

# Current Developments in Biotechnology and Bioengineering



## Deep Eutectic Solvents: Fundamentals and Emerging Applications

*Editors*

Ashish Pandey • Bhagyashree Tiwari  
Ashok Pandey • Suzana Yusup

CURRENT  
DEVELOPMENTS IN  
BIOTECHNOLOGY  
AND  
BIOENGINEERING

---

**Series Editor**

Ashok Pandey

Distinguished Scientist, Centre for Innovation and Translational Research, CSIR-Indian Institute of  
Toxicology Research, Lucknow, India

&

Distinguished Professor, Sustainability Cluster, School of Engineering, University of Petroleum and  
Energy Studies, Dehradun, India

# CURRENT DEVELOPMENTS IN BIOTECHNOLOGY AND BIOENGINEERING

## Deep Eutectic Solvents: Fundamentals and Emerging Applications

---

*Edited by*

**ASHISH PANDEY**

*Department of Chemistry, Indian Institute of Technology Delhi, New Delhi, India; Calagua Innovations Corp, Life Sciences Innovation Hub, Calgary, AB, Canada*

**BHAGYASHREE TIWARI**

*INRS - Eau, Terre et Environnement, rue de la Couronne, Québec, Canada*

**ASHOK PANDEY**

*Distinguished Scientist, Centre for Innovation and Translational Research, CSIR-Indian Institute of Toxicology Research, Lucknow, Uttar Pradesh, India; Distinguished Professor, Sustainability Cluster, School of Engineering, University of Petroleum and Energy Studies, Dehradun, India*

**SUZANA YUSUP**

*HiCoE, Center for Biofuels and Biochemical Research (CBBR), Institute of Self-Sustainable Building (ISB), Universiti Teknologi PETRONAS, Bandar Seri Iskandar, Perak, Malaysia; Department of Chemical Engineering, Universiti Teknologi PETRONAS, Bandar Seri Iskandar, Perak, Malaysia*



ELSEVIER

Elsevier

Radarweg 29, PO Box 211, 1000 AE Amsterdam, Netherlands  
The Boulevard, Langford Lane, Kidlington, Oxford OX5 1GB, United Kingdom  
50 Hampshire Street, 5th Floor, Cambridge, MA 02139, United States

Copyright © 2022 Elsevier Inc. All rights reserved.

No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording, or any information storage and retrieval system, without permission in writing from the publisher. Details on how to seek permission, further information about the Publisher's permissions policies and our arrangements with organizations such as the Copyright Clearance Center and the Copyright Licensing Agency, can be found at our website: [www.elsevier.com/permissions](http://www.elsevier.com/permissions).

This book and the individual contributions contained in it are protected under copyright by the Publisher (other than as may be noted herein).

### Notices

Knowledge and best practice in this field are constantly changing. As new research and experience broaden our understanding, changes in research methods, professional practices, or medical treatment may become necessary.

Practitioners and researchers must always rely on their own experience and knowledge in evaluating and using any information, methods, compounds, or experiments described herein. In using such information or methods they should be mindful of their own safety and the safety of others, including parties for whom they have a professional responsibility.

To the fullest extent of the law, neither the Publisher nor the authors, contributors, or editors, assume any liability for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein.

ISBN: 978-0-323-99905-2

For Information on all Elsevier publications visit our website at  
<https://www.elsevier.com/books-and-journals>

*Publisher:* Susan Dennis

*Editorial Project Manager:* Helena Beauchamp

*Production Project Manager:* Kumar Anbazhagan

*Cover Designer:* Miles Hitchen

Typeset by Aptara, New Delhi, India



# Contents

---

**Contributors** xi

**Preface** vi

## 1. Deep eutectic solvents—An introduction 1

Ashish Pandey, Bhagyashree Tiwari, Arun K Vuppaladadiyam,  
Sai Sree Varsha Vuppaladadiyam, Shao-Yuan Leu  
and Siddharth Pandey

- 1.1 Introduction 1
  - 1.1.1 Solvents—Definition and developments 2
- 1.2 Deep eutectic solvents 3
  - 1.2.1 Synthesis of deep eutectic solvents 4
- 1.3 Physicochemical properties of DESs 5
  - 1.3.1 Phase behavior 6
  - 1.3.2 Freezing point 7
  - 1.3.3 Density 8
  - 1.3.4 Viscosity 9
  - 1.3.5 Surface tension 10
  - 1.3.6 Ionic conductivity 11
- 1.4 Applications of DESs 11
  - 1.4.1 Electrochemical applications 11
  - 1.4.2 Organic synthesis 13
  - 1.4.3 Genomics 13
  - 1.4.4 Gas capture 14
- 1.5 Challenges in development and applications of DESs 14
- 1.6 Conclusions and perspectives 15
- References 15

## 2. Design strategies for the synthesis of deep eutectic solvents 21

Mariam Ameen, Mustakimah Mohamed, Marhaini Mostapha,  
Hafiza Palwasha Zafar, Farooq Sher and Suzana Yusup

- 2.1 Introduction 21
  - 2.1.1 Classification of deep eutectic solvents based on types of mixture 22
- 2.2 Deep eutectic solvents solubility in water 26
  - 2.2.1 Hydrophilic deep eutectic solvents 26

- 2.2.2 Hydrophobic deep eutectic solvents 29
- 2.2.3 Natural deep eutectic solvents 32
- 2.3 Technologies for the synthesis of deep eutectic solvents 33
  - 2.3.1 Conventional techniques 34
  - 2.3.2 Mechanochemical synthesis 34
  - 2.3.3 Microwave-assisted synthesis 35
  - 2.3.4 Ultrasound-assisted technique 39
  - 2.3.5 Electrochemical techniques 42
- 2.4 Conclusions and perspectives 43
- Acknowledgment 43
- References 43

## 3. Applications of deep eutectic solvents in gas capture 49

Akshay Malik, Harender S. Dhattarwal and Hemant K. Kashyap

- 3.1 Introduction 49
- 3.2 Computational studies on gas capture by deep eutectic solvents 53
  - 3.2.1 Mechanism of gas capture 54
  - 3.2.2 Solvation structures of gases in deep eutectic solvents 63
- 3.3 Conclusions and perspectives 67
- Acknowledgments 68
- References 68

## 4. Critical analysis of green solvent credentials of eutectic solvents 77

Esther Jaekel, Kailey Sun Marcus and Svitlana Filonenko

- 4.1 Introduction 77
- 4.2 Defining green credentials 78
  - 4.2.1 Atom economy and environmental factor 79
  - 4.2.2 Life-cycle assessment 80
  - 4.2.3 Environment, health, and safety 80
  - 4.2.4 Persistence and spatial range 81
  - 4.2.5 Planetary boundaries in application to deep eutectic solvents 81

- 4.2.6 Efficiency—Technical and economic factors 82
- 4.3 Deep eutectic solvents in terms of inherent greenness 82
- 4.3.1 Components of deep eutectic solvents 84
- 4.3.2 Toxicity of deep eutectic solvents 85
- 4.3.3 Greenness of deep eutectic solvents preparation 86
- 4.3.4 Reactivity of deep eutectic solvents 87
- 4.4 Physical properties of deep eutectic solvents 87
- 4.4.1 Macroscopic physical properties 88
- 4.4.2 Polarity and polarizability 88
- 4.5 Potential and reality of deep eutectic solvents applications 91
- 4.5.1 Extractions and separations 92
- 4.5.2 Organic reactions 94
- 4.5.3 Polymerization in deep eutectic solvent 95
- 4.5.4 Templating with deep eutectic solvents 95
- 4.5.5 Electrochemistry in eutectic media 96
- 4.6 Three components eutectic mixtures containing water 97
- 4.7 Conclusions and perspectives 98
- Acknowledgments 98
- References 98
5. Deep eutectic solvents vs. ionic liquids: Similarities and differences 105
- Filipe H.B. Sosa, João A.P. Coutinho and André M. da Costa Lopes
- 5.1 Introduction 105
- 5.2 Ionic liquids vs. deep eutectic solvents 107
- 5.2.1 Definition 107
- 5.2.2 Classification 109
- 5.3 Physicochemical properties: ILs vs. DES 112
- 5.3.1 Density and excess volume 112
- 5.3.2 Viscosity 113
- 5.3.3 Solvatochromic parameters 116
- 5.3.4 Toxicity 117
- 5.3.5 Biodegradability 119
- 5.4 A case study: Lignocellulosic biomass valorization 121
- 5.4.1 Cellulose dissolution 122
- 5.4.2 Lignin dissolution 123
- 5.4.3 Biomass fractionation 124
- 5.5 Solvent recycling 126
- 5.6 Conclusions and perspectives 129
- Acknowledgments 130
- References 131
6. Role of deep eutectic solvents as pretreatment media for biomass transformation 139
- Chung Loong Yiin, Kok Liang Yap, Dayang Salyani Abang Mahmud, Bridgid Lai Fui Chin, Serene Sow Mun Lock, Yi Heng Chan, Kin Wai Cheah, Martin J. Taylor and Georgios Kyriakou
- 6.1 Introduction 139
- 6.2 Current status of biomass pretreatment 140
- 6.3 Deep eutectic solvents and their biopolymers solubility 142
- 6.3.1 Definition and classification of DESs 142
- 6.3.2 Biopolymers solubility 143
- 6.4 Biomass pretreatment and transformation using DESs 145
- 6.4.1 Role of DESs as pretreatment media 145
- 6.4.2 Biomass transformation 150
- 6.5 Current constraints 155
- 6.6 Conclusions and perspectives 156
- Acknowledgments 157
- References 157
7. Deep eutectic solvents as efficient media for designing biocatalytic processes 161
- Ying Ki Ng, Win Yee Lim, Vannajan Sanghiran Lee, Kiat Moon Lee, Chen Wai Wong and Eric W.C. Chan
- 7.1 Introduction 161
- 7.2 Evolution of deep eutectic solvents as biocatalytic solvents 162
- 7.3 Types of deep eutectic solvents 162
- 7.3.1 Natural deep eutectic solvents (Type III and Type V) 164
- 7.4 Deep eutectic solvents compatible biocatalysts 165
- 7.4.1 Whole cells 167
- 7.4.2 Oxidoreductases 167
- 7.4.3 Hydrolases 167
- 7.4.4 Other enzymes 168
- 7.5 Process optimization using computational modeling 168
- 7.5.1 Ab initio molecular studies 169
- 7.5.2 Molecular mechanics calculations 170
- 7.5.3 Simulation techniques 170
- 7.5.4 Enhancement of biocatalytic performance 171
- 7.6 Commercially relevant biocatalytic processes involving DES 171

