Ganpat University
॥ विद्यया समाजोत्कर्षः ॥

University Journal of Research
ISSN (Online) 2455-1724

Curcumin Encapsulated Poly(Glycerol-Citric acid) (PGCA) based Dendrimers: Synthesis, Characterisation and their antimicrobial activity.

Rizwanabegam A. Harsoliya, Hitesh M. Rakhade and Ajay Kumar Gupta*

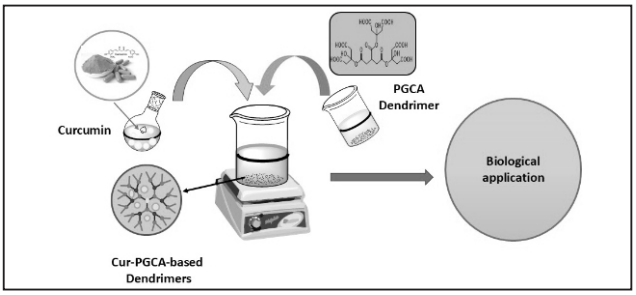
Department of Chemistry, Mehsana Urban Institute of Sciences, Faculty of Science, Ganpat University, Ganpat Vidyanagar, Dist. Mehsana, Gujarat, India.

Abstract

Poly (glycerol-citric acid) (PGCA) dendrimers were synthesised using a polyesterification process and characterized by various physico-chemical characterization techniques such as FTIR, DLS, and UV Spectroscopy etc. The PGCA dendrimer is chosen because it is non-toxic and biocompatible due to the presence of glycerol and citric acid. The latter are natural compounds that are widely used in the food and pharmaceutical industries. Curcumin is a naturally occurring antimicrobial compound that is poorly soluble in water. Curcumin was encapsulated inside the PGCA dendrimer. When tested against Gram-positive bacteria, the antimicrobial activity of the curcumin-PGCA dendrimers was found to be higher than that of free curcumin. The higher microbial activity of curcumin-PGCA dendrimers can be attributed to increased solubility of curcumin, enhanced formulation stability and efficient cellular uptake of the curcumin due to the nano-meter size of the dendrimers. The present study on PGCA-based dendrimers opens the opportunity to deliver hydrophobic drugs for antibacterial and medicinal applications.

Keywords:- Dendrimer, Curcumin, Microbial Activity, Polymer, Nanoparticles, Drug Delivery

Graphical abstract



- Poly (glycerol-citric acid) (PGCA) dendrimers were synthesised using a polyesterification process.
- Curcumin was encapsulated inside the PGCA dendrimer and characterised by various physico-chemical techniques.
- The antimicrobial activity of the curcumin-PGCA dendrimers was found to be higher than that of free curcumin.
- The higher microbial activity is due to increased solubility of curcumin, enhanced formulation stability and efficient cellular uptake.
- Opens the opportunity to deliver hydrophobic drugs for antibacterial and medicinal applications.

1. Introduction:

The dendrimers are synthetic polymers with highly structured three-dimensional arrangements, low polydispersity, and great functionality (Wang et al., 2022),(Redón et al., 2012). Dendrimers possess several advantageous properties that distinguish them from conventional polymers (Torabi Fard et al., 2024). Dendrimers are attractive candidates for drug delivery and biomedical applications due to their highly controlled molecular architecture, precise size distribution, biocompatibility, and excellent solubility in aqueous and organic media. (Said et al., 2023). The two well-known methods that are employed to synthesise the polymeric macromolecules are the convergent and divergent methods (Araújo et al., 2018). In the convergent method, the dendritic segment grows step by step and ends with the core groups. The convergent method involves the propagation of the reaction inward of the core group. Examples of convergent synthesis are polyamidoamine (PAMAM) dendrimers (Lyu et al., 2020). In the divergent approach, however, it can be difficult to separate the desired result from by-products that share characteristics with the dendrimer (Gogulapati et al., 2020). One of the most promising areas of research involving dendrimers is

*Corresponding Author
E-mail address: director.research@ganpatuniversity.ac.in

their role in enhancing the therapeutic potential of bioactive compounds (Stadler et al., 2025). Curcumin is a natural polyphenolic compound derived from the turmeric plant (Curcuma longa) (Bertoncini-Silva et al., 2024). It is well known for its wide range of biological activities, including antimicrobial, antioxidant, anti-inflammatory, and anticancer properties (Omidi and Kakanejadifard, 2020)(Zaporozhchenko and Subotyalov, 2024). However, curcumin's practical applications are limited by its poor water solubility, low bioavailability (Bertoncini-Silva et al., 2024) and rapid degradation under physiological conditions (Urošević et al., 2022). To overcome these limitations, dendrimer-based encapsulation of curcumin has emerged as a promising strategy to enhance its therapeutic efficacy (Mahjubin-Tehran et al., 2024). Encapsulating curcumin within dendrimer-based formulations offers numerous benefits. In particular, PAMAM dendrimers have been shown to significantly enhance the solubility, stability, and anticancer efficacy of curcumin. This nanocarrier-based approach holds promise for the future development of targeted chemotherapeutic agents (Wang et al., 2013). Additionally, studies have demonstrated that curcumin-loaded PAMAM dendrimers improve drug delivery across the blood-brain barrier, thereby enhancing their neuroprotective effects. This formulation shows remarkable therapeutic potential in the treatment of ischaemic stroke. This strategy advances the dendrimer-based nanomedicine for the treatment of central nervous system illnesses (Stadler et al., 2025). For preventing HIV-1 infection, the PEG-citrate dendrimer–curcumin nano-formulation provides a new, secure, and efficient method. This system exhibits controlled and sustained release properties, ensuring that curcumin remains active for an extended period, thereby improving its therapeutic effectiveness against microbial infections (Ebrahimi et al., 2024) (Barros et al., 2021). Also, the therapeutic efficacy may differ by variation in the synthesis process, storage conditions, encapsulation efficiency and exact control of curcumin release kinetics, etc. The Higher-generation PAMAM dendrimers (such as G4 and above) may be cytotoxic even though they are efficient drug carriers. This is particularly true because they contain terminal amine (-NH2) groups, which can rupture cellular membranes and harm cells (Fox et al., 2018). To overcome the harmful toxicological effects of PAMAM dendrimers, in this work, Poly(glycerol-citric acid) (PGCA) dendrimers are a class of biocompatible, biodegradable and hyperbranched polymers synthesised from citric acid, a tricarboxylic acid with multiple reactive carboxyl & hydroxyl groups and glycerol (a nontoxic triol). These dendrimers form an amphiphilic network suitable for encapsulating a variety of hydrophobic molecules, such as curcumin. PGCA dendrimers exhibit excellent water solubility, good surface chemistry, and characterised by various physico-chemical techniques. The PGCA dendrimer is non-toxic and biocompatible due to the presence of glycerol and citric acid, which are natural compounds widely used in the food and pharmaceutical industries. These PGCA dendrimers were effective in encapsulating curcumin, which is poorly soluble in water. Interestingly, after curcumin was encapsulated within PGCA dendrimers, its antibacterial activity was significantly enhanced.

