

Potential Applications of Ionic Liquids in Dentistry: A Narrative Review

Nadia Munir^[1], Raja Azman Awang^{[1]*}, Nawshad Muhammad^[2], Noor Huda Ismail^[1], Abdul Samad Khan^[3], Naveed Inayat^[4]

Abstract

Recently, the use of ionic liquids (ILs) as potential solvents in dentistry has increased. Dental polymers use ionic liquids as solvents, plasticizers, surfactants, and disinfectants. Additionally, they possess anti-bacterial and antifungal properties. This review aimed to evaluate the potential of task-specific liquids in dental applications. Methodology: The Scopus, PubMed, and Web of Science databases were searched electronically for studies published between May 2013 and May 2022. Relevant publications were retrieved, evaluated, and organized for data compilation. Results and conclusion: The

inclusion of ILs in dental cement, resin composites, or surface modifiers on dental implants could lead to the development of novel procedures in dentistry. The influence on the durability, structural rigidity, and other physical and mechanical properties of dental materials is profound. Additionally, they have attracted the attention of dental researchers worldwide as potent antimicrobial agent. However, further research is required to determine the effects of ILs on biosafety of host cells and mechanical properties of dental materials.

Keywords: Adhesive, Anti-microbial potential, Dental applications, Implant coatings, Ionic liquids

Received: February 20, 2023; *revised:* August 09, 2023; *accepted:* August 17, 2023

DOI: 10.1002/cben.202300012

1 Introduction

The need for bio-safe and environment-friendly solvents has been increased to aid in clean manufacturing processes. Conventional solvents are often harmful and volatile in the environment. Due to their negligible vapor and low flammability, ionic liquids (ILs) have gained popularity as green solvents [1, 2]. ILs are organic salts with antimicrobial potential and low melting points, with the capacity to alter their physicochemical properties by modifying their anions and cations independently [3]. They are composed of large cations such as imidazolium (IMM) and pyridinium (Py), and anions such as chloride, bromide, and nitrate [4]. The structural flexibility of ILs provides a unique architectural platform on which both the cation and anion characteristics can be independently modified. This structural flexibility of ILs enables researchers to design novel functional materials while preserving the essential desired properties [5]. The earliest application of IL was as a propellant in warfare [6]. Later, it was used as energetic materials [7], lubricants [8], disinfectants [9], and surfactants [10].

The first IL, ethylammonium nitrate, was documented by Paul Walden in 1914 [11]. Years later, in the 1970s and 1980s, alkyl-imidazolium cations-based ionic liquids, with potential use as electrolytes in batteries were developed [12, 13]. Wilkes et al. documented the first generation of ionic liquids based on methylimidazolium salt in 1982 [14], followed by a second gen-

eration in 1992 [15], which makes IL an air and water-stable solvent due to the use of dialkylimidazolium tetrafluoroborate, replacing the original moisture-sensitive anion [16]. Later, in 1999, Davis and his colleagues introduced task-specific liquids (TSILs) as the third generation of IL by adjusting liquids using ammonium thiosalicylate [17]. Fig. 1 demonstrates the generations of ionic liquids and their properties.

IL are grouped into acidic or basic, with the respective cation or anion dictating acidity and basicity. The selection of anion and cation determines the physicochemical properties such as

^[1] Dr. Nadia Munir, Dr. Raja Azman Awang (rjazman@usm.my), Dr. Noor Huda Ismail
School of Dental Sciences, Health Campus, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia.

^[2] Dr. Nawshad Muhammad
Department of Dental Materials, Institute of Basic Medical Sciences, Khyber Medical University, Peshawar, Khyber Pakhtunkhwa, 25100, Pakistan.

^[3] Dr. Abdul Samad Khan
Department of Restorative Dental Sciences, College of Dentistry, Imam Abdulrahman Bin Faisal University, Dammam 31441, Saudi Arabia.

^[4] Dr. Naveed Inayat
Department of Prosthodontics, Avicenna Dental College –Defense Housing Authority Phase 1X, 54000 Lahore, Pakistan.

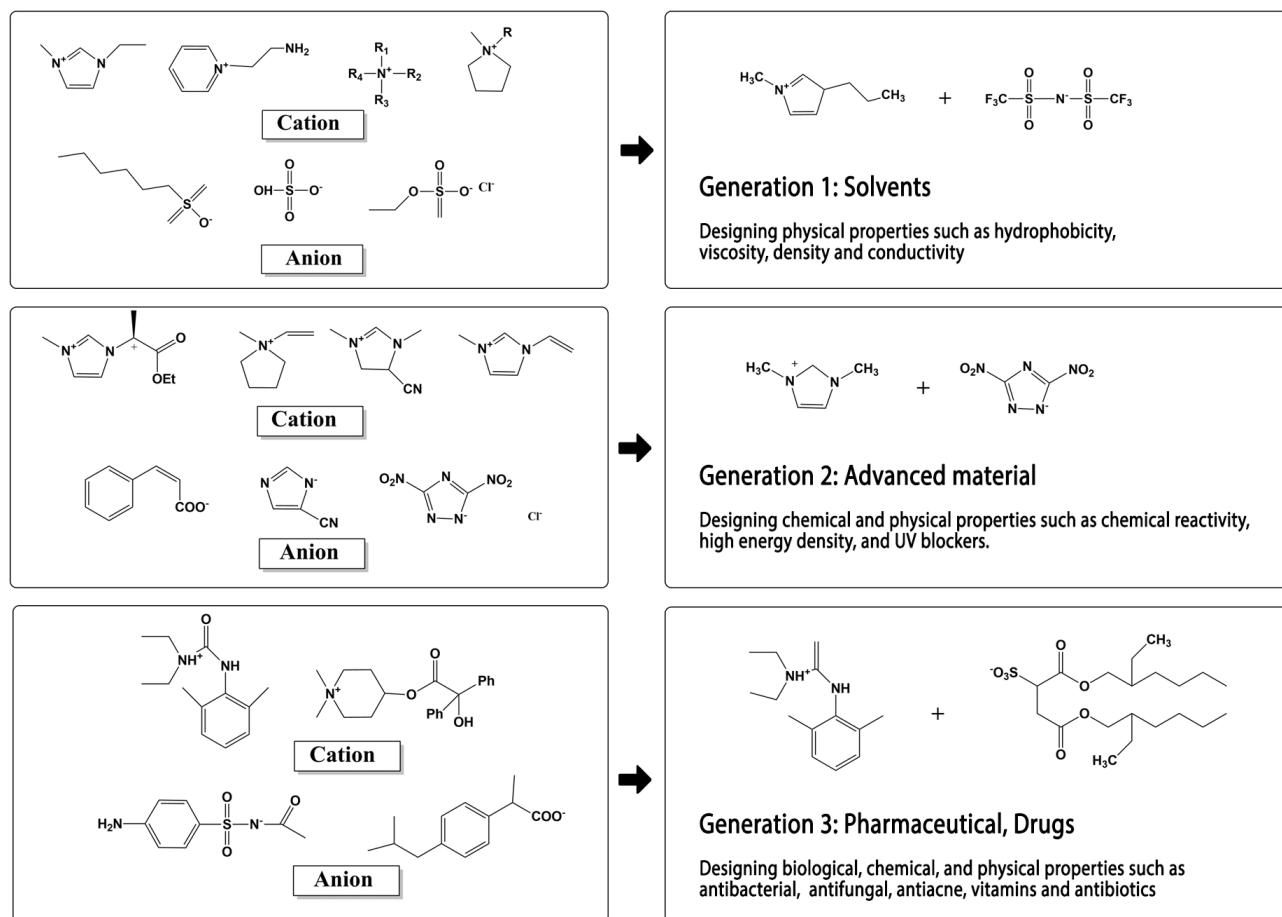


Figure 1. Generations of ionic liquids and related properties [23].

