

Original Research Article

<https://doi.org/10.20546/ijcmas.2026.sp13.002>

Green Synthesis of Pharmaceutical Polymers Using Heterogeneous Phase-Transfer Catalysis

Loganathan Subramanian^{1*}, Vidyadharani Gopalakrishnan² and Anand Balu¹

¹Department of Chemistry, Sir Theagaraya College, Chennai, India

²Department of Microbiology, Valliammal College for Women, Chennai, India

*Corresponding author

ABSTRACT

The development of environmentally sustainable synthetic methodologies has become increasingly important in pharmaceutical and polymer research. Phase-transfer catalysis (PTC) provides an efficient approach for facilitating reactions between reagents present in different phases and can improve reaction efficiency under heterogeneous conditions. In the present study, tetra-isopropylammonium chloride (PTC) was synthesized as a phase-transfer catalyst using ammonia and isopropyl chloride in ethanol under reflux conditions. The synthesized catalyst was purified by repeated ether washing and characterized using Fourier-transform infrared (FT-IR). The catalytic performance of PTC was investigated in the polymerization of styrene using an aqueous/organic biphasic system. Polymerization experiments were performed at different styrene concentrations and temperatures, both in the presence and absence of PTC. The reported results demonstrated an increase in the rate of polymerization with increasing monomer concentration. At 65 °C, the reported polymerization rate increased from 0.087 to 0.308 without PTC and from 0.125 to 0.438 in the presence of 0.5 g PTC as the styrene volume increased from 2 to 7 mL. At 75 °C, the corresponding rate increased from 0.149 to 0.519 in the presence of PTC. These findings indicate that PTC enhances the polymerization process under the investigated heterogeneous conditions. The resulting polymeric materials may have potential relevance to polymer-based pharmaceutical technologies, particularly controlled drug-delivery systems; however, direct drug loading, encapsulation, release, biocompatibility, and therapeutic studies were not included in the present investigation. Thus, the study provides a foundation for further development of PTC-assisted polymeric materials for potential drug-delivery applications.

Keywords

Green chemistry, phase-transfer catalysis, quaternary ammonium salt, heterogeneous polymerization

Article Info

Received:

10 August 2026

Accepted:

25 September 2026

Available Online:

10 October 2026

Introduction

The increasing demand for sustainable chemical processes has encouraged the development of synthetic

methodologies that minimize hazardous reagents, waste generation, energy consumption, and environmental impact. Green chemistry emphasizes the design of chemical processes that reduce or eliminate the use and

generation of hazardous substances while maintaining efficient chemical transformations. Recent developments in sustainable organic chemistry have particularly focused on reducing solvent-related waste, improving reaction efficiency, and replacing conventional reaction conditions with safer and more resource-efficient alternatives (Sharma *et al.*, 2024). Quaternary ammonium salts are among the most widely investigated PTCs because their ionic nature and structural characteristics can facilitate interaction with both aqueous and organic reaction environments. This interfacial transfer can increase the effective concentration and reactivity of the reacting species and thereby enhance the rate of heterogeneous reactions (Vermeeren, *et al.*, 2024; Sharma *et al.*, 2024).

The efficiency of the process is influenced by catalyst structure, phase composition, agitation, interfacial area, solvent characteristics, and the nature of the counterion. Recent research has continued to demonstrate that controlling transport at the liquid–liquid interface can significantly influence phase-transfer reactions, highlighting the importance of interfacial mass transfer in PTC systems (Ang *et al.*, 2024). Recent literature also emphasizes the broad chemical utility of quaternary ammonium compounds, including their application as phase-transfer catalysts and functional ionic materials. Polymer-based drug-delivery systems have attracted considerable attention because polymers can be tailored to control the incorporation, protection, and release of therapeutic agents. Conventional drug-delivery approaches may be associated with limitations such as poor aqueous solubility, rapid elimination, fluctuations in drug concentration, and nonspecific distribution (Xu, Y, *et al.*, 2025). Polymeric systems provide opportunities to improve drug-delivery performance through control of polymer composition, molecular weight, hydrophilicity, morphology, degradation behavior, and drug–polymer interactions (Aghajanpour, S. *et al.*, 2025). Depending on the characteristics of the polymeric matrix, drug release may occur through diffusion, swelling, erosion, degradation, or a combination of these mechanisms, enabling sustained or controlled release of therapeutic agents. Recent studies have highlighted the continuing importance of polymeric materials in controlled drug delivery and pharmaceutical applications (Lu *et al.*, 2024; Xu, 2025). However, successful development of a polymeric drug-delivery system requires evaluation of drug-loading capacity, encapsulation efficiency, release kinetics, physicochemical stability, biocompatibility, and potential toxicity of the polymer and its degradation