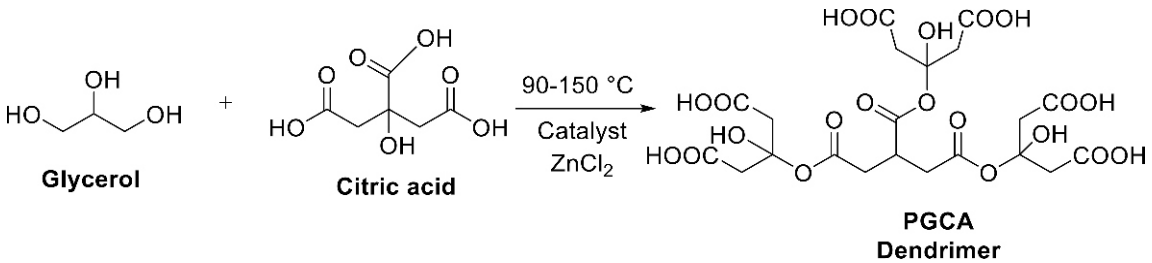
2.0 Material and Synthesis:

2.1 Material

Citric acid monohydrate (99.5%), glycerol (98%), acetone (99.5%) were purchased from ACS Chemicals, (Ahmedabad, India), tetrahydrofuran (THF) (99.5%), 99% extrapure dimethyl sulfoxide (DMSO) (99%), and curcumin were all procured from SRL Chemicals, Ahmedabad, India). All chemicals were AR grade and used without further purification. The doubly distilled water was collected from the distillation plant and used throughout the entire study.

2.2 Synthesis of PGCA Dendrimer

The Polyglycerol (citric acid) PGCA dendrimers were synthesised as reported in previous studies involving biodegradable hyperbranched polymers. A mixture of citric acid monohydrate (33 mmol) and glycerol (0.66 mmol) was prepared in a round-bottom flask fitted with a reflux condenser and a magnetic stirrer (Remi 2LPH). The initial mixture was stirred at 90°C for 30 minutes until a clear, homogenous solution was obtained, indicating complete miscibility of the reactants. Subsequently, a catalytic amount of zinc chloride ($ZnCl_2$) was added to promote esterification and enhance the reaction kinetics. The reaction mixture was then subjected to a stepwise increase in temperature under inert atmospheric conditions: 110°C for 20 minutes, followed by 130°C for 40 minutes, and finally 150°C for 60 minutes (Scheme – 1).



Scheme 1: Synthesis of hyperbranched copolymer containing Citric Acid (CA) and Glycerol (G) building blocks by thermal polycondensation.

These sequential heating steps facilitated progressive dehydration and drove the polycondensation reaction to completion by eliminating water formed as a by-product. Upon completion of the reaction, the viscous product was allowed to cool to room temperature and stored for future characterisation. The stepwise thermal treatment and catalytic assistance ensured the formation of a hyperbranched, biodegradable polyester dendrimer with pendant hydroxyl and carboxyl functional groups, suitable for drug encapsulation and biomedical applications (Adeli et al., 2013; Wrzecionek et al., 2021; Cabral et al., 2020).

2.3 Hydroxamic acid Test for ester bond conformation

Every 20 minutes, 1.0 ml of the reaction mixture was taken out of the reaction medium and transferred into a test tube. Four drops of ethanolic solution of hydroxylamine hydrochloride (5.0% w/w) and five drops of aqueous solution of potassium hydroxide (5.0% w/w) were added. The reaction mixture was heated for one minute at about 60 °C in a water bath and then cooled to room temperature. Four drops of an aqueous solution of 1.0% m/m ferric chloride (95% FeCl3) and four drops of an aqueous solution of 5.0% v/v hydrochloric acid (HCl) were then added. The solution will turn deep violet due to the presence of ester bonds (-COO-) in the medium (affirmative result). In the absence of an ester bond, the solution will remain yellow, which is typical of an aqueous solution of FeCl3 (Cabral et al., 2020).

2.4 Bromine Test for Unsaturation (alkene groups)

For the identification of an unsaturated bond in the synthesized dendrimer compound, the bromine test was used. Took 0.5 to 1 mg of the sample in a test tube and added an equal quantity of bromine water and mixed well. The dark yellow colour of the compound remain unchanged and did not become colourless indicating the absence of unsaturated alkene groups in the compound.

2.5 Encapsulation of the Curcumin with Polyglycerol (citric acid) Dendrimers

Curcumin was encapsulated in PGCA dendrimers with an encapsulation efficiency ranging from 2% to 25%. The encapsulation of curcumin occurs inside the dendrimer's hydrophobic inner domains and non-specific interactions between carboxyl groups of dendrimers and hydroxyl or carbonyl groups of curcumin molecules. The methanolic solution of curcumin was slowly added to the PGCA dendrimers, creating a uniform solution, and the mixture was vigorously stirred for two to three hours at room temperature to ensure complete encapsulation of curcumin inside the dendrimers. To create a powdered sample of curcumin-loaded dendrimer, the sample was centrifuged for 15 minutes at 10,000 RPM, rinsed with water, and then freeze-dried in a lyophilizer (Wang et al., 2019).

2.6 FTIR Spectroscopy studies

A Bruker alpha II FTIR spectrophotometer with a resolution of 4 cm-1 in the range of 400-4000 cm-1 was used in these studies. FTIR studies were done to determine the chemical structure of the synthesised dendrimer and also to ensure that the reaction had taken place. FTIR studies were also done to confirm the curcumin encapsulation inside the dendrimers.