7.6.1 Cellulosic biofuels	171
7.6.2 Lipid-base biofuels	174
7.6.3 Pulp and paper	174
7.6.4 Biotransformation	175
7.6.5 Natural product extraction	175
7.7 Conclusions and perspectives	176
References	177
8. Role of deep eutectic solvents in membrane-based separation processes	181
Irshad Kammakakam and Zhiping Lai	
8.1 Introduction	181
8.2 Deep eutectic solvents assisted or containing membranes	187
8.2.1 Selection of deep eutectic solvents in membrane matrix	187
8.2.2 Methods of DES-based membrane fabrication and basic characterizations	189
8.3 Toward applications of deep eutectic solvents-based membranes	192
8.3.1 DES-membranes in gas separation applications	192
8.3.2 DES-membranes in pervaporation applications	195
8.3.3 DES-membranes in water filtration applications	197
8.3.4 DES-membranes as polymer electrolytes	198
8.4 Conclusions and perspectives	199
References	200
9. Liquid-liquid equilibria and alcohol valorization in aqueous alcoholic systems using hydrophobic eutectic solvents	205
Rupesh Verma, Anand Bharti, Papu Kumar Naik and Tamal Banerjee	
ASPEN Licenses	00
9.1 Introduction	205
9.2 Liquid-liquid equilibria with lower alcohols	206
9.3 Process design and techno-economic assessment for the recovery of 1-butanol from aqueous solution	209
9.4 Conclusions and perspectives	218
References	220

## 10. Applications of deep eutectic solvents in remediation of emerging contaminants 223

Emmanuel A. Oke, Renu Sharma, Naved I. Malek and Sushma P. Ijardar

10.1 Introduction	223
10.2 Applications of deep eutectic solvents in the remediation of pollutants	224
10.2.1 Dyes removal	224
10.2.2 Bisphenols removal	230
10.2.3 Plasticizers removal	231
10.2.4 Application of DESs in the removal of pesticides	232
10.2.5 Application of DES in the removal of metal ions from water	239
10.2.6 Miscellaneous applications	240
10.3 Challenges and opportunities	241
10.4 Conclusions and perspectives	241
Acknowledgments	242
References	242

## 11. Cross-coupling reactions in deep eutectic solvents 247

Nerea González-Gallardo, Seyyed Emad Hooshmand, Ronak Afshari and Diego J. Ramón

11.1 Introduction	247
11.2 Carbon-carbon cross-coupling reactions	252
11.2.1 Cross-coupling reactions in DESs: The historical background	252
11.2.2 Ligand-free cross-coupling reactions in DESs	254
11.2.3 Carbon-carbon cross-coupling reactions performed in DES using ligands	257
11.3 Carbon-nitrogen cross-coupling reactions	264
11.3.1 Heterogeneous catalyst for Ullmann reactions	264
11.3.2 Homogeneous catalyst for Ullmann reaction	267
11.3.3 Ullmann reaction without external catalyst	267
11.3.4 Buchwald–Hartwig type C–N coupling reaction	268



- 11.3.5 Goldberg-type C–N coupling reaction 269
- 11.4 Carbon-oxygen cross-coupling reactions 270
- 11.5 Carbon-sulfur cross-coupling reactions 270
- 11.6 Conclusions and perspectives 275
- Acknowledgments 276
- References 276

## 12. Deep eutectic solvents (DESs) as efficient systems for drug discovery, drug delivery, and pharmaceutical applications 283

Gagandeep Singh, Meena Bisht, Eden E.L. Tanner,  
Tejwant Singh Kang, Dibyendu Mondal and Siddharth Pandey

- 12.1 Introduction 283
- 12.2 Preparation of DESs 285
- 12.3 DESs for drug applications 286
  - 12.3.1 DESs possessing drug-like properties 286
  - 12.3.2 DESs for drug solubilization 297
  - 12.3.3 Therapeutic deep eutectic solvents for improving drug bioavailability 304
  - 12.3.4 DESs-based drug delivery 308
- 12.4 Toxicological profile of DESs 310
- 12.5 Conclusions and perspectives 312
- References 313

## 13. Role of deep eutectic solvents (DESs) in CO<sub>2</sub> mitigation technologies 319

Bhawna Bhawna

- 13.1 Introduction 319
- 13.2 Deep eutectic solvents-based techniques for CO<sub>2</sub> capture 322
  - 13.2.1 Ammonium/phosphonium-functionalized deep eutectic solvents 323
  - 13.2.2 Imidazolium-derived deep eutectic solvents 328
  - 13.2.3 Amine based-deep eutectic solvents 329
  - 13.2.4 Azolide-based deep eutectic solvents 332
  - 13.2.5 Superbase-added deep eutectic solvents 333
  - 13.2.6 Hydrophobic deep eutectic solvents 337
  - 13.2.7 Miscellaneous methods 338
- 13.3 Conclusions and perspectives 340
- References 341

## 14. Deep eutectic solvents in desulfurization of fuel oil 345

Wan Nur Aini Wan Mokhtar,  
Norshahidatul Akmar Mohd Shohaimi, Susilawati Toemen,  
Wan Nazwanie Wan Abdullah, Salmiah Jamal Mat Rosid,  
Nor Hakimin Abdullah and Sarina Mat Rosid

- 14.1 Introduction 345
- 14.2 Deep eutectic solvents in desulfurization 346
- 14.3 DES in extractive desulfurization 347
- 14.4 DES in oxidative desulfurization 351
  - 14.4.1 Extractive oxidative desulfurization (EODS) 352
  - 14.4.2 Extractive catalytic oxidative desulfurization (ECODS) 352
  - 14.4.3 Aerobic oxidative desulfurization (AODS) 353
  - 14.4.4 DES in adsorptive desulfurization (ADS) 356
- 14.5 Response surface methodology of DES—Desulfurization system 359
- 14.6 Regeneration of DESs in desulfurization 360
- 14.7 Mechanisms of DES—Desulfurization process 362
- 14.8 Molecular modeling 364
- 14.9 Conclusions and perspectives 366
- References 367

## 15. Regulatory aspects of deep eutectic solvents technology and applications 373

Elisabeth Rianawati, Nadiya Pranindita, Hanafi Kusumayudha,  
Tifany Khalisa Rinaldy and Shellyn Fortuna

- 15.1 Introduction 373
  - 15.1.1 Current development of deep eutectic solvents 375
- 15.2 Regulations of deep eutectic solvents applications 376
  - 15.2.1 Regulation of solvents 376
  - 15.2.2 Regulation of deep eutectic solvents 378
- 15.3 Problems of deep eutectic solvents as sustainable solvents 379
  - 15.3.1 Unavailability of deep eutectic solvents on wider market 379
  - 15.3.2 Drawbacks of deep eutectic solvents application in various sectors 387
  - 15.3.3 Post-usage risks of deep eutectic solvents 393