products (Jiang, M, *et al.*, 2025). In the present study, the synthesized PTC was investigated primarily as a phase-transfer catalyst for styrene polymerization under heterogeneous conditions. Therefore, although the resulting polymeric materials may have potential relevance to future drug-delivery applications, direct drug loading, drug-release studies, biocompatibility evaluation, and therapeutic investigations were not performed in the present work. These aspects should be addressed in future studies to establish the suitability of the developed polymeric system for pharmaceutical drug-delivery applications.

Accordingly, the objective of this work was to synthesize and characterize PTC and evaluate its catalytic behavior during styrene polymerization under heterogeneous conditions. The study provides experimental evidence for the effect of PTC on polymerization rate and establishes a basis for subsequent investigation of the resulting polymeric systems in drug-delivery applications.

Materials and Methods

Chemicals and reagents

All chemicals and reagents used in the present study were of analytical or general reagent grade and were used as received unless otherwise specified. Ammonia and isopropyl chloride were used as the principal reactants for the synthesis of the phase-transfer catalyst (PTC), while ethanol was used as the reaction solvent. Diethyl ether was used for purification of the synthesized catalyst. Styrene was used as the monomer for polymerization and was purified before use by treatment with 5% sodium hydroxide solution, followed by 3% phosphoric acid treatment and washing with double-distilled water. Other reagents used during the polymerization experiments included potassium sulfate (K_2SO_4), sulfuric acid (H_2SO_4), potassium persulfate ($K_2S_2O_8/PS$), methanol, ethyl acetate, sodium hydroxide, chlorobenzene, diethyl ether, and acetone.

The polymerization was carried out using an aqueous/organic biphasic reaction system. Styrene was present in the organic phase containing ethyl acetate, while the aqueous phase contained the catalyst and other components required for controlling ionic strength and acidity. Potassium sulfate was used to maintain ionic strength, and sulfuric acid was used to control the hydrogen-ion concentration of the aqueous phase.

Instrumentation and Equipment

The synthesized PTC was characterized using Fourier-transform infrared (FT-IR) spectroscopy. Additional laboratory equipment included a thermostat, mechanical stirrer, reaction vessel, nitrogen supply system, melting-point apparatus, thin-layer chromatography equipment, and chromatographic facilities.

Preparation of Polymer-Based Drug-Delivery Material

The polymer obtained through the PTC-assisted styrene polymerization was considered as a polymeric matrix for potential drug-delivery application. The polymer was first purified by washing and dried under vacuum at 50–60 °C, following the polymer isolation procedure described in the present study. For a subsequent drug-delivery study, a suitable model drug would be incorporated into the polymeric matrix using an appropriate drug-loading or encapsulation method. The polymer and selected drug would be combined under controlled conditions, followed by separation of the drug-loaded polymer from the unincorporated drug.

Characterization of Drug-Loaded Polymer

The drug-loaded polymer would be characterized to determine changes in its physicochemical properties following drug incorporation. Appropriate analyses could include FT-IR spectroscopy, UV–visible spectroscopy, surface morphology used for the final formulation. Drug-release data could subsequently be fitted to suitable kinetic models to investigate the mechanism of drug release.

Results and Discussion

Synthesis of the phase-transfer catalyst

A measured amount of ammonia (1 equivalent) and isopropyl chloride (4 equivalents) was placed in a 250 mL round-bottom flask. Ethanol (40 mL) was added slowly to the reaction mixture. The resulting solution was stirred and refluxed under a nitrogen atmosphere for 48 h. After completion of the reaction, the excess solvent was removed under reduced pressure using a vacuum evaporator. The resulting crude phase-transfer catalyst (PTC) was repeatedly washed with diethyl ether (4 × 25 mL) to remove residual impurities. The purified catalyst

was subsequently dried and stored in a desiccator until further use. The synthesized PTC was characterized by FT-IR.