conductivity, viscosity, and water miscibility [7]. Acidic cations include ammonium, pyrrolidinium, and imidazolium, whereas basic ionic liquids include lactate, formate, acetate, and dicyanamide (DCA). They are known for their favorable physicochemical properties, including high thermal stability, low decomposition temperature and solubilizing function as a catalyst [18]. In the early 2000s, ILs were first utilized in biomedicine to improve the thermal stability of enzymes, model proteins and augment enzymatic activity [19]. Recent applications include IL-assisted production of chitin and chitosan derivatives, plasticizers and surfactants, and antimicrobial adhesives in dentistry [20–22].

Even though the usage of ionic liquids is on the rise worldwide, no review article on the applications of IL in dentistry has been published. Literature suggests that ILs may play an essential role in devising novel dental materials. These IL assisted materials can facilitate the longevity of dental treatment procedures in clinical practice. This review is aimed to integrate the most recent and pertinent data available, on the potential role of ionic liquids, when combined with various dental materials, as well as their use in other dental applications.

2 Methodology

The existing databases, including PubMed, Scopus, Web of Science, Medline, and Google Scholar, were searched with keywords pertaining to IL and its potential applications in dentistry. Included in the list of keywords are ionic liquids and/or biomedical applications, ionic liquids and/or dental applications, antifungal and antibacterial activity in dentistry, and ILs and adhesion in dentistry. Online and manual searches were conducted to locate studies published between May 2013 and May 2022. The papers were retrieved and evaluated, and information on IL and dentistry was searched, categorized, and tabulated according to their application.

3 Common Ionic Liquids Studied in Dentistry

ILs have been included in dental materials to achieve multiple functionalities, such as sustained antifungal and antibacterial properties, cytocompatibility, and enhanced physicochemical qualities. The most commonly used ILs include quaternary ammonium compounds, choline-based ionic liquids, and imidazolium ring-based ionic liquids, which were regularly

employed as solvents, plasticizers, surfactants, and disinfectants [9]. Although the amino acid-base IL has promising prospects as a bio-safe product in medical applications, particularly for the production of prototype medical-grade cement, it is not gaining popularity because of its preparation difficulties [24]. Tab. 1 summarizes the studies of the use of ILs in dentistry.

3.1 Quaternary Ammonium Compounds

Quaternary ammonium compounds (QAC) are a category of ionic liquids that are employed as antimicrobial agents, disinfectants, and surfactants. Due to the presence of the hydroxyethyl group, they are effective antimicrobial agents [33,34]. QACs are also known as ecofriendly ILs due to their favorable environmental impact. They are nonvolatile and chemically stable polymers because of their high molar mass. They have a detergent-like action and a broad spectrum against ESKAPE

Table 1. Studies of the use of ILs in dentistry.

Ionic Liquid	Study method	Study Outcome	Ref.
QAMP	In vitro study on the effect of QAMP incorporation, on anti-biofilm and anti-microbial activity of experimental adhesives (Clearfil™ SE Bond+-QAMP)	5 % QAMP modified resin adhesive showed sustained anti biofilm, and sustained anti-microbial activity	[25]
Dodecyl-3-methylimidazolium chloride ([DMIM][Cl])	Evaluation of imidazolium-IL protected silver nanoparticles were assessed as a root canal disinfectant and compared with CHX and NaOCl	Positively charged imidazolium ionic liquid protected silver nano particles showed antibacterial potential against <i>E. faecalis</i>	[26]
Imidazolium-based ionic liquid IL1 and IL2	Investigation of cytocompatibility behavior, of imidazolium-based coating with human 14 gingival fibroblasts (HGF-1) and pre-osteoblast (MC3T3-E1), antimicrobial assay and wear resistance on Titanium implants surfaces	Broad-spectrum antibacterial activity of IL1 against <i>Streptococcus species</i> , <i>S. muans</i> , <i>S. salivarius</i> , <i>S. gordonii</i> , and <i>S. uberis</i> cells in early stages of implantation, enhanced wear resistance but more cytotoxicity as compared to IL2	[27]
IL1 and IL2	In vitro investigation of dicationic imidazolium-based ILs as multi-functional coatings on a zirconia (ZrO ₂) surface	Increased wear resistance, decreased coefficient of friction and anti-biofilm potential against <i>Streptococcus salivarius</i> and <i>Streptococcus sanguinis</i> , while maintaining the material's compatibility with host cells (gingival fibroblasts and pre-osteoblasts) ILs. IL1 showed enhanced antimicrobial resistance as compared to IL2 and control (zirconia surface without coating)	[28]
1-Decyl-3-methylimidazolium chloride	Impact of 1-Decyl-3-methylimidazolium chloride IL on antifungal, physical and mechanical properties of conventional and nystatin incorporated tissue conditioners	Enhanced antifungal activity against <i>C. albicans</i> , reduced water solubility, increased water sorption, increased softness, and mild cytotoxicity against mouse fibroblast cells in IL and nystatin incorporated tissue conditioners	[29]
THMM	Electrical shear bond Strength reduction of trihydroxyethyl methylammonium methylsulfate IL incorporated RMGIC	Significant shear bond strength reduction and easy debonding on-demand with the trigger of electric current (smart dental cement) in IL incorporated resin modified glass ionomer cement.	[24]
BMIM	Synthesis and assessment of IL assisted, Sr-doped hydroxyapatite filled dental composites for surface area, curing depth and cell viability in breast cancer cell line (MCF-7) with MTT assay.	Increased surface area, increased curing depth, and acceptable biocompatibility in IL assisted Sr doped hydroxyapatite filled dental composites as compared to conventionally prepared HA filled dental composites.	[30]
[BMIM][Tf ₂ N]	Synthesis and evaluation of IL stabilized [BMIM][Tf ₂ N] stabilized, QD filled stabilized adhesives	Antibacterial fillers, potential cytocompatibility, maintained shear bond strength in IL stabilized quantum dot filled adhesives	[31]
[BMIM][Tf ₂ N]	1-n-butyl-3-methylimidazolium (trifluoromethanesulfonyl) imide IL (5 %, 10 %, 15 %) incorporated resin adhesives were investigated for antimicrobial potential, cytotoxicity with a degree of conversion	All groups of IL incorporated resin adhesives showed antibacterial potential, cytocompatibility, higher degree of conversion during polymerization, with less Knoop hardness and softening in solvent IL 10 % and IL 15 % groups	[32]