15.4 Recommendation: Regulatory aspects of deep eutectic solvents application	393	16. Impact of deep eutectic solvents to health, safety, and environment	407
15.4.1 Recognition of compounds as solvent	394	Mimi Haryani Hassim, Syaza Izyanni Ahmad and Saffri Sa'dan	
15.4.2 Deep eutectic solvents regulatory body	394	16.1 Introduction	407
15.4.3 Socialization on deep eutectic solvents and implementing incentives and disincentives strategy	395	16.2 Toxicity of deep eutectic solvents	408
15.4.4 Mandatory guideline for compound selection and processing	395	16.3 Safety impact of deep eutectic solvents	412
15.4.5 Regular report of technical properties assessments	396	16.4 Biodegradability of deep eutectic solvents	413
15.4.6 Standard limit usage and residue	396	16.5 Inherent safety assessment of DESs	414
15.4.7 Health and safety risk measures	397	16.6 Way forward of evaluating safety, health, and environmental impacts of deep eutectic solvents	417
15.5 Conclusions and perspectives	398	16.7 Conclusions and perspectives	419
References	399	References	419
		<b>Index</b>	<b>423</b>



# Contributors

---

- Nor Hakim Abdullah** Advanced Materials Research Cluster (AMRC), Faculty of Bioengineering and Technology, Universiti Malaysia Kelantan (UMK), Jeli, Kelantan, Malaysia
- Wan Nazwanie Wan Abdullah** School of Chemical Sciences, Universiti Sains Malaysia, USM Penang, Malaysia
- Ronak Afshari** Department of Physics, Sharif University of Technology, Tehran, Iran
- Syaza Izyanni Ahmad** Department of Chemical Engineering, Universiti Teknologi, Seri Iskandar, Perak, Malaysia
- Mariam Ameen** HiCoE, Center for Biofuels and Biochemical Research (CBBR), Institute of Self-Sustainable Building (ISB), Universiti Teknologi PETRONAS, Bandar Seri Iskandar, Perak, Malaysia
- Tamal Banerjee** Department of Chemical Engineering, Indian Institute of Technology Guwahati, Guwahati, Assam, India
- Anand Bharti** Department of Chemical Engineering, Birla Institute of Technology Mesra, Ranchi, Jharkhand, India
- Bhawna Bhawna** Chemical and Biological Engineering Department, University of Alabama, Tuscaloosa, United States
- Meena Bisht** Department of Chemistry, Indian Institute of Technology Delhi, New Delhi, India
- Eric W.C. Chan** Department of Food Science and Nutrition, Faculty of Applied Sciences, UCSI University, Kuala Lumpur, Malaysia; APEC Sustainable Coastal Cities Research Consortium, UCSI University, Kuala Lumpur, Malaysia
- Yi Herng Chan** PETRONAS Research Sdn. Bhd. (PRSB), Lot 3288 & 3289, Off Jalan Ayer Itam, Kawasan Institusi Bangi, Kajang, Selangor, Malaysia
- Kin Wai Cheah** School of Computing, Engineering and Digital Technologies, Teesside University, Borough Road, Middlesbrough, United Kingdom
- Bridgid Lai Fui Chin** Chemical and Petroleum Engineering Department, Faculty of Engineering and Science, Curtin University Malaysia, Miri, Sarawak Malaysia
- João A.P. Coutinho** CICECO – Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, Aveiro, Portugal
- Harender S. Dhatarwal** Department of Chemistry, Indian Institute of Technology Delhi, New Delhi, India
- Svitlana Filonenko** Department of Colloid Chemistry, Max Planck Institute of Colloids and Interfaces, Potsdam, Germany
- Shellyn Fortuna** Resilience Development Initiative, Bandung, Indonesia
- Nerea González-Gallardo** Department of Organic Chemistry and Institute of Organic Synthesis (ISO), Faculty of Sciences, University of Alicante, Alicante, Spain
- Mimi Haryani Hassim** Centre of Hydrogen Energy (CHE), Universiti Teknologi Malaysia, Johor Bahru, Johor, Malaysia
- Seyyed Emad Hooshmand** Department of Medical Nanotechnology, Faculty of Advanced Technologies in Medicine, Iran University of Medical Sciences, Tehran, Iran
- Sushma P. Ijardar** Department of Chemistry, Veer Narmad South Gujarat University, Surat, India
- Esther Jaekel** Department of Colloid Chemistry, Max Planck Institute of Colloids and Interfaces, Potsdam, Germany

- Irshad Kammakakam** Division of Physical Science and Engineering, King Abdullah University of Science and Technology, Thuwal 23955-6900, Saudi Arabia
- Tejwant Singh Kang** Department of Chemistry, UGC-Centre for Advance Studies – II, Guru Nanak Dev University, Amritsar, India
- Hemant K. Kashyap** Department of Chemistry, Indian Institute of Technology Delhi, New Delhi, India
- Hanafi Kusumayudha** Resilience Development Initiative, Bandung, Indonesia
- Georgios Kyriakou** Department of Chemical Engineering, University of Patras, Patras, Greece
- Zhiping Lai** Division of Physical Science and Engineering, King Abdullah University of Science and Technology, Thuwal 23955-6900, Saudi Arabia
- Kiat Moon Lee** Department of Chemical & Petroleum Engineering, UCSI University, Kuala Lumpur, Malaysia
- Vannajan Sanghiran Lee** Department of Chemistry, Faculty of Science, University Malaya, Kuala Lumpur, Malaysia
- Shao-Yuan Leu** Department of Civil & Environmental Engineering, The Hong Kong Polytechnic University, Kowloon, Hong Kong SAR, China
- Win Yee Lim** Department of Biotechnology, Faculty of Applied Sciences, UCSI University, Kuala Lumpur, Malaysia
- Serene Sow Mun Lock** CO<sub>2</sub> Research Center (CO<sub>2</sub>RES), Department of Chemical Engineering, Universiti Teknologi PETRONAS, Seri Iskandar, Malaysia
- André M. da Costa Lopes** CICECO – Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, Aveiro, Portugal; CECO-LAB – Collaborative Laboratory Towards Circular Economy, R. Nossa Senhora da Conceição, Portugal
- Dayang Salyani Abang Mahmud** Department of Chemical Engineering and Energy Sustainability, Faculty of Engineering, Universiti Malaysia Sarawak (UNIMAS), Kota Samarahan, Sarawak, Malaysia
- Naved I. Malek** Ionic Liquids Research Laboratory, Department of Chemistry, Sardar Vallabhbhai National Institute of Technology, Surat, India
- Akshay Malik** Department of Chemistry, Indian Institute of Technology Delhi, New Delhi, India
- Kailey Sun Marcus** Department of Colloid Chemistry, Max Planck Institute of Colloids and Interfaces, Potsdam, Germany; Freie Universität Berlin, Institute of Chemistry and Biochemistry, Berlin, Germany
- Mustakimah Mohamed** HiCoE, Center for Biofuels and Biochemical Research (CBBR), Institute of Self-Sustainable Building (ISB), Universiti Teknologi PETRONAS, Bandar Seri Iskandar, Perak, Malaysia
- Wan Nur Aini Wan Mokhtar** Department of Chemical Sciences, Faculty of Science and Technology, Universiti Kebangsaan Malaysia, Bangi, Selangor, Malaysia
- Dibyendu Mondal** Centre for Nano and Material Science, Jain University, Bengaluru, India
- Marhaini Mostapha** HiCoE, Center for Biofuels and Biochemical Research (CBBR), Institute of Self-Sustainable Building (ISB), Universiti Teknologi PETRONAS, Bandar Seri Iskandar, Perak, Malaysia
- Papu Kumar Naik** Department of Chemical Engineering, Indian Institute of Technology Guwahati, Guwahati, Assam, India
- Ying Ki Ng** Department of Food Science and Nutrition, Faculty of Applied Sciences, UCSI University, Kuala Lumpur, Malaysia
- Emmanuel A. Oke** Department of Chemistry, Veer Narmad South Gujarat University, Surat, India
- Ashish Pandey** Department of Chemistry, Indian Institute of Technology Delhi, New Delhi, India; Calagua Innovations Corp, Life Sciences Innovation Hub, Calgary, AB, Canada
- Siddharth Pandey** Department of Chemistry, Indian Institute of Technology Delhi, New Delhi, India
- Nadiya Pranindita** Resilience Development Initiative, Bandung, Indonesia

