MOLECULAR DYNAMICS STUDIES OF EFFECT OF EXTERNAL FACTORS ON THE STRUCTURE AND DYNAMICS OF BIO-IONIC LIQUIDS IN BULK AND INTERFACE

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by

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Submitted

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Dedicated to

My Family

Certificate

This is to certify that the thesis titled "**MOLECULAR DYNAMICS STUDIES OF EFFECT OF EXTERNAL FACTORS ON THE STRUCTURE AND DYNAMICS OF BIO-IONIC LIQUIDS IN BULK AND INTERFACE**" is being submitted by **Mr. Aditya Gupta** to the Department of Chemistry, Indian Institute of Technology Delhi, for the award of the degree of **Doctor of Philosophy**. This thesis is a record of bonafide research work carried out by him under my supervision. In my opinion, the thesis has reached the standards fulfilling the requirements of the regulations relating to the degree.

The results contained in this thesis have not been submitted to any other University or Institute for the award of any degree or diploma.

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Abstract

In this thesis, we report the effect of external factors such as dilution, temperature, and electric field on the molecular level structural arrangement and dynamics of biocompatible ionic liquids by employing all-atom molecular dynamics (MD) simulations. Recent studies have shown that biocompatibility, biodegradability, and toxicity are major issues with the conventional ionic liquids (ILs) such as imidazolium and pyridinium cation, and fluoride anion based ILs. Most of these ILs are soluble in water which possesses threat to aquatic organisms. They inhibit enzymes and therefore decreases their activity. It is also shown that cations impose higher toxicity than anion and an increase in the length of alkyl chain increases the toxicity effect of the cation. These major issues of concern led to the development of biocompatible ILs (bio-ILs). This is possible because of the designer solvent character of ILs where its properties can be modulated by tweaking their ionic components. The ionic constituents of these bio-ILs are of benign origin and hence, renewable and practically non-toxic. One of the class of these bio-ILs is cholinium amino acid ([Ch][AA]) based bio-ILs which we have explored in this thesis. These bio-ILs have been proven to have low toxicity and high biodegradability because of which they are used in different biological and industrial applications. However, as they have started gaining more importance only recently, experimental or computational studies on their microscopic structure and dynamics, and effect of external factors on them are scarce in the literature. This leads to their under-utilization in corresponding applications because of poor understanding of their fundamental properties. This has motivated us to explore the microscopic level understanding of the structure and dynamics, along with investigating the effect of dilution, temperature, and potential difference on them.

Cholinium glycinate ([Ch][Gly]) is one of the least viscous and high conductivity bio-ILs. Herein, we first investigate the effect of aqueous dilution on the molecular level structural arrangement and dynamics of the cholinium glycinate bio-IL. This has been achieved through the computation and analysis of structural correlation functions such as total X-ray scattering structure functions (S(q)), their partial components, radial distribution function (g(r)), distance-angle distribution function (g(r,θ)), and spatial distribution function (SDF). To explore the dynamics, we have explored hydrogen bond

dynamics, mean square displacement, self-diffusion coefficient, velocity autocorrelation function, and electrical conductivity of the aqueous mixtures. We extended our study in the next step to explore that how the interfacial microscopic structure and electrostatics properties of cholinium glycinate vary near graphite electrodes with the applied potential difference. In this study, we have analyzed the simulated number and charge density profiles, tangential radial distribution function, orientational order parameter, and differential capacitance of [Ch][Gly] bio-IL. Furthermore, the investigation of cholinium amino acid based bio-ILs is extended to different amino acid anions namely phenylalaninate and cysteinate. In the second half of the thesis, we have investigated the temperature dependence of the microscopic structure of cholinium phenylalaninate ([Ch][Phe]) and cholinium cysteinate ([Ch][Cys]) bio-ILs with the help of real and inverse space correlations, and isodensity surfaces along with the supporting dynamic properties such as hydrogen bond dynamics.