2.7 Dynamic Light Scatterings (DLS) studies

DLS studies by using the Horiba SZ-100 DLS instrument were done to determine the size and size distribution of the curcumin-loaded dendrimers. To make stable colloidal suspensions for the samples, the dendrimer samples were dissolved in double-distilled water. Sonication was done for 30 seconds to ensure uniform dispersion. The hydrodynamic diameters were determined by analysing the variations in intensity of the dispersed light (Kianamiri et al., 2020) (Igartúa et al., 2023).

2.8 UV-Vis Spectroscopy studies

A Shimadzu 1900 spectrophotometer was used to study the UV-visible spectrum of curcumin-encapsulated PGCA dendrimers and determine the amount of curcumin loading into the dendrimers. The sample was taken in a quartz cuvette and scanned at a wavelength range between 200–800 nm. UV spectra studies of the curcumin were done at a λ-max of 434 nm (Erez et al., 2014).

2.9 Physicochemical Studies of Curc-PGCA Dendrimer

2.9.1 Viscosity Measurements

The viscosity of the Curc-PGCA dendrimer samples was determined using an Ostwald viscometer. The measurement was based on the principle of capillary flow under the influence of gravity. The viscosity (η) was calculated using the formula:

$$\eta = k\rho t,$$

where, k is the viscometer constant, ρ is the density of the sample, and t is the flow time.

Each sample was tested in triplicate to ensure reproducibility and accuracy of the results. The average viscosity values were recorded, and standard deviations were calculated to assess the precision of the measurements. This method allows for the reliable comparison of viscosities among various formulations (Elfiyani et al., 2018).

2.9.2 Turbidity studies

Turbidity, expressed in Nephelometric Turbidity Units (NTU), provides information about the presence of suspended particles or aggregates in a dispersion system. An increase in turbidity may indicate particle aggregation or poor encapsulation stability (Wang et al., 2019). A Hanna digital turbidity meter, with a measurement range of 0–100 NTU and a resolution of 0.01 NTU, was used for turbidity measurements were carried out to for the colloidal stability and clarity of the Curc-PGCA dendrimer formulations. The samples were analysed in triplicate, and

the average turbidity values were recorded.

2.10 Anti-microbial activity studies

The antibacterial property of the cylindrical hybrid hydrogels was also tested in bacterial solution. E. coli was cultured in MHA (Mueller-Hinton Broth) at 37 ◦C with shaking at 250 rpm for 24 hrs. The bacterial solution at log phase was diluted to a series of concentrations ranging from 1.5× 108 CFU/mL. Placing the discs containing 10 µl of different concentrations (0 to 100 %). One disc in each plate was loaded with solvent alone, which served as a vehicle control, and the Ciprofloxacin disc (10µg) was taken as a positive control. The plates of Escherichia coli were incubated at 37°C for 24 hrs. A clear zone created around the disc was measured and recorded. The Antibacterial activity was checked by following the Zone Inhibition Method (Kirby-Bauer method) (Shashikala Kuruppu et al., 2022). The MHA plates were inoculated by spreading with 100 µl of Bacterial culture, Escherichia coli, as a positive control. All measurements were performed in triplicate (Figures 8 &9).

3.0 Results and Discussion

The PGCA dendrimer was synthesized by taking glycerol and citric acid in a 1:3 molar ratio. The reaction, as mentioned in experimental section 2.2, follows a polycondensation reaction mechanism where excess water is removed (Scheme 1) (Adeli et al., 2013). The reaction product, i.e. PGCA dendrimer, was confirmed by the presence of an ester bond formation and presence of unsaturation in the synthesized product. The successful synthesis of the PGCA dendrimer was confirmed through FTIR studies, which provided important structural conformation of the compound synthesized. The FTIR spectrum of PGCA dendrimers is shown in Fig.1(A) and Curcumin fig.1(B). The characteristic peaks of bonds representing the -COO ester bond formation by way of reaction between the hydroxyl group of glycerol and the carboxyl group of citric acid were observed at 1708 cm-1. Similarly, C-O carboxyl bond stretching was observed at 1175 cm-1, and C-OCH2 vibration bands were observed at 1040 cm-1 and 1114 cm-1. These peaks confirmed that the hyperbranched dendritic structure representing PGCA dendrimer was formed as a result of the reaction shown in scheme 1. FTIR spectra of curcumin encapsulated PGCA (Curc-PGCA) dendrimer were taken to confirm the drug encapsulation inside the dendrimers. FTIR spectra confirmed the structural characteristics of the Curc-PGCA dendrimer as shown in Fig.1(C). The peak located around 3300 – 3400 cm¹ is indicative of hydroxyl (-OH) groups. Aliphatic C-H stretching peak was observed at 2920–2950 cm¹. Ester bond formation was confirmed by a prominent peak at 1700–1750 cm¹. The peaks in this range may also have contributions from carboxyl (-COOH) and the keto-carbonyl (-C=O) groups of curcumin. Aromatic C=C stretching is represented by the 1620–1660 cm¹ region. The absorption peaks around 1380 and 1450 cm¹ exhibit carboxylate stretching and C-H bending, respectively. C-O and C-O-C stretching of ester bonds is confirmed at 1200–1300 cm^{-1}, whereas ether (-C-O-C) and hydroxyl (-OH) vibrations are indicated at 1000–1100 cm^{-1}. Lastly, the out-of-plane aromatic C-H bending bands at 800–900 cm-¹ validate the dendrimer contributions and the aromatic substitution pattern of curcumin (Adeli et al., 2013) (Wrzecionek et al., 2021) (Stadler et al., 2025).