- Diego J. Ramón** Department of Organic Chemistry and Institute of Organic Synthesis (ISO), Faculty of Sciences, University of Alicante, Alicante, Spain
- Elisabeth Rianawati** Resilience Development Initiative, Bandung, Indonesia
- Tifany Khalisa Rinaldy** Resilience Development Initiative, Bandung, Indonesia
- Salmiah Jamal Mat Rosid** Unisza Science and Medicine Foundation Centre, Universiti Sultan Zainal Abidin, Kuala Nerus, Terengganu, Malaysia
- Sarina Mat Rosid** Advanced Membrane Technology Research Centre (AMTEC), School of Chemical and Energy Engineering, Universiti Teknologi Malaysia, Johor Bahru, Johor, Malaysia
- Saffri Sa'dan** Department of Chemical Engineering, Universiti Teknologi, Seri Iskandar, Perak, Malaysia
- Renu Sharma** Department of Chemistry, Veer Narmad South Gujarat University, Surat, India
- Farooq Sher** Department of Engineering, School of Science and Technology, Nottingham Trent University, Nottingham, UK
- Norshahidatul Akmar Mohd Shohaimi** Faculty of Applied Sciences, UiTM Pahang, Jengka, Malaysia
- Gagandeep Singh** Department of Chemistry and Biochemistry, The University of Mississippi, MS, USA; Department of Chemistry, Indian Institute of Technology Delhi, New Delhi, India
- Filipe H.B. Sosa** CICECO – Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, Aveiro, Portugal
- Eden E.L. Tanner** Department of Chemistry and Biochemistry, The University of Mississippi, MS, USA
- Martin J. Taylor** School of Computing, Engineering and Digital Technologies, Teesside University, Borough Road, Middlesbrough, United Kingdom
- Bhagyashree Tiwari** INRS - Eau, Terre et Environnement, rue de la Couronne, Québec, Canada
- Susilawati Toemen** Department of Chemistry, Faculty of Science, Universiti Teknologi Malaysia, Skudai, Johor Bahru, Malaysia
- Rupesh Verma** Department of Chemical Engineering, Indian Institute of Technology Guwahati, Guwahati, Assam, India
- Arun K Vuppaladadiyam** Department of Civil & Environmental Engineering, The Hong Kong Polytechnic University, Kowloon, Hong Kong SAR, China
- Sai Sree Varsha Vuppaladadiyam** Department of Civil & Environmental Engineering, The Hong Kong Polytechnic University, Kowloon, Hong Kong SAR, China
- Chen Wai Wong** Department of Biotechnology, Faculty of Applied Sciences, UCSI University, Kuala Lumpur, Malaysia
- Kok Liang Yap** Department of Chemical Engineering and Energy Sustainability, Faculty of Engineering, Universiti Malaysia Sarawak (UNIMAS), Kota Samarahan, Sarawak, Malaysia
- Chung Loong Yiin** Department of Chemical Engineering and Energy Sustainability, Faculty of Engineering, Universiti Malaysia Sarawak (UNIMAS), Kota Samarahan, Sarawak, Malaysia
- Suzana Yusup** HiCoE, Center for Biofuels and Biochemical Research (CBBR), Institute of Self-Sustainable Building (ISB), Universiti Teknologi PETRONAS, Bandar Seri Iskandar, Perak, Malaysia; Department of Chemical Engineering, Universiti Teknologi PETRONAS, Bandar Seri Iskandar, Perak, Malaysia
- Hafiza Palwasha Zafar** Department of Chemistry, University of Agriculture, Faisalabad, Pakistan; International Society of Engineering Science and Technology, Coventry, UK



# Preface

---

The book titled *“Deep Eutectic Solvents – Fundamentals and Emerging Applications”* is a part of the Elsevier comprehensive book series on *Current Developments in Biotechnology and Bioengineering* (Editor-in-Chief: Ashok Pandey). Increasing sensitivity towards the health, safety, and environment has spurred increasing the research in alternative solvents that are both human and environmentally-friendly. Green solvents include biosolvents derived from the agriculture crops. Replacement to petrochemical-derived solvents that find large industrial applications is significant and at the same time, has economic viability. Deep eutectic solvents (DESs) are gaining popularity and are being increasingly used in the catalytic, separation, and electrochemical processes. Combination of Lewis or Bronsted acid and bases is the key characteristic of DESs. The bio-based DESs, known as NADESs, consist of plant-based primary metabolites such as organic acids, sugars, alcohols, amine, and amino acids. DESs are cheaper, biodegradable, and safe direct synthesis route. Owing to their potential and unique property, wholistic value-driven research is significant in promoting wider application of DESs industrially.

This book covers various topics on DESs from the fundamental studies to the emerging applications. The first chapter gives a brief introduction of DESs, followed by the design strategies to synthesize DESs, and progressing to the determination of physicochemical properties of DESs through experimental approach. Applications of DESs for gas capturing is highlighted in subsequent chapters. Owing to the importance of green

solvents and correlation with DESs, the important characteristics of DESs are highlighted. The comparison and similarities between DESs and ionic liquids are covered for better insights of the features of both the solvents. Increasing applications of biomass towards waste reduction have further expanded the applications of DESs as pretreatment media for biomass transformation. The other sectors where the applications of DESs are gaining attraction include the biocatalytic processes and in membrane-based separation which have been discussed in subsequent chapters. Predictions of the influence of DESs in the extraction processes allow further understanding of DESs through the modeling and simulation. How DESs behave in reducing the contaminants is further elaborated gearing towards environmental awareness. The role of DESs has extended in cross-coupling reactions as neoteric reaction media. DESs have applications in drug discovery and delivery as well as in pharmaceutical applications, thus widening the potential applications in health sectors. Impact of CO<sub>2</sub> and sulfur to the environment can be further reduced through the applications of DESs. Nevertheless, regulatory and impact of DESs on health, safety, and environment are among the other topics that are pertinent for larger applications and industrial deployment of DESs, which have aptly covered in the book.

The book would be of great value to the postgraduate students, researchers, scientists, practitioners, and others interested in the field of greener and biodegradable solvents. The book serves to increase the



awareness on the significant of green and biodegradable solvents and aims to increase the knowledge with state-of-art information on the fundamentals, applications, regulatory, and safety aspects of DESs.

We immensely appreciate and acknowledge the tremendous work done by the authors in compiling the pertinent information required for chapter writing, which we believe will be a valuable source for both the scientific community and general audience. We are thankful to the reviewers for providing their useful comments, which significantly helped in refining the quality of the contents in the chapters and shaping the chapter

organization, improving the scientific discussions, and overall quality of the chapters. We sincerely thank the Elsevier team comprising Dr Kostas Marinakis, Former Senior Book Acquisition Editor, Dr Katie Hammon, Senior Book Acquisition Editor, Bernadine A Miralles, Editorial Project Manager, and the entire Elsevier production team for their consistent hard work and support in publishing this book.

*Editors*

*Ashish Pandey  
Bhagyashree Tiwari  
Ashok Pandey  
Suzana Yusup*

# Role of deep eutectic solvents as pretreatment medium for biomass transformation

Chung Loong Yiin<sup>a</sup>, Kok Liang Yap<sup>a</sup>,  
Dayang Salyani Abang Mahmud<sup>a</sup>,  
Bridgid Lai Fui Chin<sup>b</sup>, Serene Sow Mun Lock<sup>c</sup>,  
Yi Heng Chan<sup>d</sup>, Kin Wai Cheah<sup>e</sup>, Martin J. Taylor<sup>f</sup>  
and Georgios Kyriakou<sup>g</sup>

<sup>a</sup>Department of Chemical Engineering and Energy Sustainability, Faculty of Engineering, Universiti Malaysia Sarawak (UNIMAS), Kota Samarahan, Sarawak, Malaysia <sup>b</sup>Chemical and Petroleum Engineering Department, Faculty of Engineering and Science, Curtin University Malaysia, Miri, Sarawak Malaysia <sup>c</sup>CO<sub>2</sub> Research Center (CO<sub>2</sub>RES), Department of Chemical Engineering, Universiti Teknologi PETRONAS, Seri Iskandar, Malaysia <sup>d</sup>PETRONAS Research Sdn. Bhd. (PRSB), Lot 3288 & 3289, Off Jalan Ayer Itam, Kawasan Institusi Bangi, Kajang, Selangor, Malaysia <sup>e</sup>School of Computing, Engineering and Digital Technologies, Teesside University, Borough Road, Middlesbrough, United Kingdom <sup>f</sup>School of Computing, Engineering and Digital Technologies, Teesside University, Borough Road, Middlesbrough, United Kingdom <sup>g</sup>Department of Chemical Engineering, University of Patras, Patras, Greece

## 6.1 Introduction

Traditionally, biomass utilization was realized through the concept of biorefineries and the purpose of using biomass was mostly energy-driven. Over the years, the concept of biomass valorization shifted its focus toward unleashing the maximum potential of biomass in downstream processing such as for the production of various energy carriers and value-added

bioproducts or chemicals. The main stepping stone toward realizing biomass transformation can be attributed to the ubiquitous nature of biomass, from which most of the biopolymers exhibited high recalcitrance in common solvents due to the heterogeneous polyphenolic structure of the lignin and the highly ordered cellulose's crystalline structure. The recalcitrance of biomass poses constraints in the biomass-to-biofuels conversion or other value-added bioproducts which typically involves three major steps: pretreatment, hydrolysis, and fermentation (Binod & Pandey, 2015). The pretreatment of biomass can be regarded as the most important step in biomass processing. In this sense, the goal of biomass pretreatment is to disintegrate the lignin barrier and make the celluloses, hemicelluloses, and other substrates accessible, as well as to enable the further processing and recovery of the valuable components embedded within the biomass.