bacteria, which include *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, etc [35,36]. It has been demonstrated that QACs are effective antibacterial agents in dental adhesives [24, 33, 37]. Experimental Clearfil™ SE Bond containing 5% QAMP showed a cumulative release of only 5.1% quaternary ammonium compounds compared to 47.2% in conventional adhesives Clearfil™ Protect bond, thus supporting a sustained antimicrobial activity [39]. Quaternary ammonium polymers are promising non-leaching contact-killing bactericidal compounds without compromising the adhesive's strength and modulus [40]. Zhang and co-workers were among the first to investigate the protein-repellant dental adhesives formulated with 2-methacryloyloxyethyl phosphorylcholine (MPC), quaternary ammonium compounds (QAC), and dimethylaminohexadecylmethacrylate (DMAHDM), where the protein-repellant action is believed to improve the contact-killing between the QAC-microbial interfaces [41].

Researchers have revealed that QACs may cause reproductive and developmental anomalies in animals [41,42]. There have been no findings on the toxicity of QACs in humans till date. To be on the safe side, the California Department of Public Health issued COVID19 recommendations for schools in July 2020, recommending the use of disinfectants that do not contain QACs. Similarly, when designing new dental materials containing QACs, vigilance should be exercised, and toxicity should be considered as an early concern in the material production process. International standard, ISO 7405:2018, which provides test methodologies for evaluating biocompatibility of medical devices used in dentistry, should be specifically referred prior to the material's commercialization [36]. Quaternary ammonium derived polyethylene (QA-PEI) nanoparticles have been documented as cytotoxic, when added at 2 wt% in endodontic sealers for antimicrobial activity. The cytotoxicity of the QA-PEI modified dental materials was tested using macrophages and fibroblast cell lines and studying its effect on the secretion of tumor necrosis factor alpha (TNF α) from the macrophages [43].

3.2 Choline-based Ionic Liquids

Choline-based ionic liquids are also known for their antifungal and antibacterial properties. They are employed as neuromuscular blocking agents, antibacterial and antifungal agents for therapeutic medication delivery [42,43]. The mechanism of action is based on the breakdown of cellular processes and lysis of bacteria. Via hydroxyl groups, they also promote cytoplasmic denaturation of microbial enzymes [44, 45].

3.3 Imidazolium Ring-based Ionic Liquids

Imidazolium ring-based ionic liquids are positively charged with the carbon chain. It has been demonstrated in numerous investigations that they can result in bacterial lysis [33, 46]. This IL has been investigated in antibacterial research as a potential agent to prevent secondary caries in orthodontic resin-based adhesives and experimental resin-based adhesives

[47], as well as potent disinfectants in root canal treatments [35]. Imidazolium-based ILs have also been used as solvents in synthesising antiviral drugs such as brivudine, stavudine and trifluridine [10]. These imidazolium-based antiviral drugs have been found to have a good yield. Trifluridine, for example, yielded 91% in 20–25 min. This antiviral drug was synthesised using 1-methoxyethyl-3-methylimidazolium methanesulfonate, 4-dimethylaminopyridine (DMAP), and acetic anhydride [48].

4 Applications of Ionic Liquids in Dentistry

The antimicrobial properties of ionic liquids have opened new vistas in overcoming the current challenges associated with combating antibiotic-resistant pathogens. The potential applications of ionic liquids in the biomedical arena, including regenerative medicine, biosensing, and drug/biomolecule delivery, are presented to stimulate the scientific community to explore their potential benefits [33,49]. In dentistry, ionic liquids modulated antimicrobial adhesives [31, 47, 50], ionic liquid-based antibacterial coating on dental implants [28], and retained therapeutic carriers system in periodontal disease [33] have been investigated.

4.1 Tissue Conditioners

Oral candidiasis is the inflammation of mucosa and a frequent complaint in long term denture wearers. The condition is associated with antifungal infection caused by *Candida albicans*. Treatments for denture stomatitis are, to remove the denture with an antifungal drug prescription. The purpose is to promote healing of the inflamed tissues. If the problem still persists, slight grinding of the tissue surface followed by an application of denture liner is advised [53].

It is known that intraoral antifungal therapy has a number of disadvantages, including the cleansing effect of saliva and muscle in the oral cavity, which reduces the drug's potency below the appropriate therapeutic concentration. Therefore recurrence of candidiasis is a prime concern [54]. Researchers have attempted to develop tissue conditioners with antifungal properties by integrating antifungal drugs, metal-containing compounds, or poly-therapeutic agents [33, 34]. The idea was to reduce the surface accumulation of microorganisms and hence prevent denture stomatitis. According to studies, the proportion of *Candida albicans* colony-forming units was decreased dramatically in tissue conditioners containing antifungal drugs [35, 37]. In addition, antifungal drugs combined with IL significantly decreased *Candida albicans* colony-forming units (Fig. 2), where the interaction between the positive charges of ILs, 1-decyl-3-methylimidazolium chloride, and the negative charges of acidic phospholipids in the microbial cell membrane causes cell membrane disruption, followed by denaturation of structural proteins, leakage of intercellular components, and cell lysis [19]. Furthermore, the antifungal-IL incorporated tissue conditioners exhibit less solubility and reduced water sorption in addition to enhanced antifungal characteristics; however, the 2.25% IL incorporated tissue conditioner was

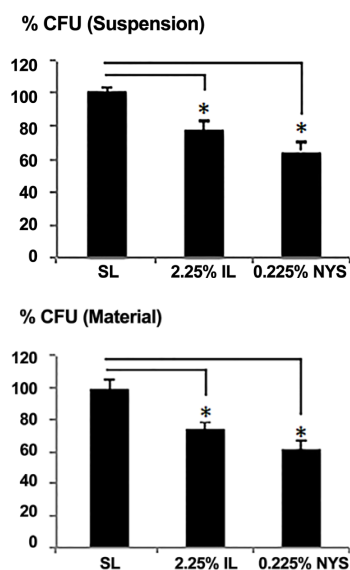


Figure 2. The percentage of colony forming unit (%CFU) of *C. albicans* from material suspension and adhered fungal cells on materials. Significant decrease in fungal cell viability was observed in both IL and NYS group, compared to control. Similar results were observed from both suspension and adhered fungal cells. *Significant difference, $p < 0.05$ [29]

found to create a stiffer tissue conditioner [29]. Another drawback of the IL-incorporated tissue conditioners was their cell cytotoxicity, which may have been caused by IL's impact on solubilizing cell membrane components, which may also be harmful to human cells [29,51]. More studies appear to be needed to address the concerns of cytotoxicity and dynamic viscoelasticity in IL-incorporated tissue conditioners.

