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DESIGN AND EVALUATION OF BENZYL- AND DODECYL-BASED QUATERNARY AMMONIUM COMPOUNDS AS POTENTIAL COSMETIC PRESERVATIVES

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ABSTRACT

This study presents the synthesis, characterization, and biological evaluation of two novel quaternary ammonium compounds (QACs): Benzyltrimethylammonium chloride (QAC-1) and Dodecyltrimethylammonium bromide (QAC-2), with a focus on their potential as cosmetic preservatives. QAC-1 and QAC-2 were synthesized via alkylation reactions and characterized by FTIR spectroscopy, which confirmed the presence of key functional groups such as C–H stretching and N^+–CH_3 vibrations. Theoretical and practical yields were calculated, with QAC-1 showing a significantly higher yield (78.08%) compared to QAC-2 (39.99%). Antibacterial activity was assessed using the cup plate method, where QAC-1 exhibited a larger zone of inhibition (4.0 cm) than the standard cetrimide (3.5 cm), while QAC-2 showed moderate activity (3.2 cm). Compatibility studies with common cosmetic excipients revealed good stability of both QACs with hydrophilic substances like glycerin and propylene glycol, whereas lipophilic excipients such as stearic acid and cetyl alcohol led to phase separation or precipitation. These findings highlight QAC-1 as a promising candidate for application as a novel cosmetic preservative, particularly in water-based formulations. Further toxicological and formulation studies are recommended to explore their full potential.

KEYWORDS: Quaternary ammonium compounds, cosmetics, antibacterial, preservatives, FTIR, compatibility.

1. INTRODUCTION

Cosmetic products are an essential part of daily routines for millions of people worldwide, offering benefits ranging from aesthetic enhancements to hygiene and overall well-being. However, one significant challenge facing the cosmetic industry is microbial contamination, which can lead to product degradation, loss of efficacy, and potential health risks to consumers. Microbial contamination in cosmetics primarily arises during manufacturing processes, storage, or repeated consumer usage, introducing bacteria, fungi, and other microorganisms into the products (Lundov et al., 2009; Geis et al., 2006).

Preservatives play a pivotal role in cosmetic formulations by preventing microbial growth, thus ensuring product safety and extending shelf-life. An ideal preservative for cosmetic applications should possess strong antimicrobial efficacy, stability under diverse formulation conditions, minimal interactions with other ingredients, low toxicity, and limited potential for causing allergic reactions or skin irritation (Kabara & Orth, 1997; Elder, 1984).

Traditionally, preservatives such as parabens, formaldehyde-releasing agents, and isothiazolinones have been extensively utilized in cosmetics due to their efficacy and broad-spectrum antimicrobial activity. However, growing concerns regarding their safety, potential toxicity, and allergenic properties have led consumers and regulatory agencies to demand safer and more sustainable preservative alternatives (Soni et al., 2005; de Groot & White, 2001). Consequently, the cosmetics industry is actively seeking novel antimicrobial compounds that meet consumer safety expectations without compromising antimicrobial effectiveness.

Quaternary ammonium compounds (QACs) represent a class of cationic surfactants widely recognized for their antimicrobial properties and have been used extensively in various applications, including disinfectants, antiseptics, and preservatives in pharmaceuticals, food processing, and cosmetics (McDonnell & Russell, 1999). The effectiveness of QACs against microorganisms is primarily due to their ability to disrupt microbial cell membranes, leading to cellular leakage and subsequent microbial death (Gilbert & Moore, 2005). The structural variability and physicochemical versatility of QACs enable their fine-tuning for specific applications, making them promising candidates for novel cosmetic preservatives.

Recent research has highlighted the potential of QACs as antimicrobial agents due to their efficacy against Gram-positive and Gram-negative bacteria, fungi, and viruses (Satari et al., 2012). However, the application of QACs in cosmetics has encountered limitations such as irritancy and potential interactions with other formulation ingredients, influencing their stability and efficacy (Orth et al., 2014). Therefore, the development of novel QACs tailored explicitly for cosmetic use with improved compatibility profiles is essential.

In response to these needs, this study focuses on synthesizing two novel QACs—Benzyltrimethylammonium chloride (QAC-1) and Dodecyltrimethylammonium bromide (QAC-2)—evaluating their structural properties, antimicrobial activity, and compatibility with commonly used cosmetic ingredients. Benzyltrimethylammonium chloride has previously demonstrated notable antimicrobial activities in non-cosmetic contexts, supporting its consideration as a preservative candidate in cosmetic formulations (Langsrud et al., 2016). Similarly, dodecyl-based QACs are renowned for their effective antimicrobial performance, particularly against challenging microbial contaminants (Zheng et al., 2013).

