDA	TA-EDA	LA-DAP	AdA-DAP	TA-DAP
MeOH	+--	+--	+--	+--	+++	+++	+++
NMP	+--	+--	+--	+--	+++	+++	+++
DMSO	+--	+--	+--	+--	+++	+++	+++
DMF	+--	+--	+--	+--	+++	+++	+++
$CHCl_3$	---	---	---	---	++-	++-	++-
DCM	---	---	---	---	++-	++-	++-

+++: highly soluble, ++-: partially soluble, +--: scarcely soluble, ---: insoluble

Morphology

The structural morphology of the synthesized amides and polyamides was scanned by SEM. The analysis image showed a flake-like structure for AcA-EDA, LA-EDA, AdA-EDA, and TA-EDA (Fig.-9) whereas amorphous morphology for LA-DAP and TA-DAP. Also, AdA-DAP has a fiber-like appearance.

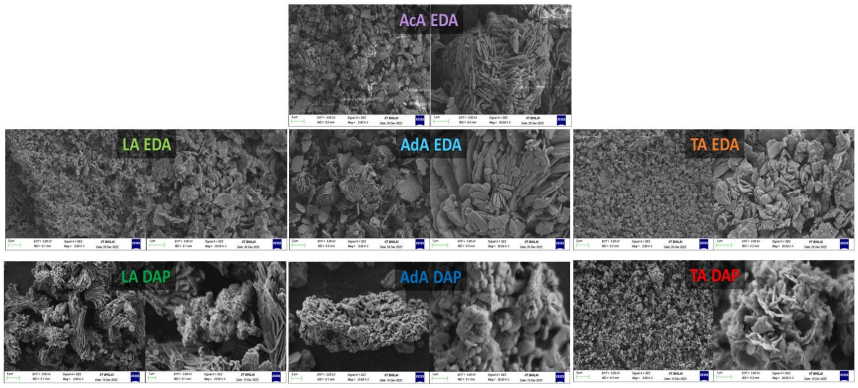

Fig.-9: SEM Images of Amides and Polyamides

Thermal Degradation

Thermal degradation via %mass loss is studied via a TGA thermogram (Fig.-10). The %mass of compounds containing EDA lost after 200 ^oC can be marked at 82%. The rate of mass loss with respect to the increase in temperature becomes steady at 80% for AcA-EDA, LA-EDA, and AdA-EDA, whereas TA-EDA shows steady loss in mass with increasing temperature. LA-DAP displays a gradual mass loss as the temperature

increases. AdA-DAP has a sudden loss of mass from 85% at 400 °C and 65% at 600 °C. TA-DAP shows a drop in %mass loss with 68% at 510 °C. Compounds containing EDA start forming char at 300 °C, whereas compounds having DAP show gradual degradation till char formation at 800 °C, which suggests that they show comparatively more thermal degradability than the former.

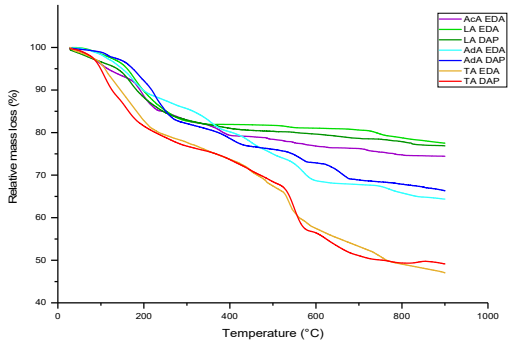

Fig.-10: TGA Thermogram of Amides and Polyamides

The DSC thermogram of AdA-DAP shows that the polyamide is completely amorphous having a wide range of glass transition temperature (Tg). The Tg of AdA-DAP ranges from 140-150 °C which represents the conversion of the polyamide from solid state to glassy form and a negligible melting endotherm (Fig.-11).