4.2 Dental Restorations

The current approach in dentistry is to use innovative restorative materials to make dentistry long-lasting, efficient, and aesthetically acceptable for the patient. As a result, resin-based composites containing bioactive remineralizing agents are in tremendous demand today. Bioactive fillers are incorporated in the resin matrix of composite restorative materials, and in vitro research has shown a sustained release of calcium and phosphate ions. Bioactive composites have been found to remineralize enamel and dentin carious lesions. These bioactive fillers can chemically bind with tooth enamel by establishing a remineralizing layer at the tooth-composite interface, making the restoration more robust [56].

Ionic liquids have been used to alter inorganic materials. They have a unique property that allows them to be utilized as templating or morphology-controlling agents, allowing them to control the nucleation and growth of nanostructures [52–54]. The desirable chemical and physical properties of ILs, such as high polarity and low toxicity, make them the preferred materials for this application.

Their intrinsic charge can hinder nanoparticle aggregation by electrostatic interaction, whereas their alkyl substituent can prevent nanoparticle aggregation via steric hindrance as demonstrated in Fig. 3 [55,56]. Studies showed that ionic liquid was released from a composite resin with strontium-doped hydroxyapatite fillers treated with bromine hydroxide ionic liquid, and this composite resin formula demonstrated effective caries remineralization by type 1 collagen [57,58].

Ionic liquids were also used in the application of smart dental cement; in which dental cement can be debond on demand, such as when secondary caries formation occurred or when the crown restoration needed to be removed. Smart dental cement, in essence, allows for a strong bond between teeth and dental materials, or between different types of dental materials, such as metal post-core and ceramic crowns, while also allowing for easy debonding when necessary. This concept is not new and is already used in adhesive engineering applications [59]. The idea is that the incorporated ILs serves as essential parts for the cement debonding process when required. Elements including heat, pH, light, and electric current are frequently used to trigger the debonding process through ILs [60,61]. However, not all of these elements are suitable for oral use. For instance, it is unsafe to apply heat in an oral environment. Although moderate pH changes and light may be acceptable for intraoral use, it is difficult to stop their actions [24]. On the other hand, small electric currents between 0.4 and 5 mA are relatively safe and easy to deactivate [62,63]. Resin-modified glass ionomer cement containing IL, tris 2-hydroxyethyl methylammonium methylsulfate, was found to exhibit significant electrical conductivity and easy debonding on-demand with the application of electric current [24], which opens the door for further investigation of IL's use in smart dental cement.

4.3 Implants Surfaces Coatings

Most early implantation failures are due to bacterial adhesion, which impedes good healing and osseointegration [28]. In post-insertion implant failures, bacterial colonization on the implant surface plays a significant role [64–66]. It has been proposed that dicationic imidazolium-based ionic liquid coatings protect implant surfaces against bacterial colonization and biofilm deposition [28,67]. Phenylalanine, an anionic component in dicationic imidazolium-based ionic liquids, is responsible for antimicrobial action and cell proliferation on titanium implant surfaces [27]. Dicationic imidazolium-based ionic liquids IL-based coatings had shown broad-spectrum anti-

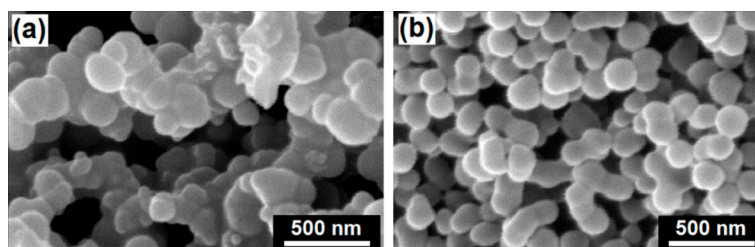


Figure 3. SEM images of the as-prepared products via hydrothermal method without (a) and with (b) ILs [30].

microbial activity in the early stage of implantation [68]. It has also been demonstrated that imidazolium-based ILs possess broad-spectrum antimicrobial activity against strains such as *Streptococcus mutans*, *Streptococcus mutants*, *Streptococcus sanguinis*, *Streptococcus salivarius*, *Streptococcus Gordonii*, and *Streptococcus uberis* [27], which are commonly found on the implant surface during the early stages of implantation.

The coatings of ILs on zirconia implants constitute a novel and potential technology for surface enhancement of implants. Dicationic imidazolium-based IL coatings, when added to the surface of commercially pure titanium (CpTi), form a thin layer of stable anti-biofilm with high adhesion strength. This coating promotes corrosion protection and improved lubrication [67,69] while maintaining biocompatibility with host tissues in vitro [28,67]. Dicationic imidazolium-based IL coating was also shown to improve wear resistance by forming a stable lubricating layer on zirconia surfaces [28]. This increased hydrophobicity results in a lower coefficient of friction and wear volume loss by shielding it against mechanical forces during insertion. IL coating not only demonstrated anti-biofilm activity and wear protection for implant fixtures, but also provided an environment for the growth and proliferation of host cells [28,71].

4.4 Ionic Liquids in Adhesives Resins

Dental adhesives are methacrylate resins, which lack inherent strength and antimicrobial potential against *S. mutans* [26]. Developments of secondary caries led to disintegration of the adhesives and compromise the bond strength at tooth dentin interface. Various attempts have been made to device antibacterial dental adhesives via contact killing or leaching of antimicrobial agents. Conventional strategies included incorporation of chlorhexidine [73], quaternary ammonium compounds [33], addition of silver [74], and zinc oxide nanoparticles [47], in resin matrix of dental adhesives. Despite of the promising antibacterial potential, these measures either provoke the esthetic concern by discoloration of teeth or cytotoxicity/metal ion releasing in biological systems in in vitro experiments.

Ionic liquids incorporation has been employed as the contemporary strategy to develop antimicrobial adhesive systems [37]. They have been proposed to provide wide, tailored antimicrobial potential either by selecting the class of cations and their counter anions as well, as by controlling the alkyl chain length of the cations [68,75].

Titanium quantum dots along with 1-n-butyl-3-methylimidazolium tetrafluoroborate (BMIM.BF₄), were used o formulae antibacterial adhesives against *S. mutans*. The carbon chain of BMIM.BF₄ and he positively charged imidazolium ring conveniently facilitated he anchoring of negatively charged cell membrane of prokaryotic bacterial cell [24].

In another research, experimental orthodontic adhesives, composed of 1-n-butyl-3-methylimidazolium bis(trifluoromethane-sulfonyl)imide IL a varying concentrations(5%, 10%, and 15%) were assessed. Significant antimicrobial potential against *S. mutans* along with the maintained degree of conversion, flexural strength and shear bond strength were evident in group with 5% ionic liquid [32].