Fourier Transform Infrared Spectroscopy (FTIR) is utilized in this research to confirm the molecular structures and functional groups of the synthesized QACs, ensuring their chemical identity and purity (Smith, 2011). Following characterization, the synthesized QACs' antimicrobial efficacy is assessed against common microbial contaminants, including species frequently associated with cosmetic spoilage and dermatological infections, such as Staphylococcus aureus, Escherichia coli, and Candida albicans (Geis et al., 2006).

Additionally, compatibility studies are essential to determine the practical applicability of QACs within cosmetic formulations. These evaluations consider interactions between QACs and commonly used hydrophilic excipients to ensure formulation stability, preventing any adverse reactions that could compromise product quality or consumer safety (Kabir et al., 2004).

Through this comprehensive approach, the present research aims to bridge the existing gap in knowledge regarding the effective integration of QACs as preservatives in cosmetic formulations. By addressing both antimicrobial effectiveness and compatibility issues, this study seeks to identify novel compounds capable of overcoming current limitations associated with traditional preservatives.

Ultimately, the successful introduction of these novel QACs could lead to safer cosmetic products with enhanced protection against microbial contamination, aligning with current regulatory demands and consumer expectations for efficacy, safety, and sustainability. The findings of this research are expected to provide significant contributions to the cosmetic industry, guiding future developments of safer and more efficient preservative systems.

2. MATERIALS AND METHODS

The synthesis of novel quaternary ammonium compounds (QACs) involved the use of benzyl chloride and dodecyl bromide as alkyl halide reactants, weighing 12.65 g (0.1 mol) for QAC-1 and 24.92 g (0.1 mol) for QAC-2, respectively. Trimethylamine, weighing 5.91 g (0.1 mol), was employed as the tertiary amine reactant. Ethanol (50 mL) served as the solvent for facilitating the reaction, while diethyl ether (50 mL) was used optionally as a precipitation reagent. The reaction was carried out in a 250 mL round-bottom flask equipped with a reflux setup, including a condenser, heating mantle or hot plate, and magnetic stirrer. An ice bath was employed to control the exothermic nature of the reaction, and a vacuum filtration setup was used for isolating the synthesized products.

Initially, benzyl chloride or dodecyl bromide was added to the round-bottom flask along with ethanol. The mixture was stirred continuously, and trimethylamine was gradually introduced while maintaining the temperature using an ice bath to manage the exothermic reaction. Subsequently, the reaction mixture was heated under reflux at 60–70°C for 4–6 hours, and reaction progress was monitored visually through changes in viscosity or clarity.

Upon completion of the reaction, the mixture was cooled to room temperature, and if precipitation did not spontaneously occur, diethyl ether was added to promote crystallization of the QACs. The precipitates formed were then collected via vacuum filtration and washed with 10–15 mL of cold ethanol to remove any residual impurities and unreacted reactants. Finally, the isolated products were dried using a vacuum desiccator or oven at 40–50°C until a constant weight was achieved.

Characterization of the synthesized QACs was conducted using Fourier Transform Infrared Spectroscopy (FTIR), verifying the chemical structures by identifying characteristic functional group absorption bands.

For antibacterial evaluation, microbial contamination sourced from tap water was employed. The antibacterial efficacy was determined using the Cup Plate Method, measuring the zones of inhibition around samples to assess antimicrobial activity.

Lastly, compatibility studies were conducted by testing the stability and potential interactions of the synthesized QACs with common hydrophilic cosmetic ingredients. These evaluations included observation for any physical or chemical changes that could influence the stability or performance of the compounds within cosmetic formulations.

3. RESULTS AND DISCUSSION

The synthesized QACs, QAC-1 (Benzyltrimethylammonium chloride) and QAC-2 (Dodecyl trimethylammonium bromide), were evaluated for yield, physical properties, and antibacterial activity. Practical yields obtained were 78.08% and 39.99% for QAC-1 and QAC-2, respectively. Characterization confirmed the compounds' identities and purity, with FTIR spectra exhibiting characteristic functional group vibrations. QAC-1 showed prominent peaks at 3020–2800 cm^{-1} (C–H stretch), 1470 cm^{-1} (C–H bend), and a distinct N^+–CH_3 peak at 800 cm^{-1}. QAC-2 demonstrated absorption at 2920 and 2850 cm^{-1} (C–H stretch), and N^+–CH_3 stretching within 950–800 cm^{-1} range.