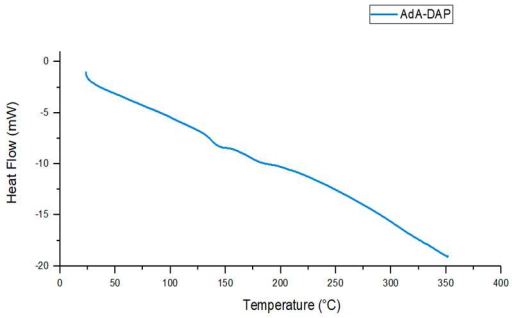

Fig.-11: DSC Thermogram of AdA-DAP

Biodegradation

DH5α strain of *E. coli* was incubated with 10 mg of synthesized products in shaking condition at 37°C for 15 days (Fig.-12). The isolated growth media was kept under controlled conditions without any microorganisms. The samples were analyzed visually under a microscope and structurally via FT-IR at an interval of 7 days.

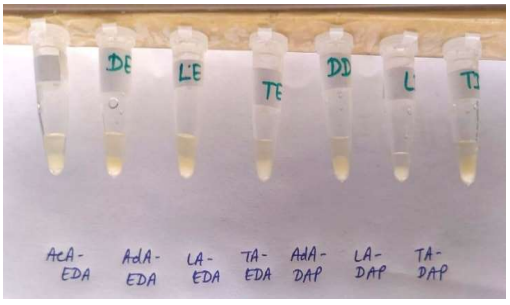

Fig.-12: Degradation of Samples on Day 15 of Biological Treatment

Figure-13 shows the FT-IR graph of the biodegraded products at the end of 15 days of microbial treatment. The graphs showed the diminished peaks of amides, amines, and carboxylic acids, signifying the successful structural degradation of the samples.[14]

CONCLUSION

Aliphatic and semi-aromatic amides and polyamides were synthesized biodegradable dicarboxylic acids with two aliphatic diamines by Yamazaki-Higashi phosphorylation reaction. This direct polycondensation

method evades the stoichiometric pre-activation by hazardous acyl chlorides or in situ activation reagents mandatory in conventional polyamidation process and gives a much greener process having a high atomic economy.

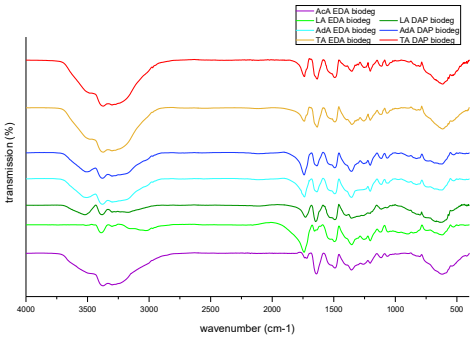

Fig.-13: FT-IR Spectra of Amides and Polyamides after Biodegradation

The synthesized products were structurally confirmed by FT-IR and ^{1}H NMR. SEM analysis showed the amorphous morphology of the products having good solubility in various polar solvents. Their thermal behavior study by TGA proved that the aromaticity of TA in TA-EDA decreased its thermal degradability in comparison to other products containing EDA. The T_g of 140 °C for AdA-DAP confirming its amorphous nature was studied via DSC. An increase in the carbon chain of the diamine backbone increases the solubility and decreases the thermal degradability of the amides and polyamides. The diminishing of amide group peaks in the FT-IR spectra of the biodegraded samples signifies the depolymerization of samples at the end of 15 days of microbial treatment. Owing to the extensive importance of functional amides and polyamides, biodegradability studies of these products have also been carried out, given their potential to be considered for structural arms in the synthesis of star-shaped biodegradable polymers for drug-delivery systems.