4.5 Ionic Liquids Incorporated Endodontic Sealants

Endodontic treatment eliminates the underlying reason of infection in the root canal space. Instrumentation, irrigation, and intracanal medicaments are all employed during the root canal treatment process. This procedure seeks to eliminate all bacteria and their byproducts. However, investigations have shown that bacteria can persist in the dentinal tubules and cementum, where they can cause inflammation and infection [38]. The most common microbe in infected root canals is *E. faecalis*, which has the potential to infiltrate deeply into dentinal tubules while resisting intracanal operations and living in filled canals [70]. The development of antibacterial endodontic medicaments, intracanal posts, and resins for core build-ups might aid in the restoration of apical and periapical tissues [72].

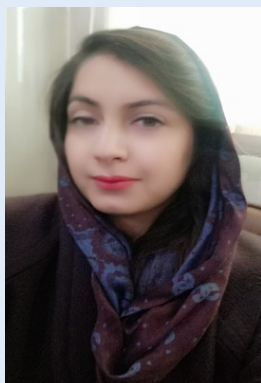
Silver nanoparticles are now established antimicrobials in root canal irrigants [76,77]. Ionic liquid is active against *Enerococcus faecalis* in endodontic infections. The antibacterial potency of AgNp is dependent upon their size, shape, charge and surface coatings. Agglomeration of silver nanoparticles in suspension is of concern, as it decreases he surface area and hinder he antibacterial potential [78]. Abbas [76], documented, positively charged imidazolium based IL; dodecyl-3-methylimidazolium chloride ([C1MIM][Cl]), protected silver nanoparticles maintained lasting antimicrobial potential against *E. Faecalis*. Non-agglomerated, positively charged IL, protected AgNp, could conveniently anchor the negatively charged prokaryotic cell membrane of bacteria. When compared with the chlorhexidine and sodium hypochlorite incorporated silver nanoparticles.

5 Conclusion

Ionic liquids have been studied as prospective candidates for various new dental application strategies. Their antifungal and antibacterial qualities make them an excellent candidate for incorporation in denture tissue conditioners, dental adhesive resins, and an active pharmaceutical ingredient in anti-inflammatory medications to enhance drug efficacy. ILs are increasingly being used to modify the surface of titanium dental implants. These stable coatings are anticipated to improve wear performance on zirconia implant surfaces through intrinsic lubrication, anti-biofilm activity, biocompatible cell interactions, and implant stability. There are also potential applications for ILs in novel dental applications, such as smart dental resin modified lass ionomer cement, which can be used to debond on demand, and prototype medical grade cement, which requires further work. However, biosafety is a challenge because the IL concentration must be precisely controlled to guarantee biocompatibility. In addition, the incorporation of ILs decreases the material's viscoelasticity, which is unfavorable to the oral mucosa.

Conflicts of Interest

The authors declare no conflict of interest.



Nadia Munir is a Ph.D. scholar at Universiti Sains Malaysia Kelantan Malaysia and currently working as Associate Professor of Dental Materials at Avicenna Dental College Lahore Pakistan. She did her Bachelor of Dental Surgery (BDS) in Pakistan, and in 2014, her M. Phil in Dental Materials at University of Health Sciences (UHS) Lahore, Pakistan. She also holds a post graduate diploma in medical

education from the University of Liverpool. Her research interests include synthesis and characterizations choline based ionic liquids, investigation of impact of ionic liquids on various properties of ionic liquids, bioactive dental composites and interfacial study of restorative resins.



Raja Azman Awang is a periodontist and lecturer at the School of Dental Sciences, Universiti Sains Malaysia, where he has worked since 1999. He teaches periodontology to dentistry students at the undergraduate and graduate levels and is currently the Head of Periodontics unit at the School of Dental Sciences, USM. He received his Ph.D. in Periodontal Immunology from the University of Glasgow in

2014. He completed his specialist training in Periodontics (2004) and his first degree in Dentistry (1997) at the Universiti Malaya. In addition to treating patients and teaching dentistry, his research interests include periodontal clinical studies and immunology, as well as dental biomaterials.



Nawshad Muhammad obtained his M. Phil from University of Peshawar in the field of Dental Polymeric Materials and Biochemistry and his Ph.D. from PETRONAS Ionic Liquid Center, Universiti Teknologi PETRONAS Malaysia in the domain of green chemistry and sustainable biotechnology. He obtained a postdoctoral certificate from China Ionic Liquid Laboratory, Dalian Institute of Chemical Physics, Chinese Academy of

Sciences in the field of green processing of bioactive materials. Currently he is working as Associate Professor in Khyber Medical University Peshawar Pakistan. His research interests include synthesis of ionic liquids for extraction and processing of biopolymers.



Noor Huda Ismail is a prosthodontist and lecturer at the School of Dental Sciences, Universiti Sains Malaysia (USM). She started as a dental officer at USM following her graduation with a Bachelor of Dental Surgery from the University of Malaya. Then, she became a trainee lecturer before continuing her studies at the University of Dundee in prosthodontic and graduated in 2012. She is a member of

the Malaysian Association of Prosthodontics. She is also a member of the Royal College of Physicians and Surgeons of Glasgow. Her main clinical interest and research field include fixed and removable prosthodontics, endodontically treated teeth, and dental biomaterials.



Abdul Samad Khan is currently working as an Associate Professor of Dental Biomaterial at the Department of Restorative Dental Sciences, College of Dentistry, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia. He did his Bachelor of Dental Surgery (BDS) in 1999 in Pakistan and in 2005 his M.Sc. Dental Materials at Queen Mary University of London (QMUL), UK. He

completed his Ph.D. in 2009 at QMUL, UK. In 2013–2014 he did a Postdoctoral Associateship at the University of Sheffield, UK. His research is driven by several different approaches, mainly synthesis and characterizations of resin-based composites and Adhesives based on bioactive nanomaterials.



Naveed Inayat is an Associate Professor of Prosthodontics at Avicenna Dental College, Lahore, Pakistan. He received his bachelor's degree from the de' Montmorency College of Dentistry, Lahore, in 2003. As a facilitator, he conducts regular workshops on fixed prosthodontics and aesthetic dentistry for undergraduate and post graduate students, accredited with university of health sciences Lahore. Apart from

Academic teaching he wants to pursue his career in clinical practice of Maxillo-Facial prosthodontics and its specific implications to implantology. Growing concerns toward replacement of missing oral and Maxillo-Facial structures can make ways for further advancement and scope in the field.

Acknowledgements

The authors are grateful to Dr Azmat Mehmood from department of Chemistry; Islamia college Lahore for consistent support in review and organization of the manuscript.