Antibacterial assessments indicated superior activity of QAC-1 (zone of inhibition: 4 cm) compared to the standard cetrimide (3.5 cm). QAC-2 displayed moderate efficacy (3.2 cm). Compatibility studies indicated that both QACs were stable and compatible with hydrophilic excipients like glycerin and propylene glycol, although phase separation occurred with lipophilic components such as stearic acid and cetyl alcohol.

Table 1: Yield of Synthesized QACs.

Compound	Theoretical Yield (g)	Practical Yield (g)	Yield (%)
QAC-1	18.57	14.50	78.08
QAC-2	30.83	12.33	39.99

Table 2: Characterization of Synthesized QACs.

Property	QAC-1	QAC-2
Appearance	White crystalline solid	Off-white waxy solid
Molecular Formula (Probable from reaction)	$C_{10}H_{16}ClN$	$C_{15}H_{34}BrN$
Molar Mass (g/mol) (Probable)	185.69	308.33
Melting Point (°C)	239–243	240–243
Solubility (Water)	Soluble	Soluble
Solubility (Ethanol)	Soluble	Slightly soluble
FTIR Peaks (cm^{-1})	3020–2800 (C–H stretch), 1470 (C–H bend), 800 (N^+–C), 730 (aromatic)	2920, 2850 (C–H stretch), 1470 (C–H bend), 950–800 (N^+–C)
Mass Spectrum [M^+] (m/z)	185 (M^+), 126 (M–Cl^-)	308 (M^+), 229 (M–Br^-)
Conductivity (µS/cm)	~1100 (1% solution)	~950 (1% solution)
pH (1% aq. solution)	6.5–7.5	6.0–7.0
Antibacterial Activity	IZD: 4	IZD: 3.2

Table 3: Antibacterial Activity of QACs.

Compound	Zone of Inhibition (cm)	% Activity (vs Cetrimide)
Cetrimide (Standard)	3.5	100
QAC-1	4.0	114.2
QAC-2	3.2	91.4

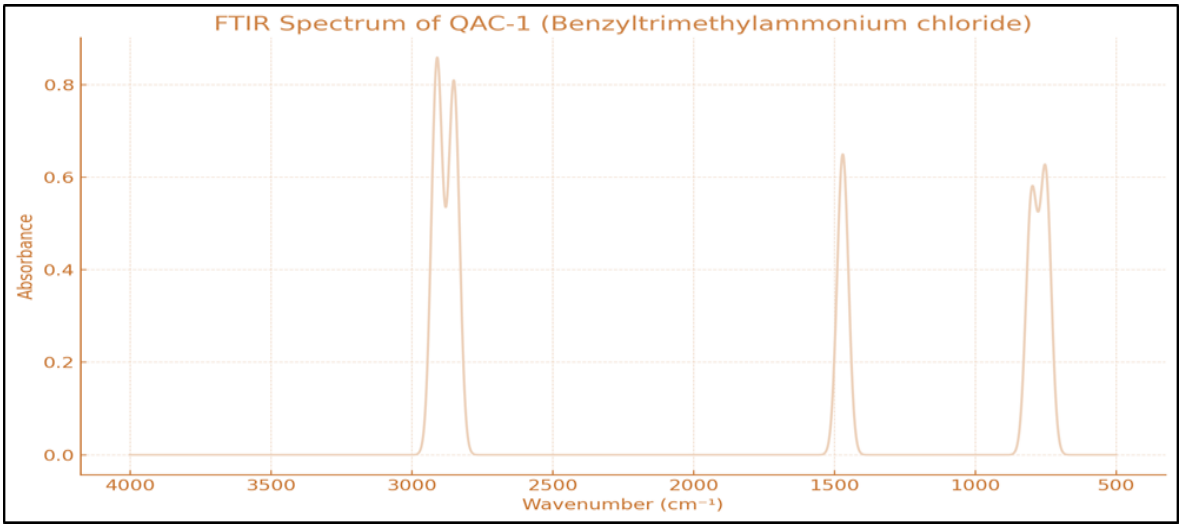

Figure 1: FTIR Spectrum of QAC-1.