ACKNOWLEDGMENTS

The authors acknowledge the Department of Chemistry, School of Sciences, Gujarat University, Ahmedabad, Gujarat, India for basic infrastructural facilities and the Department of Biochemistry and Forensic Science, School of Sciences, Gujarat University, Ahmedabad, Gujarat, India for biodegradation facilities. The authors also acknowledge the characterization conveniences of MNIT Jaipur for IR, IIT Roorkee for NMR; IIT Bhilai for LCMS; IIT Bhilai for SEM; Delhi University for TGA, and SAIC, Tezpur University for DSC.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

All the authors contributed significantly to this manuscript, participated in reviewing/editing, and approved the final draft for publication. The research profile of the authors can be verified from their ORCID IDs, given below:

Siddhi S. Panchal https://orcid.org/0000-0002-5628-8803
Dilip V. Vasava https://orcid.org/0000-0001-8513-7580
Rishikesh Joshi https://orcid.org/0000-0003-3772-5569

REFERENCES

1. Y. Jiang and K. Loos, *Polymers*, **8(7)**, 243(2016), http://dx.doi.org/10.3390/polym8070243
2. S. S. Panchal and D. V. Vasava, *ACS Omega*, **5(9)**, 4370(2020), http://dx.doi.org/10.1021/acsomega.9b04422

3. M. Anwar, F. Muhammad and B. Akhtar, *Journal of Drug Delivery Science and Technology*, **64**, 102638(2021), http://dx.doi.org/10.1016/j.jddst.2021.102638
4. S. S. Panchal and D. V. Vasava, *International Journal of Polymeric Materials and Polymeric Biomaterials*, **73(6)**, 478(2023), http://dx.doi.org/10.1080/00914037.2023.2167081
5. P. Sahariah, D. Cibor, D. Zielinska, M. A. Hjalmarsdottir, D. Stawski and M. Masson, *International Journal of Molecular Sciences*, **20(7)**, 1743(2019), http://dx.doi.org/10.3390/ijms20071743
6. S. Hajebi, S. Yousefiasl, I. Rahimmanesh, A. Dahim, S. Ahmadi, F. B. Kadumudi, N. Rahgozar, S. Amani, A. Kumar, E. Kamrani, M. Rabiee, A. Borzacchiello, X. Wang, N. Rabiee, A. Dolatshahi-Pirouz and P. Makvandi, P., *Advanced Healthcare Materials*, **11(20)**, e2201583(2022), http://dx.doi.org/10.1002/adhm.202201583
7. S. D. Ghodke, A. B. Tamboli, A. V. Diwate, V. P. Ubale and N. N. Maldar, *Designed Monomers and Polymers*, **23(1)**, 177(2020), http://dx.doi.org/10.1080/15685551.2020.1826705
8. S. S. Panchal, D. V. Vasava, *International Journal of Polymeric Materials and Polymeric Biomaterials*, **71(18)**, 1407(2021), http://dx.doi.org/10.1080/00914037.2023.2167081
9. S. Lee, Y. R. Lee, S. J. Kim, J. S. Lee and K. Min, *Chemical Engineering Journal*, **454**, 140470(2020), http://dx.doi.org/10.1016/j.cej.2022.140470
10. J. Zhao, H. Xu, J. Fang and J. Yin, *Journal of Applied Polymer Science*, **126(1)**, 244(2012), http://dx.doi.org/10.1002/app.36979
11. M. M. Abe, M. C. Branciforti and M. Brienzo, *Recycling*, **6(1)**, 22(2021), http://dx.doi.org/10.3390/recycling6010022
12. J. Ruthi, M. Cerri, I. Brunner, B. Stierli, M. Sander and B. Frey, *Frontiers in Microbiology*, **14**, 1178474(2023), http://dx.doi.org/10.3389/fmicb.2023.1178474
13. S. Wang, X. Yang, L. Zhou, J. Li and H. Chen, *Journal of Materials Chemistry B*, **8(15)**, 2974(2020), http://dx.doi.org/10.1039/c9tb02845e
14. S. S. Panchal and D. V. Vasava, *Oriental Journal of Chemistry*, **40(1)**, 258(2024), http://dx.doi.org/10.13005/ojc/400131

[RJC- 8742/2023]