Abbreviations

AgNp	silver nanoparticles
BMIM	1-butyl-3-methylimidazolium
BMIM-decane	diphenylalanine- 1, 10-Bis (3-methylimidazolium-1-yl) decane diphenylalanine

BMIM-decane dimethionine	1, 10-bis (3-methylimidazolium-1-yl)decane dimethionine
[BMIM][Tf ₂ N]	1-butyl-3-methylimidazolium bis [(trifluoromethyl)sulfonyl]imide
CpTi	commercially pure titanium
DMAHDM	dimethyl amino hexadecyl methacrylate
DMAP	4- dimethylaminopyridine
[DMIM][Cl]	dodecyl-3-methy- limidazolium chloride
ESKAPE	<i>Enterococcus faecium</i> , <i>Staphylococcus aureus</i> , <i>Klebsiella pneumonia</i> , <i>Acinetobacter baumannii</i>
IL	ionic liquid
IL1	1,10-bis(3-methylimidazolium-1-yl)decane diphenylalanine
IL2	1,10-bis(3-methylimidazolium-1-yl)decane dimethionine
MPC	2-methacryloyloxyethyl phosphorylcholine
NaOCl	sodium hypochlorite
QAC	quaternary ammonium compounds QAMP
	quaternary ammonium methacrylate polymer
QA-PEI	quaternary ammonium derived polyethylene
RMGIC	resin modified glass ionomer cements
THMM	tris 2-hydroxyethyl methylammoniummethyl sulfate

References

- [1] B. Nanda, M. Sailaja, P. Mohapatra, R. K. Pradhan, B. B. Nanda, *Mater. Today: Proc.* **2021**, *47*, 1234–1240. DOI: <https://doi.org/10.1016/j.matpr.2021.06.458>
- [2] M. Bystrzanowska, F. P. Pereira, L. Marcinkowski, M. Tobiszewski, *Ecotoxicol. Environ. Saf.* **2019**, *174*, 455–458. DOI: <https://doi.org/10.1016/j.ecoenv.2019.03.014>
- [3] R. M. Moshikur, M. R. Chowdhury, M. Moniruzzaman, M. Goto, *Green Chem.* **2020**, *22* (23), 8116–8139. DOI: <https://doi.org/10.1039/D0GC02387F>
- [4] A. Bhattarai, *J. Eng. Sci.* **2012**, *1*, 15–22.
- [5] F. Plamper, W. Richtering, *Acc. Chem. Res.* **2017**, *50* (2), 131–140. DOI: <https://doi.org/10.1021/acs.accounts.6b00544>
- [6] Suresh, J. S. Sandhu, *Green Chem. Lett. Rev.* **2011**, *4* (4), 289–310. DOI: <https://doi.org/10.1080/17518253.2011.572294>
- [7] S. Singh, A. Savoy, *J. Mol. Liq.* **2020**, *297*, 112038. DOI: <https://doi.org/10.1016/j.molliq.2019.112038>
- [8] P. Calandra, E. Szerb, D. Lombardo, V. Algieri, A. D. Nino, L. Maiuolo, *Appl. Sci.* **2021**, *11* (12), 5677. DOI: <https://doi.org/10.3390/app11125677>
- [9] D. Hodyna, V. Kovalishyn, I. Semenyuta, V. Blagodatnyi, S. Rogalsky, L. Metelytsia, *Comput. Biol. Chem.* **2018**, *73*, 127–138. DOI: <https://doi.org/10.1016/j.compbiolchem.2018.01.012>