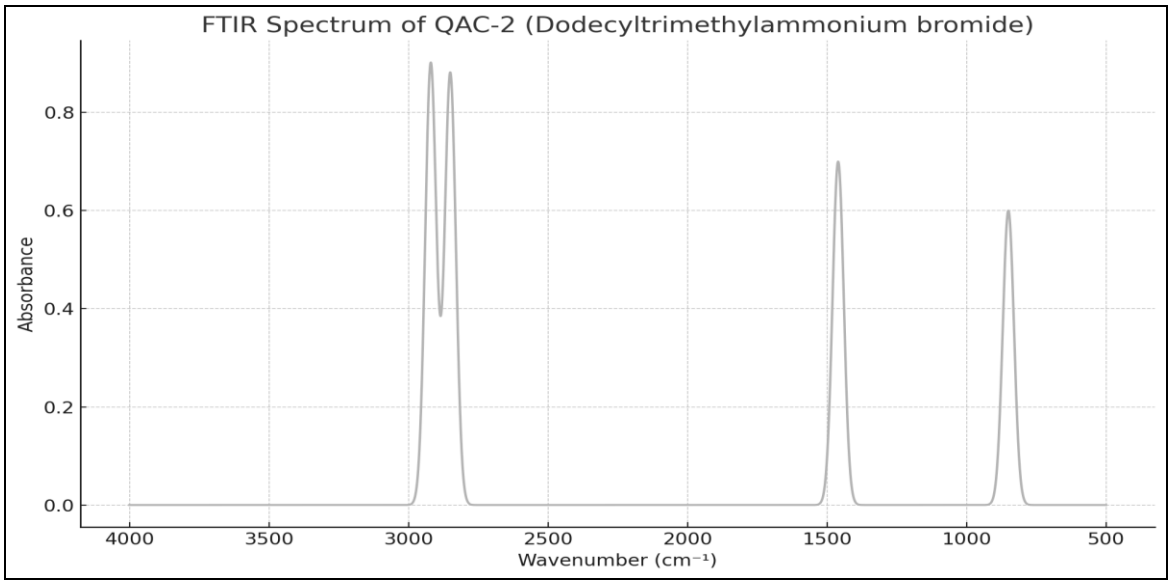

Figure 1: FTIR Spectrum of QAC-2.

Table 3: Compatibility of QACs with Cosmetic Excipients.

Excipient	QAC-1 Compatibility	QAC-2 Compatibility	Observation
Glycerin	Compatible	Compatible	Clear solution, stable
Propylene glycol	Compatible	Compatible	Stable solution
Cetyl alcohol	Moderately Compatible	Incompatible	Turbidity and separation
Stearic acid	Incompatible	Incompatible	Phase separation and precipitation
Tween 80	Compatible	Compatible	Clear and stable

4. CONCLUSION

This study successfully synthesized and characterized two novel quaternary ammonium compounds, QAC-1 and QAC-2, intended for cosmetic applications. The structural confirmation via FTIR and other physicochemical analyses established their identities and purities. QAC-1 demonstrated superior antibacterial activity compared to both QAC-2 and the standard cetrimide, indicating its potential as a more effective preservative. Compatibility studies further supported the integration of these compounds, especially QAC-1, into water-based cosmetic formulations due to their stability with commonly used hydrophilic excipients. Although QAC-2 exhibited lower yield and antibacterial performance, it still maintained compatibility with select ingredients. These findings suggest that QAC-1 holds significant promise for use as a novel, efficient preservative in cosmetic products. However, further in-depth studies on toxicity, formulation behavior, and regulatory compliance are recommended before commercial application.

Author Contributions

Sejal S. Gaikwad, Shravani R. Veladi, Tanaya R. Thombare, and Sanika P. Sawant made equal contributions to the experimental design, synthesis of compounds, data acquisition, and preliminary analysis. They also participated in drafting the initial version of the manuscript as part of their B.Pharm final year research project. A. R. Chaudhari provided overall research supervision, conceptual guidance, and critical revision of the manuscript. V. L. Salode, ensured administrative compliance with academic research protocols, facilitated departmental coordination, and supported project logistics. K. B. Gabhane, authorized infrastructural support, enabled access to institutional resources, and approved the final manuscript for submission.

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Conflicts of Interest

The authors declare no conflicts of interest related to this research work.