Pretreatment methods such as physical, chemical, biological, physicochemical, biochemical, and green solvents have been studied including some commercialized methods while others are still in development or struggling to be scaled up. Conventional pretreatment methods include physical and chemical pretreatment which were considered as effective and matured technologies. Although the efficiency of these conventional pretreatment approaches is high enough for the successful transformation of biomass resources, the extensive usage of caustic and volatile chemicals or the high energy requirement of these conventional pretreatment methods are considered drawbacks. More attention should be devoted to environmental sustainability as the world realized the irreversible environmental impact due to human activities and began emphasizing green chemistry. Apart from that, the choice of pretreatment technology is of utter importance since it has a direct impact on the operating costs related to feedstock (i.e., chemicals, solvents, catalysts, etc.), utility consumption (i.e., steam, electricity, etc.), labor charges, and effluent treatment which often make up 60% of the total production costs (Cheng et al., 2019). Recently, deep eutectic solvents (DESs) emerged as an ideal low-cost, environmentally friendly, and prospective biomass pretreatment media since they first demonstrated biomass solubilizing capability in a novel study (Francisco et al., 2012).

## 6.2 Current status of biomass pretreatment

The pretreatment of biomass represents a crucial significance in biomass processing where it is the first and also the key step toward the accessibility of the substrates trapped within the recalcitrant shield of the lignin-carbohydrate complex of biomass. At the moment, there are five mainstream biomass pretreatment approaches which include physical, chemical, biological, combinatorial pretreatment (i.e., physicochemical, biochemical, etc.), and green solvents pretreatment. The conventional pretreatment approaches, inter alia, most typically include physical and chemical pretreatment methods that were already widely commercialized and applied in the industries while more recent techniques such as the use of green solvents as biomass pretreatment media are on an uprising interest and are currently still in development.

Physical pretreatment is an approach to reduce and minimize particle size. It is essential for biomass to undergo size reduction through mechanical or manual processing to achieve increased surface area, a reduced degree of polymerization, and a reduction in crystallinity for further processing to be carried out smoothly and effectively. Physical pretreatment can be

further categorized into various processes such as microwave irradiation, milling, extrusion, and ultrasonication. These physical pretreatment methods can be regarded as environmentally friendly as they are unlikely to produce toxic or pollutants that harm the environment. However, most physical pretreatment methods require large capital investment and intensive consumption of energy in the form of machinery operation.

Chemical pretreatment involves of organic or inorganic compounds with capability of lignin dissolution through chemical interactions that modify the interpolymer bonds of lignin, cellulose, and hemicellulose which further break down biomass's recalcitrant structure. It consists of organosolv pretreatment, ozonolysis, alkaline pretreatment, and acid pretreatment. For instance, acidic pretreatment is one of the most matured and long-established technologies among various biomass pretreatment methodologies. However, the apparent disadvantages when it comes to using chemical pretreatment would never escape from the concerns over their caustic nature and causing corrosion to the processing equipment. Apart from that, the formation of inhibitors during the pretreatment process will impede the immediate commercialization of the resulting products due to the added cost needed to remove these inhibitors. Generally, chemical pretreatment can be considered as an effective pretreatment procedure but the high chemical usage and operating costs make it a rather expensive process apart from the fact that secondary pollution problems might follow.

Biological pretreatment of biomass is commonly associated with the enzymatic actions of microorganisms that are able to disintegrate the lignocellulosic materials. Fungi with a capability of enzyme production that aids in lignin degradation are often employed for biological biomass pretreatment. For instance, soft-rot, brown fungi and white-rot are recognized for the removal of hemicellulose and lignin while keeping the cellulose content intact (Nauman Aftab et al., 2019). The biological pretreatment method offers several advantages over other pretreatment methods including little or no generation of toxic substances, high yield of desired products, and low energy demand. However, the main drawbacks of the biological pretreatment method are attributed to the extremely long residence time of 10–14 days with stringent requirements on the conditions of fungal growth with a large space for conducting biological pretreatments, making this method of pretreatment being regarded as too slow and less attractive for the industry (Agbor et al., 2011). Additionally, the fact that a fraction of the embedded carbohydrate in the biomass could be consumed by the microbes also makes this method less viable. Although biological pretreatments could take weeks to complete, it was reported to be a very selective and efficient approach (Agbor et al., 2011; Anukam et al., 2020).

Combinations of one or more pretreatment methods such as combining chemical treatments with temperature or pressure or a biological step are often explored with the target of enhancing the fractionation of the biomass feedstocks. In this sense, physicochemical pretreatment is a hybrid technique that affects both the physical parameters and the chemical structures through bond cleavage and intermolecular interactions. Some instances of physicochemical pretreatment include supercritical carbon dioxide (CO<sub>2</sub>) and ammonia fiber explosion, steam explosion as well as liquid hot water. On the other hand, biochemical pretreatment method is less commonly reported but typically involves bio-organosolv pretreatment. However, the implementation of various pretreatment approaches comes with an extra cost on the feedstocks, utilities, and operating expenses, often even higher than any of the pretreatment methods alone. In terms of environmental impacts, methods such as supercritical CO<sub>2</sub> and

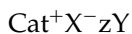
liquid hot water pretreatment are generally environmentally benign but other approaches that combine with caustic chemicals could often be a problem.

The conventional biomass pretreatment technologies either require substantial capital investment and high utility utilization or depend heavily on nonenvironmentally friendly solvents with their characteristics of highly carcinogenic, corrosive, volatile, nonbiodegradable, etc. The growing focus on green solvents development for biomass transformation aims to formulate green solvents that satisfy both the economic viability and environmental sustainability without compromising on the green solvents' performance in biomass pretreatment. Green solvents consist of those that are low-cost, biodegradable, nonvolatile, nontoxic and preferably sourced from readily available materials or through natural means. Several green solvents were exploited for pretreatment of biomass which includes ionic liquids (ILs) and DESs. ILs exhibited high solvating ability in biomass pretreatment proven through active studies since a few decades back. However, the key obstacles that held back the extensive application of ILs in industry are mainly associated with economic constraints and environmental imperatives. Their complex synthesis and purification process, controversial ecotoxicological data, and nonbiodegradability often raise questions on their qualifications as green solvents. On the other hand, new and emerging DESs are considered green solvents that are analogous to ILs but in addition, offer many advantages such as simple and straightforward synthesis without any aids of external solvents and subsequent purification, low cost, biodegradable, nontoxic, and highly tunable. Active studies revealed the capability of certain DESs to solubilize high amounts of lignin from biomass with minimal or no effects on the cellulose and hemicellulose. Therefore, DESs could take a significance role in performing selective solubilization or lignin removal from biomass time keeping the complete cellulose and hemicellulose contents for further processing with minimum deprivation of sugars.

### 6.3 Deep eutectic solvents and their biopolymers solubility

#### 6.3.1 Definition and classification of DESs

DESs are emerging subclass of sustainable ILs that have received extensive attention from researchers and industrial practitioners in the past two decades (Hansen et al., 2021). They are commonly composed of a mixture of at least one proton acceptor and proton donor. The term "eutectic" was coined in 1884 by Frederick Guthrie and derived from the Greek word eútēktos for low melting point (Liu et al., 2018). The term DESs refers to any liquid with the lowest melting point at a particular molar composition of the individual components. In general, DESs can be expressed by the common formula below:



where Cat<sup>+</sup> refers to any sulfonium, phosphonium, or ammonium cation, X is a Lewis base, and Y is either a Bronsted or Lewis base, and z is the Y molecules' number.

The concept and definition of DESs mixture was firstly introduced by Abbott et al. (2003), where he and his co-worker observed the changes in the physical state of powdered choline chloride, ChCl ( $T_m = 320^\circ\text{C}$ ) and crystalline urea ( $T_m = 133^\circ\text{C}$ ) mixture from solid to liquid under room temperature and the mixture with 33 mol% of ChCl exhibited the lowest melting

TABLE 6.1 Classification of DESs with the general formula (Tomé et al., 2018).

Type	General formula	Terms
Type I	$\text{Cat}^+ \text{X}^- z\text{MCl}_x$	$\text{M} = \text{Zn, Sn, Fe, Al, Ga, In}$
Type II	$\text{Cat}^+ \text{X}^- z\text{MCl}_x \cdot y\text{H}_2\text{O}$	$\text{M} = \text{Cr, Co, Cu, Ni, Fe}$
Type III	$\text{Cat}^+ \text{X}^- z\text{RZ}$	$\text{Z} = \text{CONH}_2, \text{COOH, OH}$
Type IV	$\text{MCl}_x + \text{RZ} = \text{MCl}_{x-1}^+ \cdot \text{RZ} + \text{MCl}_{x+1}^-$	$\text{M} = \text{Al, Zn, Z} = \text{CONH}_2, \text{OH}$

point of 12°C. Chemically, DESs are usually strongly associated with each other via interactions of hydrogen bond, which allow it to reduce the anion–cation electrostatic force of the system and thus dissociate to generate a new eutectic phase with a lower melting point compared to the individual component (<100°C) (Perna et al., 2020). The significant depression in the melting point of the DESs was mainly attributed from the charge delocalization between the hydrogen bond acceptors (HBA) and hydrogen bond donors (HBD) (Paiva et al., 2014).