The FT-IR spectrum of the synthesized PTC exhibited characteristic absorption bands at approximately 3000 and 2932 cm^{-1} , attributed to C–H stretching vibrations. The band at 1473 cm^{-1} was assigned to C–H bending, while the absorption at 1178 cm^{-1} was attributed to C–N⁺ stretching. These characteristic bands support the presence of the aliphatic ammonium structure in the synthesized PTC

Potential Drug-Delivery Application of the Polymer

The polymer obtained through the PTC-assisted polymerization of styrene was considered as a potential polymeric matrix for drug-delivery applications. The polymerization results demonstrated that the presence of PTC enhanced the rate of polymerization under the investigated heterogeneous conditions. At 65 °C, the polymerization rate increased from 0.087–0.308 in the absence of PTC to 0.125–0.438 in the presence of 0.5 g PTC as the styrene volume increased from 2 to 7 mL. Further, at 75 °C, the polymerization rate increased from 0.149 to 0.519 over the same monomer-volume range.

These results indicate that the PTC-assisted polymerization system can produce polymeric material under the investigated conditions. From a drug-delivery perspective, such polymeric materials may provide a matrix for the incorporation and controlled release of therapeutic compounds.

The physicochemical characteristics of the polymer, including its structure, morphology, hydrophobicity, and interaction with a drug, would be expected to influence drug incorporation and release behavior. Therefore, the polymer obtained in the present study may serve as a basis for subsequent investigation as a drug-delivery material.

Characterization of Calcium Polystyrene Sulfonate

The FT-IR spectrum of the synthesized calcium polystyrene sulfonate exhibited characteristic absorption bands associated with the polystyrene backbone and sulfonate functionality.

Figure.1 Synthesis of tetra-isopropylammonium chloride (PTC) from ammonia and isopropyl chloride in ethanol under reflux conditions at 75 °C for 48 h.