- [10] B. Nagay, S. Bitencourt, B. Commar, E. D. Silva, D. D. Santos, E. Rangel, M. Goiatob, A. Curya, A. Filhod, V. Barãoa, *Arch. Oral Biol.* **2020**, *117*, 104822. DOI: <https://doi.org/10.1016/j.archoralbio.2020.104822>
- [11] F. Brunel, C. Lautard, F. Garzino, J. Raimundo, J. Bolla, M. Camplo, *Bioorg. Med. Chem. Lett.* **2020**, *30* (18), 127389. DOI: <https://doi.org/10.1016/j.bmcl.2020.127389>
- [12] V. Koch, L. Miller, R. Osteryoung, *J. Am. Chem. Soc.* **1975**, *97* (15), 3264–3265. DOI: <https://doi.org/10.1021/ja00844a081>
- [13] *Dialkylimidazolium*, in *Encyclopedia of Lubricants and Lubrication* (Ed: T. Mang), Springer, Berlin **1982**, 374. DOI: https://doi.org/10.1007/978-3-642-22647-2_100172
- [14] J. Wilkes, J. Levisky, R. Wilson, C. Hussey, *Inorg. Chem.* **1982**, *21* (3), 1263–1264. DOI: <https://doi.org/10.1021/ic00133a078>
- [15] J. S. Wilkes, M. J. Zaworotko, *J. Chem. Soc., Chem. Commun.* **1992**, (13), 965–967. DOI: <https://doi.org/10.1039/C39920000965>
- [16] M. Nasrollahzadeh, M. Ghasemzadeh, H. Gharoubi, Z. Nezafat, *J. Mol. Liq.* **2021**, *342*, 117559. DOI: <https://doi.org/10.1016/j.molliq.2021.117559>
- [17] B. Gadilohar, G. Shankarling, *J. Mol. Liq.* **2017**, *227*, 234–261. DOI: <https://doi.org/10.1016/j.molliq.2016.11.136>
- [18] G. Thomas, J. Wilson, P. Valderrama, D. Rodrigues, *J. Periodontol.* **2014**, *85* (5), 657–660. DOI: <https://doi.org/10.1902/jop.2013.130353>
- [19] A. Curreri, S. Mitragotri, E. Tanner, *Adv. Sci.* **2021**, *8* (17), 2004819. DOI: <https://doi.org/10.1002/advs.202004819>
- [20] K. Azuma, S. Ifuku, T. Osaki, Y. Okamoto, S. Minami, *J. Biomed. Nanotechnol.* **2014**, *10* (10), 2891–920. DOI: <https://doi.org/10.1166/jbn.2014.1882>
- [21] S. Blöcher, R. Frankenberger, A. Hellak, M. Schauseil, M. Roggendorf, M. K. Steiner, *BMC. Oral Health* **2015**, *15*, 42. DOI: <https://doi.org/10.1186/s12903-015-0024-8>
- [22] K.-L. Chang et al., *Bioresour. Technol.* **2017**, *1* (227), 388–392. DOI: <https://doi.org/10.1016/j.biortech.2016.11.085>
- [23] N. Kajimoto, E. Uyama, K. Sekine, K. Hamada, *Dent. Mater. J.* **2018**, *37* (5), 768–774. DOI: <https://doi.org/10.4012/dmj.2017-361>
- [24] M. Pupo, V. Farago, M. Nadal, A. Esmerino, F. Maluf, F. Zawadzki, M. Michéle, F. Santos, A. Gomes, J. Carlos, *J. Biomater. Sci. Polym. Ed.* **2013**, *24* (12), 1443–1458. DOI: <https://doi.org/10.1080/09205063.2013.766784>
- [25] A. Abbaszadegan, M. Nabavizadeh, A. Gholami, S. Aleyasin, S. Dorostkar, M. Saliminasa, Y. Ghasemi, B. Hemmateenejad, H. Sharghi, *Int. Endod. J.* **2015**, *48* (8), 790–800. DOI: <https://doi.org/10.1111/iej.12377>
- [26] M. Gindri, K. Palmer, A. Siddiqui, S. Aghyarian, P. Frizzo, A. Martins, D. Rodrigues, *RSC Adv.* **2016**, *6* (43), 36475–36483. DOI: <https://doi.org/10.1039/C6RA01003B>
- [27] P. Sandhu, I. Gindri, D. Siddiqui, D. Rodrigues, *J. Func. Biomater.* **2017**, *8* (4), 50. DOI: <https://doi.org/10.3390/jfb8040050>
- [28] K. Kanjanamekanant, N. Limpuangthip, M. Arksornnukit, *Mater. Sci. Appl.* **2017**, *8* (5), 376–388. DOI: <https://doi.org/10.4236/msa.2017.85026>
- [29] K. Moradi, A. Alvani, D. Poelman, *Materials* **2019**, *12* (14), 2339. DOI: <https://doi.org/10.3390/ma12142339>
- [30] M. Garcia, S. Souza, C. Hellriegel, D. Scholten, M. Collares, *J. Dent. Res.* **2019**, *98* (6), 682–688. DOI: <https://doi.org/10.1177/0022034519835203>
- [31] I. Garcia, C. Ferreira, S. de Souza, V. Leitune, W. Samuel, G. Balbinot, A. Mottac, F. Visiolid, J. Scholtenb, F. Collares, *Dent. Mater.* **2019**, *35* (8), 1155–1165. DOI: <https://doi.org/10.1016/j.dental.2019.05.010>
- [32] N. Nikfarjam, M. Ghomi, T. Agarwal, M. Hassanpour, E. Sharifi, D. Khorsandi, *Adv. Funct. Mater.* **2021**, *31* (42), 2104148. DOI: <https://doi.org/10.1002/adfm.202104148>
- [33] Y. Nam, *J. Adv. Prosthodont.* **2011**, *3* (1), 20–24. DOI: <https://doi.org/10.4047/jap.2011.3.1.20>
- [34] J. Flaczyk, J. Walentowska, *Int. Biodeterior. Biodegrad.* **2013**, *84*, 412–415. DOI: <https://doi.org/10.1016/j.ibiod.2012.05.025>
- [35] A. Sahoo, S. Swain, A. Behera, G. Sahoo, K. Mahapatra, K. Panda, *Front. Microbiol.* **2021**, *12*, 661195. DOI: <https://doi.org/10.3389/fmicb.2021.661195>
- [36] S. Parhi, S. Pal, S. Das, P. Ghosh, *Biotechnol. Bioeng.* **2021**, *118*, 4590–4622. DOI: <https://doi.org/10.1002/bit.27948>
- [37] M. Garcia, S. Souza, D. Scholten, M. Collares, *J. Adhes. Dent.* **2020**, *22* (2), 207–214. DOI: <https://doi.org/10.3290/j.jad.a44285>
- [38] C. Poggio, F. Trovati, M. Ceci, M. Chiesa, M. Colombo, G. Pietrocola, *J. Clin. Exp. Dent.* **2017**, *9* (3), e387–393. DOI: <https://doi.org/10.4317/jced.53464>
- [39] P. Ramburrun, A. Pringle, A. Dube, Z. Adam, S. D'souza, M. Aucamp, *Materials* **2021**, *14*, 3167. DOI: <https://doi.org/10.3390/ma14123167>
- [40] F. Zhang, R. Wu, Y. Fan, S. Liao, Y. Wang, T. Wen, *J. Dent. Res.* **2014**, *93* (12), 1283–1289. DOI: <https://doi.org/10.3390/pharmaceutics13111820>
- [41] C. Hrubec, E. Melin, S. Shea, E. Ferguson, C. Garofola, M. Repine, W. Chapman, R. Patel, M. Razvi, E. Sugrue, H. Potineni, G. Magnin-Bissel, A. Hunt, *Birth. Defects. Res.* **2017**, *109* (14), 1166–1178. DOI: <https://doi.org/10.1002/bdr2.1064>
- [42] V. E. Melin, T. E. Melin, J. Dessify, T. Nguyen, S. Shea, C. Hrubec, *Reprod. Toxicol.* **2016**, *59*, 159–166. DOI: <https://doi.org/10.1016/j.reprotox.2015.10.006>
- [43] M. Chrószcz, I. Ryberek, *Polymers* **2020**, *12* (11), 2551. DOI: <https://doi.org/10.3390/polym12112551>
- [44] N. Gandhewar, P. Shende, *Ionics* **2021**, *27* (9), 3715–3728. DOI: <https://doi.org/10.1007/s11581-021-04201-y>
- [45] J. Huh, J. K. Won, *J. Control. Release* **2011**, *156* (2), 128–145. DOI: <https://doi.org/10.1016/j.jconrel.2011.07.002>
- [46] F. Siopa, T. Figueiredo, R. Frade, I. Neto, A. Meirinhos, P. Reis, R. Sobral, C. Afonso, P. Rijo, *ChemistrySelect* **2016**, *1* (18), 5909–5916. DOI: <https://doi.org/10.1002/slct.201600864>
- [47] N. Muhammad, I. Hossain, Z. Man, M. El-harbawi, A. Bustam, A. Noaman, N. Alitheen, M. Ng, G. Hefter, C. Yin, *J. Chem. Eng. Data* **2012**, *57*, 2191–2196. DOI: <https://doi.org/10.1016/j.jddst.2021.102694>
- [48] J. Shi, M. Wang, Z. Sun, Y. Liu, J. Guo, M. Hailei, F. Yan, *Acta Biomater.* **2019**, *9*, 247–259. DOI: <https://doi.org/10.1016/j.actbio.2019.07.039>