Generally, most of DESs exhibit safe characteristics such as low toxicity, biodegradability and renewability as well as low production cost (Tomé et al., 2018). It is also well accepted in the literature that DESs are excellent and versatile substitutes for conventional ILs and emerging as new generation of ILs. Conventional ILs may possess ionic characteristics, but DESs generally have melting points remarkably lower than the starting material. Furthermore, the sustainability of ILs is frequently questioned and challenged due to its inherent poor biocompatibility and biodegradability (Paiva et al., 2014). Also, the preparation method of DESs is cheaper and more environmentally friendly than ILs. As showed in Table 6.1, DESs can be broadly divided into two main categories: those that contain metal salt and those that do not. DESs with metal salts can be further classified based on whether the metal salt is hydrated or not. Generally, there are four different types of DESs: Type I (quaternary ammonium salt + metal halide), Type II (quaternary ammonium salt + hydrated metal halide), Type III (quaternary ammonium salt + HBD such as polyol, carboxylic acid or amine, and Type IV (metal halide + HBD).

### 6.3.2 Biopolymers solubility

At the present stage, there is a major bottleneck in commercialization of bio-based facilities due to challenges for lignin removal from polysaccharides at attractive cost and industrial scale production of fermentable sugars and value-added products. Since DESs have been reported to be a flexible proton donor and acceptor, its presence is able to enhance interaction with biomolecules through its extensive hydrogen bond network, which enhances the solubility as an end effect. The recent progress in elucidation of biopolymers solubility, which includes lignin, cellulose and hemicellulose, using DESs has been provided in Table 6.2. Based on summary of Table 6.2, it is found that majority of the studies have been devoted to determination of lignin solubility, which demonstrates great potential. Nonetheless, DESs have been found to be not so effective in solubilizing cellulose as compared to lignin, while the study of hemicellulose has been scarcely available. Thus far, only a limited number of studies are available that demonstrate higher cellulose solubilization, such as that reported by Malaeke et al. (2018) by

TABLE 6.2 Solubility of lignin, cellulose, and hemicellulose biopolymers using DESs.

Salt	HBR	Salt: HBR molar ratio	Temperature (K)	Lignin (wt. %)	Cellulose (wt. %)	Hemicellulose (wt. %)	Reference
Choline chloride	Amide (Urea)	1:2	383.15	–	1.43	–	Ren et al. (2016b)
Choline chloride	Amide (Urea)	1:2	383.15	–	<0.20	–	Zhang et al. (2012)
Choline chloride	Amide (Thiourea)	1:2	373.15	–	10.00	–	Sharma et al. (2013)
Choline chloride	Amide (Acetamide)	1:2	383.15	–	0.22	–	Ren et al. (2016b)
Choline chloride	Aromatic alcohol (Phenol)	2:1	363.15	40.40	4.70	1.55	Malaeké et al. (2018)
Choline chloride	Aromatic alcohol ( $\alpha$ -Naphthol)	1:1	363.15	23.91	3.39	0.92	Malaeké et al. (2018)
Choline chloride	Aromatic alcohol (Resorcinol)	1:1	363.15	48.15	6.10	1.96	Malaeké et al. (2018)
Choline chloride	Carboxylic acids (lactic acid)	1:2	333.15	5.38	0.00	–	Francisco et al. (2012)
Choline chloride	Carboxylic acids (lactic acid)	1:5	333.15	7.77	0.00	–	Francisco et al. (2012)
Choline chloride	Carboxylic acids (lactic acid)	1:10	333.15	11.82	0.13	–	Francisco et al. (2012)
Choline chloride	Carboxylic acids (lactic acid)	1:10	333.15	13.00	<3.00	<5.00	Lynam et al. (2017)
Choline chloride	Carboxylic acids (formic acid)	1:2	333.15	14.00	<1.00	<1.00	Lynam et al. (2017)
Choline chloride	Carboxylic acids (acetic acid)	1:2	333.15	12.00	<1.00	<1.00	Lynam et al. (2017)
Choline chloride	Carboxylic acids (oxalic acid)	1:1	333.15	3.65	2.5	–	Lynam et al. (2017)
Choline chloride	Carboxylic acids (maleic acid)	1:1	363.15	38.13	2.57	0.85	Malaeké et al. (2018)
Choline chloride	Aromatic (imidazole)	3:7	383.15	–	2.48	–	Ren et al. (2016b)
Allyl triethyl ammonium chloride	Carboxylic acids (oxalic acid)	1:1	383.15	–	6.48	–	Ren et al. (2016a)

using 1:1 Choline Chloride: Resorcinol with 6.1 wt.% solubilization (Malaek et al., 2018) by using 1:1 Allyl triethyl Ammonium Chloride: Oxalic Acid by achieving 6.48 wt.% removal (Ren et al., 2016a) and Sharma et al. who has achieved 10 wt.% using 1:1 Choline Chloride: Thiourea (Sharma et al., 2013). To further enhance the solubility of biopolymers within DESs, it has been proposed to add cosolvent within the pristine solvent. It has been demonstrated that via incorporation of 5 wt.% polyethylene glycol (PEG) as cosolvents in choline chloride: imidazole DESs, it decreases hydrophobicity of cellulose, which ultimately enhances solubility to 4.57 wt.% (Ren et al., 2016a).

Although it has been well-acknowledged that DESs can potentially degrade the resultant biomass, majority of the studies have not reported the molecular weight before and after applying DESs, which suggest that the reported solubilities may be misleading (Häkkinen & Abbott, 2019). Another concern is although it is found that aromatic alcohol-based DESs demonstrate superior biopolymers solubility performance as compared to the other HBDs, phenolic nature of the compounds may be carcinogenic and toxic, which make greenness and feasibility of the solvent to be questionable. Hence, more studies are required to enhance the performance using other greener and safer HDBs while expanding the interrogation to different biopolymers to increase the feasibility in industrial scale application.

## 6.4 Biomass pretreatment and transformation using DESs

### 6.4.1 Role of DESs as pretreatment media

Lignin is a natural occurring heteropolymer that is found abundantly in biomass. Generally, lignin is a mixture of p-hydroxyphenyl (H), guaiacyl (G) and syringyl (S) units bonded by ether and C-C linkages (Liu et al., 2020; Owhe et al., 2021). Due to its complex and highly branched aromatic structure that intertwines with cellulose and hemicellulose, lignin has a recalcitrant nature and exhibits strong resistance against enzymatic attack and hydrolysis (Malaek et al., 2018; Oh et al., 2020). Besides, use of organic solvents and ILs in biomass fractionation raises environmental and operating cost issues. This has rendered isolation of lignin from biomass a challenging process, posing difficulties in the pretreatment and fractionation of biomass for further downstream valorization.

DESs have emerged as a green, recyclable and sustainable solvent or agent to extract lignin from biomass. Lignin recovered from biomass could further be converted into value-added chemicals or fuels, such as resins, composites, aromatic monomers, adhesives, and antioxidants (Ma et al., 2021; Song et al., 2020; Zhang et al., 2021). Extraction of lignin from a plethora of biomass has been studied and evaluated using various combinations of HBA (choline chloride, betaine, guanidine hydrochloride, and proline) and HBD (carboxylic acids, amines, and polyols) (Chen et al., 2020). Generally, the lignin recovered by DESs possesses superior qualities in comparison to the native lignin present in the biomass, which include low sulfur content hence causing less environmental pollution (Liu et al., 2020), reduced molecular weight hence easing further processing to value-added products (Oh et al., 2020), as well as increased molecular weight distribution range and higher heating values hence suitable to be used as plasticizers and sustainable fuels (Owhe et al., 2021).



Choline chloride (ChCl) has been extensively researched due to its superiority compared to other HBAs and higher lignin dissolution ability (Fernandes et al., 2021; Liu et al., 2020). ChCl-based DESs with varying HBD counterparts have been scrutinized in terms of their lignin removal efficiency, in view of varying physicochemical properties of the DESs when different HBA and HBD are paired. Oh et al. (2020) reported a direct correlation between the polarity and hydrogen bond acidity of the DESs toward the lignin removal efficiency. Having higher polarity and hydrogen bond acidity, ChCl-based DESs containing carboxylic acids as HBD have shown better lignin removal capabilities, as compared to DESs containing hydroxyl- and amide-based HBDs (Oh et al., 2020). The highest lignin removal efficiency of 72% was achieved by ternary ChCl/lactic acid/formic acid DESs, which registered the highest polarity and hydrogen bond acidity among other ternary DESs (Oh et al., 2020). Besides, the effect of carboxylic acids used as HBD in the ChCl-based DESs was also investigated by Fernandes et al. (2021). Higher selectivity of lignin extraction was exhibited by acids having additional OH (alpha-hydroxy) groups (such as tartaric acid, glycolic acid, and lactic acid), leading to increased polarity and enhanced interactions with lignin.