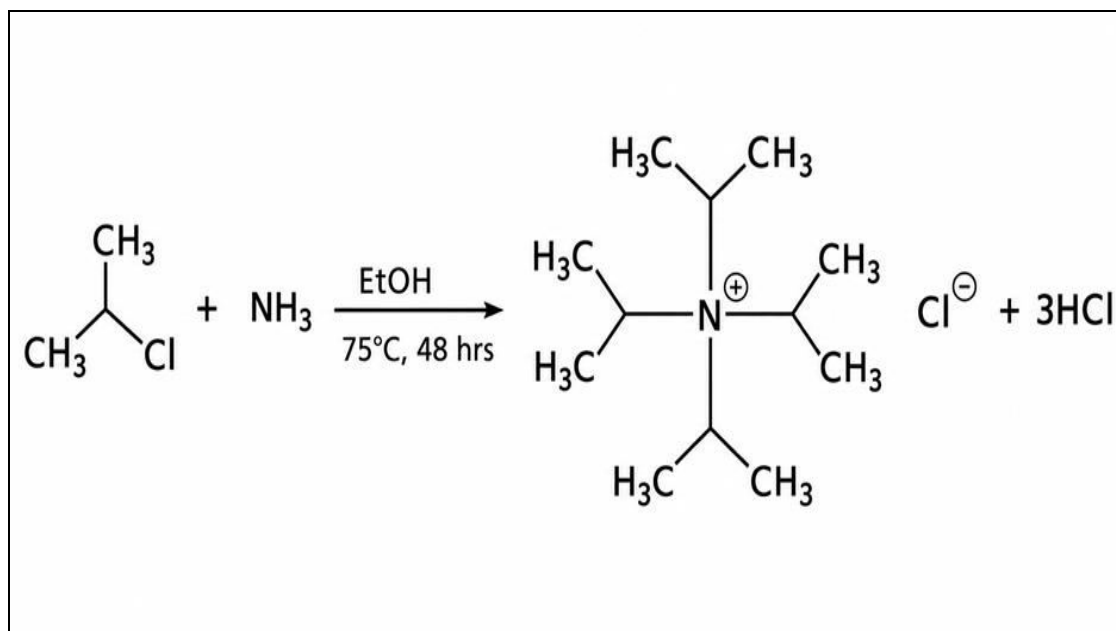


Figure.2 FT-IR spectrum of the synthesized PTC

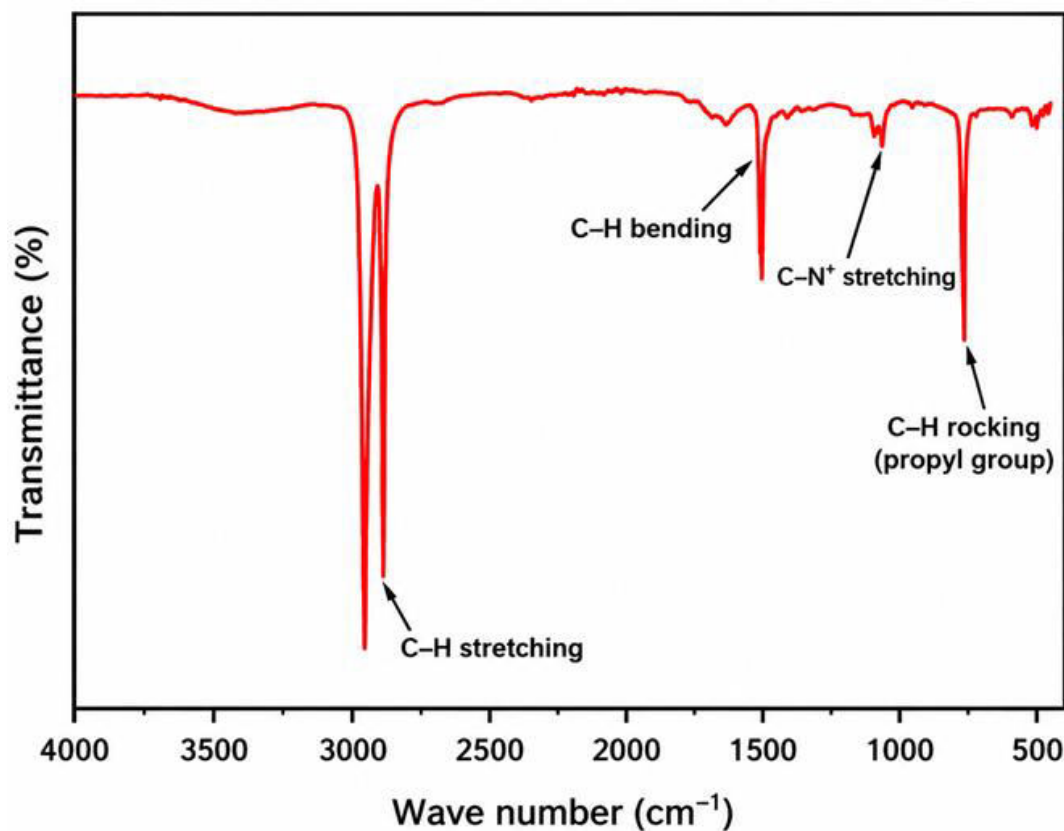


Figure.3 Effect of styrene volume, temperature, and PTC on the rate of polymerization

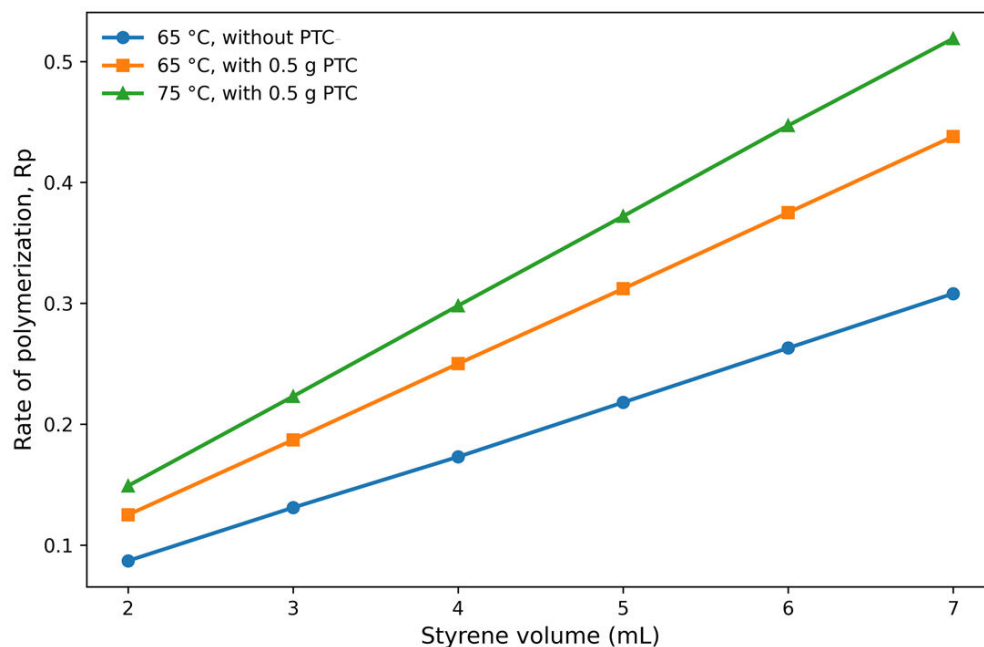


Figure.4 FT-IR spectrum of calcium polystyrene sulfonate (CPS) showing characteristic aromatic and sulfonate functional-group vibrations.