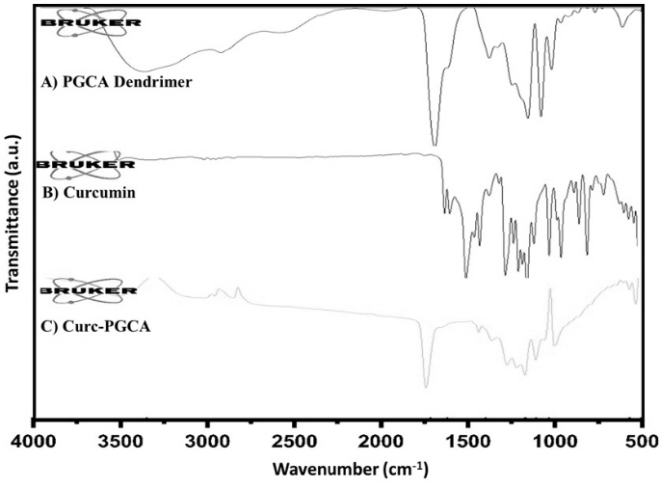


Figure 1: FTIR spectrum of A) PGCA Dendrimer, B) Curcumin and C) Curcumin encapsulated PGCA dendrimers (Curc-PGCA).

UV-Visible spectrophotometer was used for the quantitative analysis of the curcumin inside the PGCA dendrimers. The UV-Visible spectrum was taken in the 200-800 nm region to determine the λ-max value of the curcumin. Because of the π-π interaction of the diketone moiety, curcumin was found to have λ-max value at 434 nm (Figure 2A and 2B). Curcumin encapsulation within the PGCA dendrimer exhibit a broad absorbance peak at 434 nm. This data also indicates the improved aqueous stability and effective encapsulation, as shown in Figure 2 (Pande and Crooks, 2011) (Agrawal and Jaiswal, 2022).

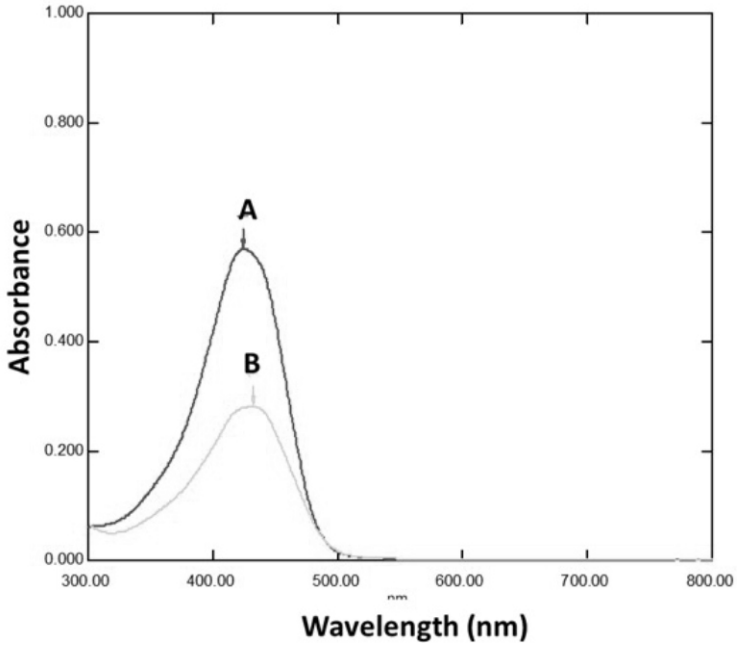


Figure 2: UV-Visible Spectroscopy of A) Curcumin and B) Curc-PGCA Dendrimer.

Dynamic Light Scattering Studies

The particle size and size distribution of the dendrimer and curcumin-encapsulated dendrimers were determined by using a Horiba particle size analyser. According to DLS analysis, the PGCA dendrimer showed an average hydrodynamic diameter of roughly 80 nm with a narrow size distribution, as shown in Figure 3 (A), but the Curc-PGCA dendrimer showed a much greater size of about 181 nm (Figure 3(B)), showing successful curcumin encapsulation. The nanoparticles of Curc-PGCA Dendrimers exhibit greater stability (Elfiyani et al., 2018).

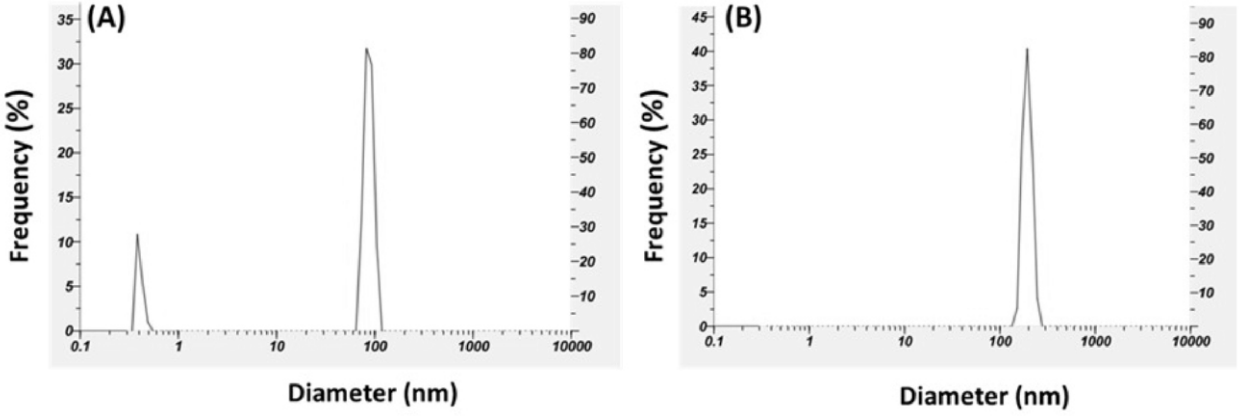


Figure 3: Dynamic light scattering of A) PGCA Dendrimer, B) Curc-PGCA Dendrimer

Physiochemical Studies of Curcumin Encapsulated PGCA Dendrimer

Viscosity studies

Viscosity plays an important role in determining the stability of dendrimer-based formulations and further application in drug delivery applications. It can be seen from Figure 4 that the viscosity of the sample increases with an increase in concentration of the dendrimers in the sample. At 50 ppm, the viscosity of the sample was about 0.41 cP, while at a concentration of 10 ppm, the viscosity was found to be about 0.32 cP. This is because of the high number of dendrimer molecules present at the higher concentration, making the flow of liquid slower. The flow time of the Curc-PGCA was 82 seconds at a concentration of 50 ppm, whereas the flow time was about 65 seconds at a concentration of 10 ppm, suggesting a fluidic character of the dendrimer samples.