In addition, parameters such as extraction temperature, time, and HBA:HBD molar ratio are often optimized for maximizing the delignification efficiency of DESs. Oh et al. (2020) found that higher temperature and prolonged reaction time positively affected the lignin removal from pine wood until an optimum (plateau) was attained, after which further increase in temperature and reaction time showed insignificant influence on lignin removal. Similar trends were also reported by Fernandes et al. (2021). The molar ratio of HBA and HBD is also an important parameter that influences the properties of DESs such as conductivity, density, viscosity, stability and pH, which will in turn affect the mass transfer, solute-solvent interaction, and hence the delignification efficiency (Ji et al., 2020). In a study by Zhou et al. (2021), higher molar fraction of HBD (p-TsOH) in DESs resulted in higher lignin removal, due to higher lignin solubility in such concentration of DESs. Similar observation was also reported by Fernandes et al. (2021). Using ternary DES composed of lactic acid/tartaric acid/ChCl, it was found that as the HBD:HBA ratio increased from 1:1 to 5:1, the lignin extraction yield increased from 13% to 27%. In particular, increasing molar ratio of lactic acid to tartaric acid was desirable for lignin extraction due to lower concentration tartaric acid (a dicarboxylic acid containing the bulky COOH group) in the mixture, resulting in less entanglement and better mixing (Fernandes et al., 2021).

Lignin extractability is often enhanced or synergized by coupling the DESs pretreatment with a variety of technologies or sequential pretreatment, such as microwave, ultrasonic, or acid/alkali pre- or post-DESs treatments. For example, microwave and ultrasonic irradiations have significantly improved the purity and yield of lignin extracted by DESs, due to more efficient, selective and rapid heating mechanism, along with the synergy and compatibility with DESs (Ji et al., 2020, 2021; Li et al., 2019; Ma et al., 2021; Ong et al., 2019). Apart from that, acid treatment prior to DESs pretreatment (sequential pretreatment) was able to produce lignin with simplified structure and improved thermal stability (Liu et al., 2020). Also, due to the high viscosity of some DESs, lignin dissolved in the leftover DESs might deposit and precipitate on the surface of the pretreated residue, leading to lower delignification efficiency. Thus, this requires post-treatment to further recover the fractionated lignin. In this context, Zhou et al. (2021) performed the alkali (NaOH) post-treatment of DESs pretreated poplar sawdust residues and revealed that lignin recovered was enhanced to 80.9–92.2% as compared

to that of without alkali post-treatment (71.0–78.5 %). [Table 6.3](#) summarizes the studies on lignin removal by DESs.

Cellulose is prominent as chain polysaccharides having a similar structure to starch and also a major component of plant cell walls. It is a perfect candidate for production of bioethanol since cannot be absorbed by animals or humans. Thus, it has become the greatest challenge in biorefinery ([Sun et al., 2016](#)). Besides, celluloses are functioning as hydrophilicity, stereoregularity, biocompatibility, and reactive hydroxyl groups. It also serves as an adaptable resource for derivatized materials such as films, composites, fibers along with fuels and chemicals ([Baruah et al., 2018](#)). It is believed that the crystallinity of cellulosic substances is the significant factor that determines their digestibility and highly influences the dimensional stability, strength, and heat resistance of the materials ([Li et al., 2021](#)). Moreover, the initial enzymatic hydrolysis rate of cellulose is closely associated with the crystallinity index of cellulose ([Sun et al., 2016](#)). The presence of covalent bonds, hydrogen bonding, and van der Waals forces is contributing to the ultrastructure of cellulose. The formation of highly crystalline supramolecular structures hinders its dissolution, from the angle of inter- and intramolecular hydrogen bonds in cellulose.

Dissolution is the crucial step in utilization and transformation of cellulose. However, most of the traditional solvents displayed a very poor ability in dissolving cellulose since there are plenty of intra- and intermolecular hydrogen bonds in cellulose structure. Dissolving cellulose via conventional techniques is highly unstable, toxic, and difficult to recycle, and therefore fails to satisfy the development requirements of the green chemical industry ([Zhang et al., 2020](#)). In this sense, DESs have been targeted as an alternative for dissolving cellulose. DESs have received an extensive attention and recognition due to its outstanding swelling effect and solubility in biomass ([Li et al., 2021](#)). A recent study by [Tong et al. \(2021\)](#) has discovered a low-cost DES that is composed of zinc chloride, water, and phosphoric acid for the efficient dissolution of cellulose. This solvent is featured as having both the superior hydrogen bonding acidity and the hydrogen bonding basicity, and thus can act as a hydrogen bond molecular scissors to cleave the hydrogen bonds within cellulose. The highlight of the study is the experiment was conducted at room temperature. Microcrystalline cellulose can be easily dissolved in the solvent at room temperature with a dissolution ratio of up to 15 wt%. The dissolved cellulose can also be recovered without any derivatization.

Another up-to-date research was conducted by [Sharma et al. \(2021\)](#) whereby zwitterion-based DESs have opted for cellulose dissolution and the subsequent processing. Zwitterion-based DESs were prepared by mixing four types of saccharide at various ratios. Twenty-two combinations of zwitterion/saccharide mixtures formed DESs in liquid state below 100°C. The combinations with saccharide ratio of 5 wt% successfully dissolved cellulose due to the low saccharide load was sufficient for liquefaction but did not disrupt the intrinsic cellulose dissolution ability of zwitterions. From the perspective of spectroscopic investigation and quantum chemical calculations, IR, and NMR spectra indicated hydrogen bonds were the main driving forces for dissolution. Furthermore, theoretical analyses indicate HBA and HBD in DESs can affect the dissolution of cellulose. Intermolecular interactions in the complexes have been identified as noncovalent interactions, especially hydrogen bonds, which were considered to be the driving force of dissolution ([Fu et al., 2020](#)).

Hemicellulose is the secondary component of biomass, a heteropolymer with side chains that consists of short chains of different polysaccharides such as pentoses (xylans), alternating

TABLE 6.3 Studies on biomass delignification by DESs.

Feedstock	DESs	Main findings	References
Pure lignin and wheat straw biomass	<ul style="list-style-type: none"> <li>• ChCl/Phenol (ChCl-Ph)</li> <li>• ChCl/<math>\alpha</math>-naphthol (ChCl-Npt)</li> <li>• ChCl/resorcinol (ChCl-Res)</li> <li>• ChCl/maleic acid (ChCl-Mal)</li> </ul>	<ul style="list-style-type: none"> <li>• Highest solubility of lignin was obtained by ChCl-Res (48.15 w/w%), followed by ChCl-Ph (40.43 w/w%), ChCl-Mal (38.13 w/w%), ChCl-Npt (23.91 w/w%).</li> <li>• Lignin solubility of 41.67 w/w% obtained from delignification of wheat straw biomass by ChCl-Res.</li> </ul>	<a href="#">Malaeké et al. (2018)</a>
Raw corn straw and lactic acid (Lac) pretreated corn straw	<ul style="list-style-type: none"> <li>• ChCl/Lac</li> <li>• Betaine/Lac</li> </ul>	<ul style="list-style-type: none"> <li>• Lignin isolated by DESs was in higher purity (86.43–89.15%) as compared to that obtained by enzymatic hydrolysis (47.85–74.65%).</li> <li>• Acid pretreatment prior to DESs (ChCl/Lac) treatment produced lignin of simplified structure, reduced molecular weight, enhanced thermal stability and higher reactivity.</li> </ul>	<a href="#">Liu et al. (2020)</a>
Control and transgenic poplar woods	<ul style="list-style-type: none"> <li>• ChCl/ethylene-glycol/<math>\text{AlCl}_3 \cdot 6\text{H}_2\text{O}</math></li> <li>• ChCl/glycerol/<math>\text{AlCl}_3 \cdot 6\text{H}_2\text{O}</math></li> </ul>	<ul style="list-style-type: none"> <li>• Delignification ratios of transgenic poplars by DESs were higher (92.98–95.13%) than that of control poplars (90.66–92.55%).</li> <li>• Lignin yields from DESs treatment of transgenic poplars were higher (45.38–54.30%) than that of control poplars (37.25–38.86%).</li> <li>• DESs extracted lignin exhibited homogeneous lignin fractions and enriched phenolic OH groups with excellent antioxidant properties.</li> </ul>	<a href="#">Ma et al. (2021)</a>
Sugarcane bagasse	ChCl/glycerol/ $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$	<ul style="list-style-type: none"> <li>• High lignin removal efficiency of 82.71% was obtained, and it was enhanced to 86.39% when DES was synergized with ultrasound ethanol treatment.</li> <li>• Recovered lignin exhibited preserved structures of <math>\beta</math>-O-4 and <math>\beta</math>-<math>\beta</math> linkages.</li> </ul>	<a href="#">Ji et al. (2021)</a>
<i>Roystonea regia</i> leaves (LR) and leaf sheaths (LSR)	In situ DESs generated by adding ChCl to liquid hot water (LHW)	<ul style="list-style-type: none"> <li>• Lignin removal efficiencies were greatly enhanced by in situ DESs, i.e., 44.6% and 53.6% for LR and LSR, respectively, compared to that of LHW (19.1% and 29.9% for LR and LSR, respectively).</li> </ul>	<a href="#">Yu et al. (2019)</a>
<i>Pinus bungeana</i> Zucc. wood	ChCl/Lac	<ul style="list-style-type: none"> <li>• Microwave-assisted DESs pretreatment achieved lower lignin removal (42.81%) as compared to that of DESs pretreatment without microwave (66.59%).</li> <li>• Microwave-assisted DESs pretreatment efficiently removed high-substituted xylan and lignin, causing significant disruption to the morphology and porosity of the cell wall structure.</li> </ul>	<a href="#">Li et al. (2019)</a>
Woody poplar sawdust (PS) and herbaceous <i>miscanthus</i> (MC)	ChCl/p-toluene sulfonic acid (p-TsOH)	<ul style="list-style-type: none"> <li>• Increased in p-TsOH content in the DESs promoted the lignin removal from PS and MC, at the optimum ChCl:p-TsOH molar ratio of 1:2.</li> <li>• NaOH (1%) treatment post DESs extraction further increased the lignin removal from 71.0–78.5% to 80.9–92.2% for PS. Similar trend was also observed for MC.</li> </ul>	<a href="#">Zhou et al. (2021)</a>