- [49] M. Garcia, S. Souza, D. Souza, F. Visioli, B. Leitune, D. Scholten, F. Collares, *J. Dent.* **2020**, *102*, 103477. DOI: <https://doi.org/10.1016/j.jdent.2020.103477>
- [50] N. Pedro, R. Freire, D. Silvestre, G. Freire, *Int. J. Mol. Sci.* **2020**, *21* (21), 8298. DOI: <https://doi.org/10.3390/ijms21218298>
- [51] R. Macfarlane, M. Forsyth, C. Howlett, M. Kar, S. Passerini, M. Pringle, H. Ohno, M. Watanabe, F. Yan, W. Zheng, S. Zhang, J. Zhang, *Nat. Rev. Mater.* **2016**, *1*, 15005. DOI: <https://doi.org/10.1038/natrevmats.2015.5>
- [52] W. Li, M. Qi, X. Sun, M. Chi, Y. Wan, X. Zheng, C. Li, L. Wang, B. Dong, *Microporous Mesoporous Mater.* **2020**, *299*, 110113. DOI: <https://doi.org/10.1016/j.micromeso.2020.110113>
- [53] R. Rautemaa, G. Ramage, *Crit. Rev. Microbiol.* **2011**, *37* (4), 328–36. DOI: <https://doi.org/10.3109/1040841X.2011.585606>
- [54] A. Ellepola, P. Samaranyake, *Dent. Update* **2000**, *27*, 165–174. DOI: <https://doi.org/10.12968/denu.2000.27.4.165>
- [55] R. Arunkumar, N. Abraham, R. Shukla, J. Drummond, L. Greaves, *J. Mol. Liq.* **2020**, *314*, 113602. DOI: <https://doi.org/10.1016/J.MOLLIQ.2020.113602>
- [56] A. Khan, M. Syed, *Dent. Mater. J.* **2019**, *38* (2), 163–76. DOI: <https://doi.org/10.4012/dmj.2018-039>
- [57] J. Luczak, M. Paszkiewicz, A. Krukowska, A. Malankowska, A. Medynska, *Adv. Colloid. Interface Sci.* **2016**, *230*, 13–28. DOI: <https://doi.org/10.1016/j.cis.2015.08.006>
- [58] F. Zhou, Y. Liang, W. Liu, *Chem. Soc. Rev.* **2009**, *38* (9), 2590–2599. DOI: <https://doi.org/10.1039/b817899m>
- [59] Y. Zhou, *Curr. Nanosci.* **2006**, *1* (1), 35–42. DOI: <https://doi.org/10.2174/1573413052953174>
- [60] J. Luczak, J. Hupka, J. Thöming, C. Jungnickel, *Colloids Surf. A* **2008**, *329* (3), 125–133. DOI: <https://doi.org/10.1016/j.colsurfa.2008.07.012>
- [61] F. Bernardi, J. Scholten, G. Fecher, J. Dupont, J. Morais, *Chem. Phys. Lett.* **2009**, *479*, 113–116. DOI: <https://doi.org/10.1016/j.cplett.2009.07.110>
- [62] C. Capuccini, P. Torricelli, E. Boanini, M. Gazzano, R. Giardino, A. Bigi, *J. Biomed. Mater. Res., Part A* **2009**, *89* (3), 594–600. DOI: <https://doi.org/10.1002/jbm.a.31975>
- [63] T. Thuy, H. Nakagaki, K. Kato, P. Hung, J. Inukai, S. Tsuboi, H. Nakagaki, M. Hirose, S. Igarashi, C. Robinson, *Arch. Oral Biol.* **2008**, *53* (11), 1017–1022. DOI: <https://doi.org/10.1016/j.archoralbio.2008.06.005>
- [64] Y. Lu, J. Broughton, P. Winfield, *Int. J. Adhes. Adhes.* **2014**, *50*, 119–127. DOI: <https://doi.org/10.1016/j.jadhadh.2014.01.021>
- [65] C. Heinzmann, S. Coulibaly, A. Roulin, G. Fiore, C. Weder, *ACS Appl. Mater. Interfaces* **2014**, *6* (7), 4713–4719. DOI: <https://doi.org/10.1021/am405302z>
- [66] X. Luo, K. Lauber, P. Mather, *Polymer* **2010**, *51* (5), 1169–1175. DOI: <https://doi.org/10.1016/j.polymer.2010.01.006>
- [67] H. E. Kim, H. K. Kwon, B. I. Kim, *J. Oral Rehabil.* **2009**, *36* (10), 770–775. DOI: <https://doi.org/10.1111/j.1365-2842.2009.01992.x>
- [68] H. E. Kim, B. I. Kim, *Oral Health Prev. Dent.* **2016**, *14* (2), 177–182. DOI: <https://doi.org/10.3290/j.ohpd.a35007>
- [69] A. Mombelli, F. Décaillet, *J. Clin. Periodontol.* **2011**, *38*, 203–213. DOI: <https://doi.org/10.1111/j.1600-051X.2010.01666.x>
- [70] E. Al. Shwaimi, D. Bogari, R. Ajaj, S. A. Shahrani, K. Almas, A. Majeed, *J. Endod.* **2016**, *42* (11), 1588–1597. DOI: <https://doi.org/10.1016/j.joen.2016.08.001>
- [71] D. Rodrigues, P. Valderrama, T. Wilson, K. Palmer, A. Thomas, S. Sridhar, A. Adapalli, M. Burbano, C. Wadhvani, *Materials* **2013**, *6* (11), 5258–5274. DOI: <https://doi.org/10.3390/ma6115258>
- [72] A. Shrestha, A. Kishen, *J. Endod.* **2016**, *42* (10), 1417–1426. DOI: <https://doi.org/10.1016/j.joen.2016.05.021>
- [73] D. Siddiqui, I. Gindri, D. Rodrigues, *J. Bio. Tribo. Corros.* **2016**, *2* (4), 27. DOI: <https://doi.org/10.1007/s40735-016-0057-9>
- [74] I. Gindri, D. Siddiqui, C. Frizzo, M. Martins, D. Rodrigues, *ACS Appl. Mater. Interfaces* **2015**, *7* (49), 27421–27431. DOI: <https://doi.org/10.1021/acsami.5b09309>
- [75] I. Gindri, D. Siddiqui, P. Bhardwaj, L. Rodriguez, K. Palmer, C. Frizzo, M. Martins, D. Rodrigues, *RSC. Adv.* **2014**, *4* (107), 62594–62602. DOI: <https://doi.org/10.1039/C4RA09906K>
- [76] M. Mathew, S. Abbey, N. Hallab, D. Hall, C. Sukotjo, M. Wimmer, *J. Biomed. Mater. Res., Part B.* **2012**, *100B* (6), 1662–1671. DOI: <https://doi.org/10.1002/jbm.b.32735>
- [77] W. Zhou, S. Liu, X. Zhou, M. Hannig, M. Rumpf, J. Feng, X. Peng, L. Cheng, *Int. J. Mol. Sci.* **2019**, *20* (3), 723. DOI: <https://doi.org/10.3390/ijms20030723>
- [78] T. Maravić, A. Comba, S. R. Cunha, V. Angeloni, M. Cadenaro, E. Visinitini, C. O. Navarra, S. Salgarello, L. Breschi, A. Mazzoni, *J. Dent.* **2019**, *84*, 60–66. DOI: <https://doi.org/10.1016/J.JDENT.2019.03.004>
- [79] F. W. Degrazia, V. C. B. Leitune, I. Garcia, R. A. Arthur, S. M. W. Samuel, F. M. Collares, *J. Appl. Oral Sci.* **2016**, *24* (4), 404–410. DOI: <https://doi.org/10.1590/1678-775720160154>

Recently, the use of ionic liquids (ILs) as potential solvents in dentistry has increased. Dental polymers use ionic liquids as solvents, plasticizers, surfactants, and disinfectants. Additionally, they possess antibacterial and antifungal properties. This review aims to evaluate the potential of task-specific liquids in dental applications.

Potential Applications of Ionic Liquids in Dentistry: A Narrative Review

Nadia Munir, Raja Azman Awang*,
Nawshad Muhammad,
Noor Huda Ismail, Abdul Samad Khan,
Naveed Inayat

ChemBioEng Rev. **2023**, *10* (X),
XXX ··· XXX

DOI: 10.1002/cben.202300012