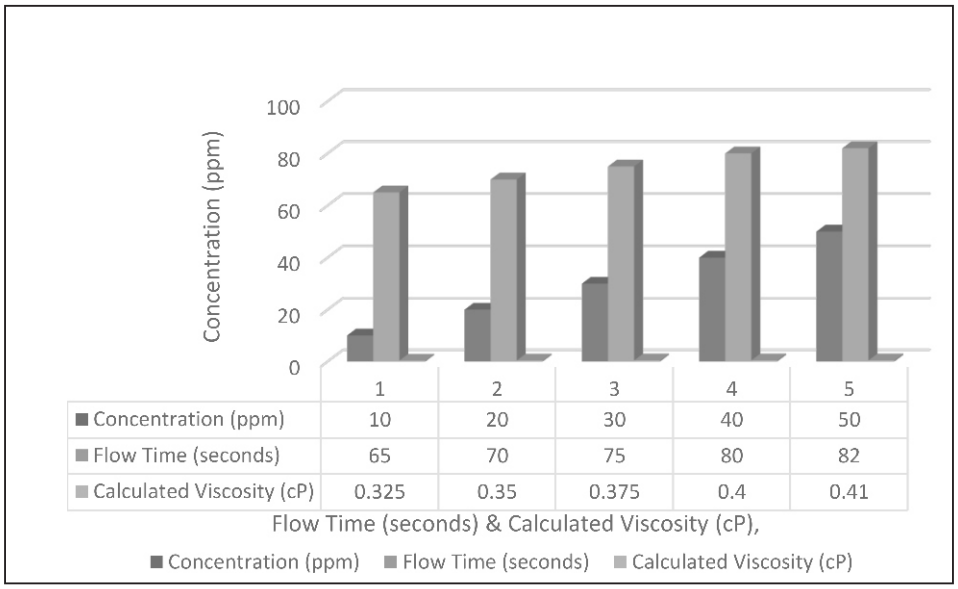


Figure 4: Viscosity of Curc-PGCA at different concentrations

pH studies

Curc-PGCA Dendrimer's pH fluctuates based on its surroundings and formulation. Because pure curcumin is poorly soluble in water, its pH is slightly basic (~8.5 pH). PGCA dendrimer solution, on the other hand, has carboxyl (-COOH) groups, which make it extremely acidic (~3.8 pH). A PGCA dendrimer's pH becomes somewhat acidic (~4.8) when curcumin is encapsulated, depending on the dendrimer's structural characteristics. The pH of the dendrimer formulations encapsulating curcumin was adjusted to about 6.8, which makes it appropriate for use in biomedical applications (Figure 5).

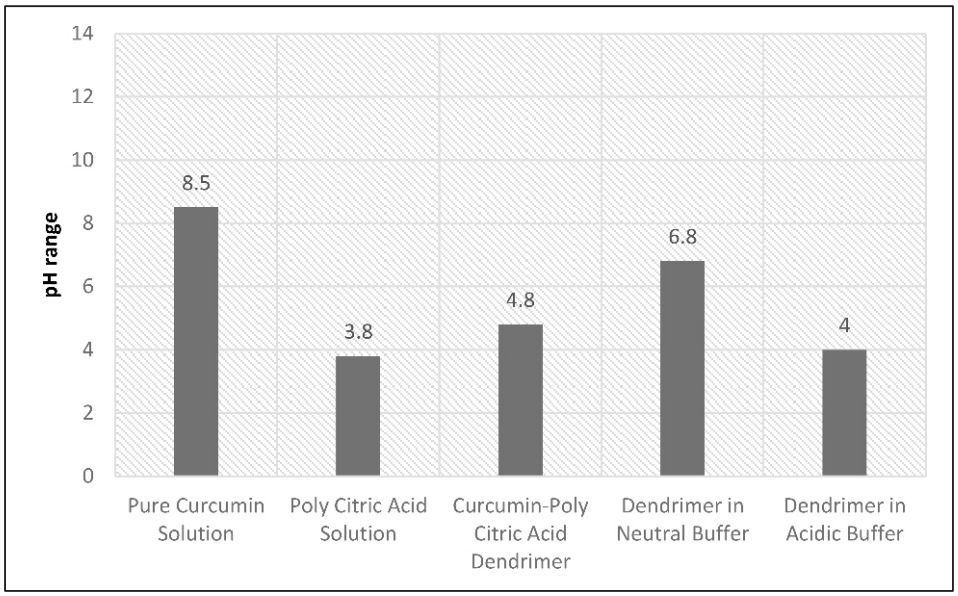


Figure 5: pH studies of different solutions

Conductivity studies

The ability of the Curc-PGCA dendrimer to facilitate ion transport is demonstrated by its moderate ionic conductivity, which rises from 267 µS at 10 ppm to 1335 µS at 50 ppm. The linear increase of electrical conductivity with concentration indicates a direct correlation between electrical conductivity and ionization potential of carboxylic groups on the dendrimer surfaces. This exceptional ionic activity at various water concentrations is caused by the ionisable groups of the dendrimer. Figure 6 illustrates how the PGCA dendrimer successfully encapsulates the curcumin when the conductivity rises, increasing the compound's potential for usage in biological applications.

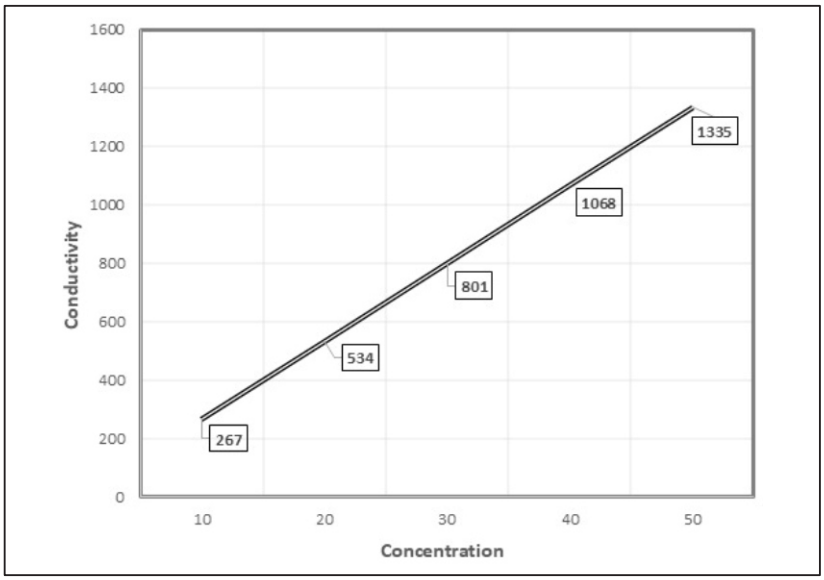


Figure 6: Conductivity studies of Curc-PGCA dendrimer at different concentrations.