सार

इस थीसिस में, हम सभी परमाणु आणविक गतिशीलता (एमडी) सिमुलेशन को नियोजित करके आणविक स्तर की संरचनात्मक व्यवस्था और बायोकंपैटिबल आयनिक तरल पदार्थों की गतिशीलता पर बाहरी कारकों जैसे कमजोर पड़ने, तापमान और विद्युत क्षेत्र के प्रभाव की रिपोर्ट करते हैं। हाल के अध्ययनों से पता चला है कि बायोकम्पैटिबिलिटी, बायोडिग्रेडेबिलिटी और विषाक्तता पारंपरिक आयनिक तरल पदार्थ (आईएल) जैसे कि इमिडाज़ोलियम और पाइरिडिनियम धनायन, और फ्लोराइड ऋणायन आधारित आईएल के साथ प्रमुख मुद्दे हैं। इनमें से अधिकांश आईएल पानी में घुलनशील हैं जो जलीय जीवों के लिए खतरा हैं। वे एंजाइमों को रोकते हैं और इसलिए उनकी गतिविधि को कम कर देते हैं। यह भी दिखाया गया है कि धनायन आयनों की तुलना में अधिक विषाक्तता लगाते हैं और एल्काइल श्रृंखला की लंबाई में वृद्धि से धनायन के विषाक्तता प्रभाव में वृद्धि होती है। चिंता के इन प्रमुख मुद्दों ने जैव-संगत आईएल (बायो-आईएल) के विकास को जन्म दिया। यह आईएल के डिज़ाइनर सॉल्वेंट कैरेक्टर के कारण संभव है, जहां इसके गुणों को उनके आयनिक घटकों को बदलकर संशोधित किया जा सकता है। इन बायो-आईएल के आयनिक घटक सौम्य मूल के हैं और इसलिए, नवीकरणीय और व्यावहारिक रूप से गैर विषैले हैं। इन जैव-आईएल के वर्ग में से एक कोलीनियम एमिनो एसिड ([सीएच][एए]) आधारित जैव-आईएल है जिसे हमने इस थीसिस में खोजा है। इन बायो-आईएल में कम विषाक्तता और उच्च बायोडिग्रेडेबिलिटी साबित हुई है, जिसके कारण इन्हें विभिन्न जैविक और औद्योगिक अनुप्रयोगों में उपयोग किया जाता है। हालाँकि, जैसा कि उन्होंने हाल ही में अधिक महत्व प्राप्त करना शुरू कर दिया है, उनकी सूक्ष्म संरचना और गतिशीलता पर प्रयोगात्मक या कम्प्यूटेशनल अध्ययन, और उन पर बाहरी कारकों का प्रभाव साहित्य में दुर्लभ है। यह उनके मौलिक गुणों की खराब समझ के कारण संबंधित अनुप्रयोगों में उनके कम उपयोग की ओर जाता है। इसने हमें पानी की सघनता बढ़ने का प्रभाव, तापमान और उन पर लागू विद्युत रासायनिक संभावित अंतर के प्रभाव की जांच के साथ-साथ संरचना और गतिशीलता की सूक्ष्म स्तर की समझ का पता लगाने के लिए प्रेरित किया है।

कोलिनियम ग्लाइसीनेट ([सीएच][ग्लाइ]) कम से कम चिपचिपा और उच्च चालकता जैव-आईएल में से एक है। इसके साथ ही, हम पहले आणविक स्तर की संरचनात्मक व्यवस्था और कोलीनियम ग्लाइसीनेट बायो-आईएल की गतिशीलता पर पानी की सघनता बढ़ने के प्रभाव की जांच करते हैं। यह कुल एक्स-रे स्कैटरिंग स्ट्रक्चर फ़ंक्शंस (एस(क्यू)), उनके आंशिक घटकों, रेडियल वितरण फ़ंक्शन (जी(आर)), दूरी-कोण वितरण फ़ंक्शन (जी(आर,θ)), और स्थानिक वितरण समारोह (एसडीएफ) जैसे संरचनात्मक सहसंबंध कार्यों की गणना और विश्लेषण के माध्यम से प्राप्त किया गया है। गतिकी का पता लगाने के लिए, हमने हाइड्रोजन बॉन्ड डायनामिक्स, माध्य वर्ग विस्थापन, स्व-प्रसार गुणांक, वेग ऑटोसहसंबंध फ़ंक्शन और जलीय मिश्रण की विद्युत चालकता का पता लगाया है। हमने अगले चरण में अपने अध्ययन का विस्तार यह पता लगाने के लिए किया कि कैसे लागू संभावित अंतर के साथ ग्रेफाइट इलेक्ट्रोड के पास कोलीनियम ग्लाइसीनेट की इंटरफेसियल सूक्ष्म संरचना और इलेक्ट्रोस्टैटिक्स गुण भिन्न होते हैं। इस अध्ययन में, हमने सिमुलेशन संख्या और चार्ज घनत्व प्रोफाइल, स्पर्शरेखा रेडियल वितरण फ़ंक्शन, ओरिएंटल ऑर्डर पैरामीटर और [सीएच][ग्लाइ] बायो-आईएल के अंतर समाई

का विश्लेषण किया है। इसके अलावा, कोलीनियम एमिनो एसिड आधारित बायो-आईएल की जांच विभिन्न एमिनो एसिड आयनों जैसे फेनिलएलनिनेट और सिस्टीनेट तक बढ़ा दी गई है। थीसिस के दूसरे भाग में, हमने वास्तविक और व्युत्क्रम अंतरिक्ष सहसंबंध, समरूपता सतह, और हाइड्रोजन बॉन्ड डायनामिक्स जैसे सहायक गतिशील गुणों की मदद से कोलीनियम फेनिलएलनिनेट ([सीएच][पीएचई]) और कोलीनियम सिस्टीनेट ([सीएच][सिस]) बायो-आईएल की सूक्ष्म संरचना की तापमान निर्भरता की जांच की है।

Permissions

Permissions have been taken for the following publications from the respective Journals.

List of Publications Related to Work Presented in this Thesis as on Thesis Submission Date

1. **Aditya Gupta**; Supreet Kaur; Hemant K. Kashyap. How Water Permutes the Structural Organization and Microscopic Dynamics of Cholinium Glycinate Biocompatible Ionic Liquid. *J. Phys. Chem. B* **2019**, *123*, 2057-2069.

2. **Aditya Gupta**; Hemant K. Kashyap. Nanoscale Heterogeneity, Hydrogen Bonding and their Temperature Dependence in Cholinium Phenylalaninate Bio-ionic Liquid. *J. Mol. Liq.* **2021**, *326*, 115329.

3. **Aditya Gupta**; Harender S. Dhattarwal; Hemant K. Kashyap. Structure of Cholinium Glycinate Biocompatible Ionic Liquid at Graphite Electrode Interface. *J. Chem. Phys.* **2021**, *154*, 184702.

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