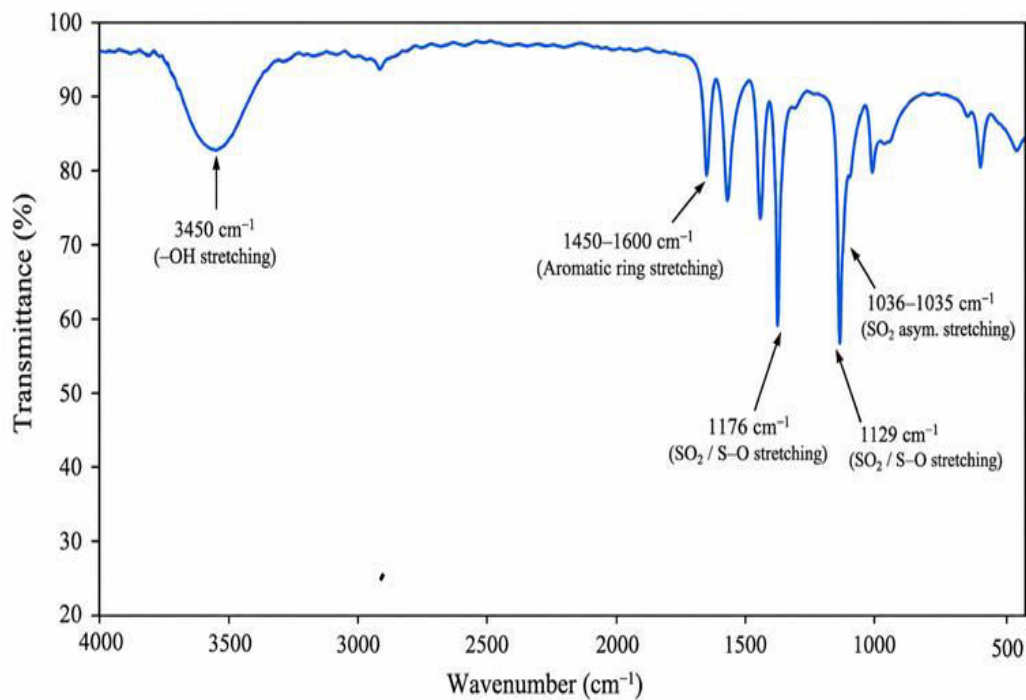


Table.1 FT-IR spectral assignments of the synthesized PTC

Wavenumber (cm ⁻¹)	Assignment	Functional group
3000	C–H stretching	Aliphatic C–H
2932	C–H stretching	Aliphatic C–H
1473	C–H bending	C–H deformation
1178	C–N ⁺ stretching	Quaternary ammonium group
Lower-wavenumber region	C–H rocking	Propyl/isopropyl group

Table.2 FT-IR spectral assignments of calcium polystyrene sulfonate

Wavenumber (cm ⁻¹)	Assignment	Interpretation
~3450	O–H stretching	Adsorbed moisture/hydrogen-bonded hydroxyl groups
1450–1600	Aromatic ring stretching	Polystyrene backbone
~1176	Sulfonate/S–O stretching	Sulfonate functional group
~1129	Sulfonate/S–O stretching	Sulfonate functional group
1036–1035	S–O/sulfonate stretching	Sulfonate functionality

The broad band observed near 3450 cm⁻¹ can be attributed to O–H stretching, which may arise from adsorbed moisture or hydrogen-bonded species. The bands in the 1450–1600 cm⁻¹ region are associated with aromatic-ring vibrations of the polystyrene backbone. Characteristic absorption bands observed at approximately 1176, 1129, and 1036–1035 cm⁻¹ are associated with sulfonate/S–O vibrations. Similar absorption bands near 1040 and 1180 cm⁻¹ have been reported for sulfonated polystyrene and have been used as characteristic spectral evidence for the introduction of sulfonate groups onto the polystyrene backbone. □

The observed spectral features therefore support the formation of a sulfonated polystyrene-based material. Calcium polystyrene sulfonate is a cation-exchange resin with established pharmaceutical use for potassium binding in the gastrointestinal tract, where calcium is exchanged for potassium.