Stability studies

Turbidity, expressed in Nephelometric Turbidity Units (NTU), is a measure of the Curc-PGCA dendrimer's stability, solubility and aggregation behaviour under different physiological conditions. The data from Figure 7 showed that particle aggregation increases as the concentration of the dendrimer in the sample rises. Good solubility is indicated by the solution's continued clarity at ≤20 ppm, but turbidity dramatically increases at ≥50 ppm, suggesting possible aggregation or phase separation. Stabilisation is necessary for uniform dispersion, as this increase may impact the effectiveness of drug delivery. Optimisation is required for stability at higher concentrations, even though the formulation exhibits good solubility at lower concentrations.

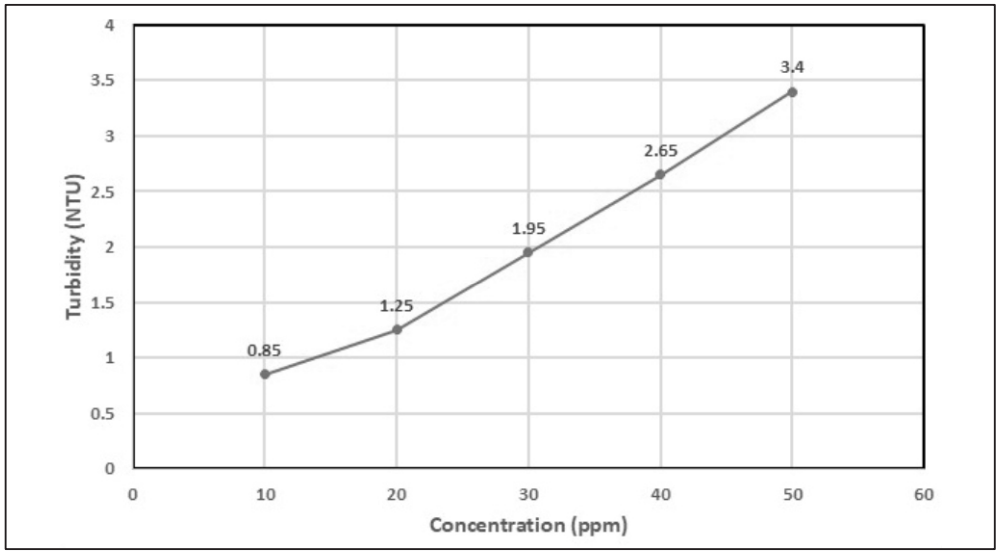


Figure 7: Stability studies of Curc-PGCA at different concentrations

Antimicrobial Studies

The antibacterial activity of Curcumin-loaded PGCA (Curc-PGCA) dendrimer was evaluated against Escherichia coli using the agar well diffusion method at various concentrations ranging from 0 % to 100% per disc. As shown in Figures 8 and 9, the Curc-PGCA dendrimer exhibited a concentration-dependent inhibitory effect. At the highest concentration tested (100 %/disc), the dendrimer produced a significant inhibition zone of approximately 15.5 mm, while lower concentrations (6.25–50 %/disc) showed moderate zones around 8±1 mm. Ciprofloxacin (10 µg), used as the positive control, demonstrated a much larger zone of inhibition, 22±1 mm, consistent with its known antibacterial potency. Although the inhibition zones of Curc-PGCA dendrimer were smaller than that of ciprofloxacin, the results indicate appreciable antibacterial activity, especially at higher concentrations (Shashikala Kuruppu et al., 2022).

All experiments were performed in triplicate, and the consistent minimum inhibitory concentration (MIC) values across replicates confirm the reproducibility and reliability of the observed antibacterial effects. These findings support the potential of Curc-PGCA dendrimers as a natural and biocompatible antimicrobial platform Table No. 1.

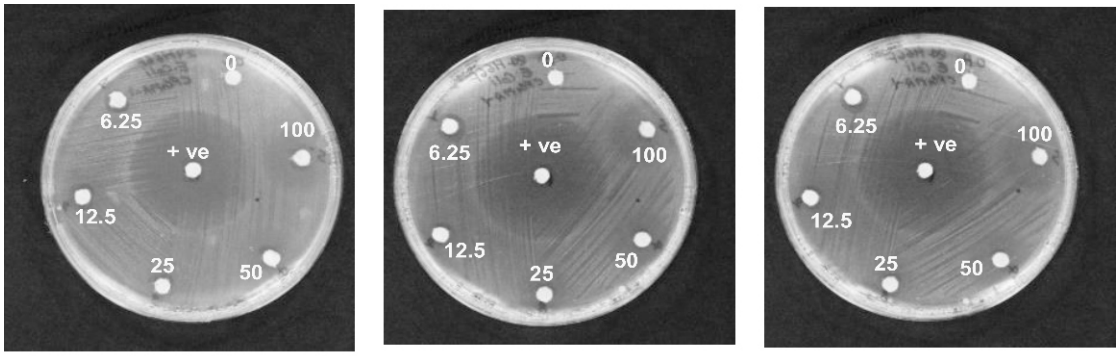


Figure 8: Inhibition Zones Developed in Agar Medium by Curc-PGCA Dendrimer at Various Concentrations (A, B, C shows disc containing 10 µL of the test sample at specified concentrations (%). Ciprofloxacin (10 µg/disc) was used as the positive control.)