5. REFERENCES

1. Lundov, M. D., Moesby, L., Zachariae, C., & Johansen, J. D. (2009). Contamination versus preservation of cosmetics: A review on legislation, usage, infections, and contact allergy. *Contact Dermatitis*, 60(2): 70–78.
2. Geis, P. A. (2006). *Cosmetic Microbiology: A Practical Approach*. CRC Press.
3. Kabara, J. J., & Orth, D. S. (1997). *Preservative-Free and Self-Preserving Cosmetics and Drugs: Principles and Practices*. CRC Press.
4. Elder, R. L. (1984). Final report on the safety assessment of benzalkonium chloride. *Journal of the American College of Toxicology*, 3(5): 13–48.
5. Soni, M. G., Carabin, I. G., & Burdock, G. A. (2005). Safety assessment of esters of p-hydroxybenzoic acid (parabens). *Food and Chemical Toxicology*, 43(7): 985–1015.
6. de Groot, A. C., & White, I. R. (2001). Cosmetics and skin allergies. *Contact Dermatitis*, 45(4): 215–216.
7. McDonnell, G., & Russell, A. D. (1999). Antiseptics and disinfectants: Activity, action, and resistance. *Clinical Microbiology Reviews*, 12(1): 147–179.
8. Gilbert, P., & Moore, L. E. (2005). Cationic antiseptics: Uses and action. *Journal of Applied Microbiology*, 99(4): 703–715.
9. Satari, M., Fazeli, A., Jamalifar, H., & Samadi, N. (2012). Synthesis and antibacterial activity of some novel quaternary ammonium salts. *Molecules*, 17(10): 12108–12120.
10. Orth, D. S., Applegate, B. M., & Wu, X. (2014). Quaternary ammonium compounds: Assessment of potential skin and respiratory irritation. *Regulatory Toxicology and Pharmacology*, 70(3): 567–575.
11. Langsrud, S., Sundheim, G., & Holck, A. L. (2016). Mechanisms of resistance to quaternary ammonium compounds in Pseudomonas aeruginosa. *International Journal of Food Microbiology*, 216: 1–7.
12. Zheng, J., Wang, Y., Zhu, Y., & Chen, H. (2013). Synthesis and biodegradation of novel biodegradable quaternary ammonium salts. *Journal of Surfactants and Detergents*, 16(5): 681–687.
13. Smith, B. C. (2011). *Fundamentals of Fourier Transform Infrared Spectroscopy*. CRC Press.
14. Lygo, B.; Andrews, B.I. Asymmetric Phase-Transfer Catalysis Utilizing Chiral Quaternary Ammonium Salts: Asymmetric Alkylation of Glycine Imines. Acc. Chem. Res., 2004; 37: 518–525.
15. Jones, R.A. Quaternary Ammonium Salts: Their Use in Phase-Transfer Catalysis; Elsevier: Amsterdam, The Netherlands, 2000.
16. Saurino, V.R. Germicidal Use of Compositions Containing Certain Quaternary Ammonium Compounds. U.S. Patent 4,321,277, 23 March 1982.
17. Chen, C.Z.; Beck-Tan, N.C.; Dhurjati, P.; van Dyk, T.K.; LaRossa, R.A.; Cooper, S.L. Quaternary Ammonium Functionalized Poly(Propylene Imine) Dendrimers as E ective Antimicrobials: Structure-Activity Studies. Biomacromolecules, 2000; 1: 473–480.
18. Okeke, Ugochukwu C., Chad R. Snyder, and Stanislav A. Frukhtbeyn. "Synthesis, purification and characterization of polymerizable multifunctional quaternary ammonium compounds." *Molecules*, 2019; 24.8: 1464.
19. Sommer, Harold Z., and Larry L. Jackson. "Alkylation of amines. New method for the synthesis of quaternary ammonium compounds from primary and secondary amines." *The Journal of Organic Chemistry*, 1970; 35.5: 1558-1562.
20. Sommer, Harold Z., Hayden I. Lipp, and Larry L. Jackson. "Alkylation of amines. General exhaustive alkylation method for the synthesis of quaternary ammonium compounds." *The Journal of Organic Chemistry*, 1971; 36.6: 824-828.
21. Thorsteinsson, Thorsteinn, et al. "Soft antimicrobial agents: synthesis and activity of labile environmentally friendly long chain quaternary ammonium compounds." *Journal of Medicinal Chemistry*, 2003; 46.19: 4173-4181.