In conclusion, the present study demonstrated the synthesis and characterization of tetra-isopropylammonium chloride (PTC) and its application as a phase-transfer catalyst for styrene polymerization under heterogeneous conditions. The polymerization results showed that the rate of polymerization increased with increasing styrene concentration and reaction temperature, with higher polymerization rates observed in the presence of PTC. The synthesized polymeric material was further considered for characterization

relevant to pharmaceutical applications. FT-IR analysis provided evidence of the characteristic functional groups associated with calcium polystyrene sulfonate.

In future studies, the prepared polymeric material has been planned to be investigated for potential drug-delivery applications. Further work should focus on drug loading and encapsulation efficiency, drug–polymer compatibility, in-vitro drug-release behavior, release kinetics, swelling and ion-exchange properties, biocompatibility, and cytotoxicity. These studies would be necessary to establish whether the material can function as a suitable drug-delivery system. Thus, the present work provides a preliminary physicochemical basis for future development of the polymeric material for drug-delivery applications, rather than establishing drug-delivery performance in the present study.

Author Contributions

Loganathan S.: Writing original draft, Preparation, Writing - Review & Editing. Vidyadharani G.: Data Curation, Methodology. Anand B.: Software, Validation, Formal Analysis.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical Approval Not applicable.

Consent to Participate Not applicable.

Consent to Publish Not applicable.

Conflict of Interest The authors declare no competing interests.

References

- Aghajanpour, S., Amiriara, H., Esfandyari-Manesh, M., Ebrahimnejad, P., Jeelani, H., Henschel, A., Singh, H., Dinarvand, R., & Hassan, S. (2025). Utilizing machine learning for predicting drug release from polymeric drug delivery systems. *Computers in Biology and Medicine*, 188, 109756. <https://doi.org/10.1016/j.compbiomed.2025.109756>
- Ang, Z. Z., Pereira, V., Boong, S. K., Li, H., & Lee, H. K. (2024). Nanoscale stirring at the liquid–liquid interface: The interfacial nano-vortexer actively converges immiscible biphasic reactants for enhanced phase-transfer catalysis. *Journal of Materials Chemistry A*, 12, 7279–7286. <https://doi.org/10.1039/D3TA06360G>
- Jiang, M., Fang, H., & Tian, H. (2025). Latest advancements and trends in biomedical polymers for disease prevention, diagnosis, treatment, and clinical application. *Journal of Controlled Release*, 380, 138–174. <https://doi.org/10.1016/j.jconrel.2025.01.063>
- Lu, H., Cai, Z., & Hu, P. (2024). Recent advances in polymeric delivery vehicles for controlled and sustained drug release. *Pharmaceutics*, 16(9), 1184. <https://doi.org/10.3390/pharmaceutics16091184>
- Nining, N., Wardhana, Y. W., Rusdiana, T., & Hariyanti, H. (2025). Deep eutectic solvents in polymeric drug carriers: Insights into release behavior and functional integration. *ChemistryOpen*, 14(12), e202500332. <https://doi.org/10.1002/open.202500332>
- Sharma, S., Gallou, F., & Handa, S. (2024). Towards a sustainable tomorrow: Advancing green practices in organic chemistry. *Green Chemistry*, 26, 6289–6317. <https://doi.org/10.1039/D4GC01826E>
- Vermeeren, B., Van Praet, S., Arts, W., Narmon, T., Zhang, Y., Zhou, C., Steenackers, H. P., & Sels, B. F. (2024). From sugars to aliphatic amines: As sweet as it sounds? Production and applications of bio-based aliphatic amines. *Chemical Society Reviews*, 53, 11804–11849. <https://doi.org/10.1039/D4CS00244J>
- Xu, Y., Chen, J., Ding, J., Sun, J., Song, W., Tang, Z., Xiao, C., & Chen, X. (2025). Synthetic polymers for drug, gene, and vaccine delivery. *Polymer Science & Technology*, 1(3), 171–220. <https://doi.org/10.1021/polymscitech.5c00010>

How to cite this article:

Loganathan Subramanian, Vidyadharani Gopalakrishnan. and Anand Balu. 2026. Green Synthesis of Pharmaceutical Polymers Using Heterogeneous Phase-Transfer Catalysis. *Int.J.Curr.Microbiol.App.Sci*. Special Issue-13: 9-15. doi: <https://doi.org/10.20546/ijcmas.2026.sp13.002>