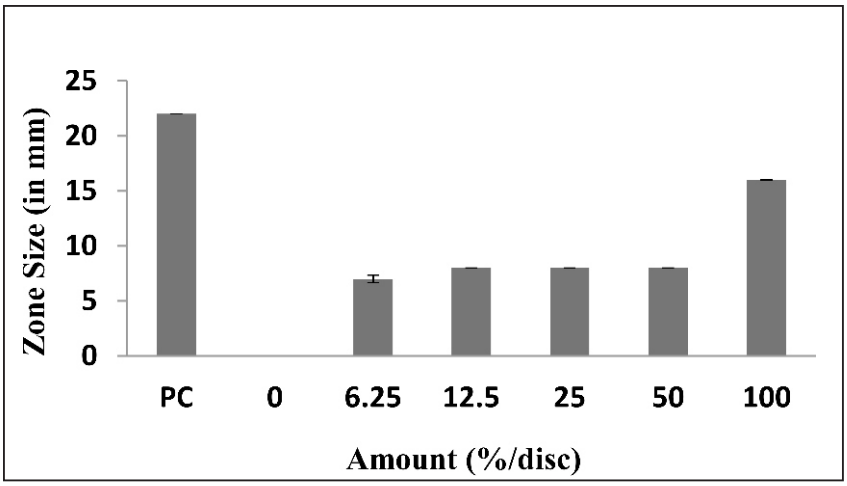


Figure 9: Antibacterial Activity of Curc-PGCA Dendrimer Against Escherichia coli at different concentrations

Although the inhibition zone of Curc-PGCA was smaller than that of ciprofloxacin, its substantial bactericidal effect, as shown by the minimal cell survival percentage, highlights its potential as a natural, biocompatible antimicrobial agent. These results collectively support the effectiveness of Curc-PGCA dendrimers in suppressing bacterial growth and suggest their promise as an alternative antibacterial platform. All measurements were performed in triplicate to ensure reproducibility and statistical reliability (Melone et al., 2019).

Table No. 1: Minimum Inhibitory Concentration (MIC) for Curc-PGCA dendrimers

Material	**Escherichia coli**	
	Effective Amount (in %)	Average Zone at Effective Amount (in mm)
Ciprofloxacin (PC)	10µg	22 ± 1 mm
PGCA Dendrimer	6.25 %	8± 1 mm

For the first time, we have reported the use of PGCA dendrimers for curcumin encapsulation for biomedical and drug delivery applications. The improved solubility of curcumin when encapsulated inside the dendrimer system is responsible for the observed higher antibacterial activity. Furthermore, the dendritic structure encourages close interaction with bacterial membranes, which may compromise membrane integrity and impede cellular functions. These outcomes are in line with earlier research showing that dendrimer-based delivery methods enhanced the antibacterial activity of hydrophobic medications. In other applications, the binding of Cur-

PGCA dendrimers to cotton fabric for antimicrobial coatings, medical textiles, and wound dressings—all of which require surface-bound bacterial control in various daily applications. This study highlights Cur-PGCA dendrimer's potential as a practical and environmentally friendly substitute for synthetic antibiotics, particularly for topical and surface-based applications.

Conclusions:

Novel Curc-PGCA dendrimer formulations developed in this study represent a scientific advancement in nanomedicine and antimicrobial therapy. By addressing curcumin's limitations and enhancing its bioavailability and therapeutic efficacy, dendrimers offer a novel platform for combating microbial infections and other diseases. As research in this field expands, biodegradable and non-toxic dendrimer-based drug delivery systems hold great promise for future biomedical applications, potentially revolutionising the treatment of infectious diseases and improving overall healthcare outcomes.

Funding: This research work was supported by the funding from Gujarat Council on Science and Technology (GUJCOST), Govt. of Gujarat, India, in the form of a research project (Sanction order No. GUJCOST/STI/2023-24/253) dated 25th April, 2023.

Acknowledgements: The Authors want to acknowledge Ganpat University for providing the facility to conduct this research.

References

- Adeli, M., Rasoulian, B., Saadatmehr, F., Zabihi, F., 2013. Hyperbranched poly(citric acid) and its application as anticancer drug delivery system. J of Applied Polymer Sci 129, 3665–3671. https://doi.org/10.1002/app.39028
- Agrawal, N., Jaiswal, M., 2022. Bioavailability enhancement of curcumin via esterification processes: A review. European Journal of Medicinal Chemistry Reports 6, 100081. https://doi.org/10.1016/j.ejmcr.2022.100081
- Araújo, R.V.D., Santos, S.D.S., Igne Ferreira, E., Giarolla, J., 2018. New Advances in General Biomedical Applications of PAMAM Dendrimers. Molecules 23, 2849. https://doi.org/10.3390/molecules23112849
- Barros, C.H.N., Hiebner, D.W., Fulaz, S., Vitale, S., Quinn, L., Casey, E., 2021. Synthesis and self-assembly of curcumin-modified amphiphilic polymeric micelles with antibacterial activity. J Nanobiotechnol 19, 104. https://doi.org/10.1186/s12951-021-00851-2
- Bertoncini-Silva, C., Vlad, A., Ricciarelli, R., Giacomo Fassini, P., Suen, V.M.M., Zingg, J.-M., 2024. Enhancing the Bioavailability and Bioactivity of Curcumin for Disease Prevention and Treatment. Antioxidants 13, 331. https://doi.org/10.3390/antiox13030331
- Cabral, T.O., Sarrouh, B., Naves, F.L., Lofrano, R.C.Z., 2020. Insights on the preparation and characterization of the poly(glycerol-co-malic acid) from renewable sources. Clean Techn Environ Policy 22, 735–742. https://doi.org/10.1007/s10098-020-01814-1
- Ebrahimi, S., Sadeghizadeh, M., Aghasadeghi, M.R., Ardestani, M.S., Amini, S.A., Vahabpour, R., 2024. Inhibition of HIV-1 infection with curcumin conjugated PEG-citrate dendrimer; a new nano formulation. BMC Complement Med Ther 24, 350. https://doi.org/10.1186/s12906-024-04634-8
- Elfiyani, R., Srifiana, Y., Al Rasyied, F.D., 2018. Curcumin encapsulation using dendrimer PAMAM G4 conjugated with polyethylene glycol to improve the properties of gel dossage form. Pharmaciana 8, 107. https://doi.org/10.12928/pharmaciana.v8i1.8940
- Erez, Y., Simkovitch, R., Shomer, S., Gepshtein, R., Huppert, D., 2014. Effect of Acid on the Ultraviolet–Visible Absorption and Emission Properties of Curcumin. J. Phys. Chem. A 118, 872–884. https://doi.org/10.1021/jp411686d
- Fox, L.J., Richardson, R.M., Briscoe, W.H., 2018. PAMAM dendrimer - cell membrane interactions. Advances in Colloid and Interface Science 257, 1–18. https://doi.org/10.1016/j.cis.2018.06.005
- Gogulapati, N., Manalan, B.V., Nadendla, R.R., 2020. Poly (propylene imine) Dendrimer: Synthesis, characterization and applications in various drug delivery. Asian J Pharm Pharmacol 6, 190–203. https://doi.org/10.31024/ajpp.2020.6.3.10
- Igartúa, D.E., González-Lizárraga, F., Martinez, C.S., Alonso, S.D.V., Ávila, C.L., Chehín, R., Chiaramoni, N.S., Prieto, M.J., 2023. PAMAM dendrimers of generation 4.5 loaded with curcumin interfere with α-synuclein aggregation. OpenNano 11, 100140. https://doi.org/10.1016/j.onano.2023.100140
- Kianamiri, S., Dinari, A., Sadeghizadeh, M., Rezaei, M., Daraei, B., Bahsoun, N.E.-H., Nomani, A., 2020. Mitochondria-Targeted Polyamidoamine Dendrimer–Curcumin Construct for Hepatocellular Cancer Treatment. Mol. Pharmaceutics 17, 4483–4498. https://doi.org/10.1021/acs.molpharmaceut.0c00566
- Lyu, Z., Ding, L., Dhumal, D., Ya-Ting Huang, A., Kao, C.-L., Peng, L., 2020. CHAPTER 4. Poly(amidoamine) (PAMAM) Dendrimers: Synthesis and Biological Applications, in: Malkoch, M., García Gallego, S. (Eds.), Monographs in Supramolecular Chemistry. Royal Society of Chemistry, Cambridge,

pp. 85–113. https://doi.org/10.1039/9781788012904-00085

- Mahjubin-Tehran, M., Khandan-Nasab, N., Kesharwani, P., Sahebkar, A., 2024. Dendrimer-Encapsulated Curcumin: Illuminating pathways to cancer treatment excellence. European Polymer Journal 218, 113358. https://doi.org/10.1016/j.eurpolymj.2024.113358
- Melone, P., Vitiello, G., Di Napoli, M., Zanfardino, A., Caso, M.F., Silvestri, B., Varcamonti, M., D'Errico, G., Luciani, G., 2019. Citric Acid Tunes the Formation of Antimicrobial Melanin-Like Nanostructures. Biomimetics 4, 40. https://doi.org/10.3390/biomimetics4020040
- Omidi, S., Kakanejadifard, A., 2020. A review on biological activities of Schiff base, hydrazone, and oxime derivatives of curcumin. RSC Adv. 10, 30186–30202. https://doi.org/10.1039/D0RA05720G
- Pande, S., Crooks, R.M., 2011. Analysis of Poly(amidoamine) Dendrimer Structure by UV–Vis Spectroscopy. Langmuir 27, 9609–9613. https://doi.org/10.1021/la201882t
- Redón, R., Carreón-Castro, M.P., Mendoza-Martínez, F.J., 2012. Langmuir-Blodgett Films of Supported Polyester Dendrimers. ISRN Organic Chemistry 2012, 1–9. https://doi.org/10.5402/2012/906839
- Said, A.I., Staneva, D., Grabchev, I., 2023. New Water-Soluble Poly(propylene imine) Dendrimer Modified with 4-Sulfo-1,8-naphthalimide Units: Sensing Properties and Logic Gates Mimicking. Sensors 23. https://doi.org/10.3390/s23115268
- Shashikala Kuruppu, Upendra Rathnayake, Madhavi De Silva, Thilini Rupasinghe, Chanaka Sandaruwan, 2022. Anti-microbial Nanohybrids Based on Naturally Derived Citric Acid Intercalated Layered Double Hydroxides. VJScience 25. https://doi.org/10.31357/vjs.v25i01.5929
- Stadler, J., Garmo, L.G., Doyle, D., Cheng, C.-I., Richardson, G., Waheed, Z., Tofan, T., Srinageshwar, B., Sharma, A., Petersen, R.B., Dunbar, G.L., Rossignol, J., 2025. Curcumin encapsulated in PAMAM dendrimers for the therapeutic treatment of ischemic stroke in rats. Front. Cell Dev. Biol. 12, 1467417. https://doi.org/10.3389/fcell.2024.1467417
- Torabi Fard, N., Ahmad Panahi, H., Moniri, E., Reza Soltani, E., Mahdavijalal, M., 2024. Stimuli-Responsive Dendrimers as Nanoscale Vectors in Drug and Gene Delivery Systems: A Review Study. J Polym Environ 32, 4959–4985. https://doi.org/10.1007/s10924-024-03280-y
- Urošević, M., Nikolić, L., Gajić, I., Nikolić, V., Dinić, A., Miljković, V., 2022. Curcumin: Biological Activities and Modern Pharmaceutical Forms. Antibiotics 11, 135. https://doi.org/10.3390/antibiotics11020135
- Wang, J., Li, B., Qiu, L., Qiao, X., Yang, H., 2022. Dendrimer-based drug delivery systems: history, challenges, and latest developments. J Biol Eng 16, 18. https://doi.org/10.1186/s13036-022-00298-5
- Wang, P., Guo, X., Wu, C., Huang, Q., Xu, X., Zhou, G., Bai, Y., 2019. Hydrophobic-assembled curcumin–porcine plasma protein complex affected by pH. Int J of Food Sci Tech 54, 891–897. https://doi.org/10.1111/ijfs.14011
- Wrzecionek, M., Matyszczak, G., Bandzerewicz, A., Ruśkowski, P., Gadomska-Gajadhur, A., 2021. Kinetics of Polycondensation of Citric Acid with Glycerol Based on a Genetic Algorithm. Org. Process Res. Dev. 25, 271–281. https://doi.org/10.1021/acs.oprd.0c00492
- Zaporozhchenko, A.A., Subotyalov, M.A., 2024. The Biological Activity and Therapeutic Potential of Curcuma longa: Literature Review. Cell Tiss. Biol. 18, 265–272. https://doi.org/10.1134/S1990519X24700202