(continued on next page)

TABLE 6.3 Studies on biomass delignification by DESs—cont'd

Feedstock	DESs	Main findings	References
Pine wood	ChCl-based DESs (containing acids, hydroxyl, amide, binary HBD)	<ul style="list-style-type: none"> <li>• Among 25 ChCl-based DESs screened, the lignin removal ranged from ~10% (ChCl/triethylene glycol) to 72% (ChCl/lactic acid/formic acid).</li> <li>• Purity of lignin recovered from DESs ranged from 90 to 97%.</li> <li>• Delignification efficiency was positively correlated to the polarity and hydrogen bond acidity of the DESs.</li> </ul>	Oh et al. (2020)
Garlic skin (GS) and green onion root (GOR)	ChCl-based DESs (containing glycerin, oxalic acid, urea and metal chloride as HBD)	<ul style="list-style-type: none"> <li>• Under four different heating methods of DESs pretreatment (i.e., oil bath, microwave, ultrasonic + oil bath and ultrasonic + microwave), lignin removal from GS and GOR were 55.34–90.14% and 39.53–92.34%, respectively.</li> <li>• The optimum ternary DESs for GS and GOR delignification was choline chloride/glycerol/aluminum chloride (ChCl-Gly-AlCl<sub>3</sub>•6H<sub>2</sub>O) at the optimum heating method of ultrasonic and microwave combined.</li> </ul>	Ji et al. (2020)
Rice husks, sugarcane bagasse, coffee chaff, corn stover	<ul style="list-style-type: none"> <li>• ChCl/Formic acid</li> <li>• ChCl/Lactic acid</li> <li>• ChCl/Acetic acid</li> </ul>	<ul style="list-style-type: none"> <li>• The lignin yield (with respect to original biomass) extracted by DESs ranged from 9.6 to 21.1%.</li> <li>• Lignin extracted by DESs exhibited reduced molecular weight and increased molecular weight distribution range (PDI: 1.06–1.92) and higher heating values compared to the control black liquor-derived lignin.</li> </ul>	Owhe et al. (2021)
Maritime pine wood ( <i>Pinus pinaster</i> Ait.) sawdust	<ul style="list-style-type: none"> <li>• Binary DESs (HBA: ChCl, betaine, urea and HBD: acetic acid, glycolic acid, propionic acid, lactic acid, tartaric acid, citric acid, lactic acid)</li> <li>• Ternary DESs (HBA: ChCl and HBD: Lactic acid + tartaric acid, glycolic acid + citric acid)</li> </ul>	<ul style="list-style-type: none"> <li>• Among the HBAs, ChCl gave superior performance in lignin extraction compared to betaine and urea.</li> <li>• Among different binary ChCl-based DESs, ChCl/Lactic acid produced highest lignin extraction yield (~32 wt%), whereas ChCl/tartaric acid produced lignin with the highest purity (~87%).</li> <li>• Ternary DESs ChCl/Lactic acid/Tartaric acid achieved the optimum lignin extraction efficiency, with lignin recovery and purity of 95% and 89 wt%, respectively.</li> </ul>	Fernandes et al. (2021)
Oil palm frond	ChCl/Urea	<ul style="list-style-type: none"> <li>• Ultrasonic treatment significantly enhanced the efficiency of lignin removal by DESs, from 14.02% (DESs treatment only) to 17.73–36.42% (ultrasound + DESs treatment).</li> </ul>	Ong et al. (2019)

units of mannose and glucose, galactomannan, glucuronoxylan, arabinoxylan, glucomannan, and xyloglucan that are held together by  $\beta$ -(1,4)- and/or  $\beta$ -(1,3)-glycosidic bonds. It is known that hemicellulose polymer matrix contain highly polymerized phenolic lignin which makes the conversion process tough, however it is readily degradable into monosaccharides due to low degree of polymerization and noncrystalline nature and thereby widely used in

industrial applications such as drug carriers, hydrogels, and cosmetics (Baruah et al., 2018). Hemicellulose hydrolysis is one of the primary biomass fractionation mechanisms by DESs, mainly based on the cleavage of ether bonds between lignin and ether/ester bonds between hemicellulose in lignin-carbohydrate complex (LCC) (Wang & Lee 2021). It was discovered that the breaking down of the covalent bonds linked lignin-hemicellulose and hydrogen bonds linked lignin-cellulose, the biomass fractionation toward lignin via DES mainly relies on the cleavage of aryl ether (C-O bond) and carbon-carbon linkages (C-C bond) in lignin. There is also occurrence of other chemical reactions for instance hydroxylation, demethoxylation, condensation, or crosslinking of depolymerized compounds derived from the reactions (Hong et al., 2020).

Acidic DESs exhibited higher solubility than basic DESs, whereby choline chloride-oxalic acid (CC-OA) DESs have effectively separated lignin and hemicellulose. It was proven that the hemicellulose thermal degradation at 150–300°C was denoted prior to DESs pretreatment (Li et al., 2021). DES synthesized from choline chloride with monobasic acid, dibasic acid, and polyol can effectively remove hemicellulose from corncob (Li et al., 2021; Zhang et al., 2016). Hou et al. (2017) has proven that 95.8% of the hemicellulose was hydrolyzed within 4 hours at 120 °C with strongly acidic DESs (ChCl:oxalic acid) and marginal hemicellulose removal was observed in mildly acidic DESs. In addition, current study on the sequential pretreatment methods has remarkable ability for the selective extraction of lignin and hemicellulose from the watermelon rind (WMR) biomass while preserving cellulose. The ultrasonic cavitation disintegrates the water molecules into free radicals which assist in the breakage of bonds by cleaving the linkages in lignin-xylan networks, removes hemicellulose and provides easy access for the penetration of the DESs in order to increase the accessibility of cellulose nanocrystals (Fakayode et al., 2021).

In other aspect, the results from Loow et al. (2018) showed that the effectiveness of ChCl:urea in delignification was attributed to its ability to form hydrogen bonds with phenolic compounds and displayed synergistic effect. Recently, a study with DESs that consists of benzyltrimethylammonium chloride/formic acid (BTMAC/FA) has shown an improvement in delignification and hemicelluloses-removal capacity. It was clarified that the removal ratio of DESs to hemicelluloses and lignin can be controlled by changing the reaction temperature. Effective removal of hemicelluloses after DESs pretreatment led to an reduced nonproductive absorption and diminished coating effect, followed by the breakdown of moieties and linkages of lignin-carbohydrates complexes (LCCs) which further enhanced the enzymatic hydrolysis (Xie et al., 2021). Nonetheless, further study is still required in systematic exploration of quantitative structure-activity relationship of hydrogen bond donor properties such as acidity, polarity, functional groups, and molecular structure on delignification and removal of hemicellulose for development of economically and environmentally viable solvents (Xu et al., 2020).

#### 6.4.2 Biomass transformation

Biomass transformation is a generic term referring to the valorization and conversion of biomass into a wide range of value-added products such as biofuels, biochemicals, bioenergy, etc. In this framework, the role of the neoteric DESs is indispensable in realizing the concept of biorefinery as existing studies discovered several roles of DESs in biomass transformation,

including dissolution, extraction, exfoliation, and conversion (Chen & Mu, 2019). Predominantly, the use of DESs as pretreatment solvents, extraction solvents, cosolvents, catalysts, or reaction media is prevalent at the moment. According to Loow et al. (2017), the implementation of DESs in biomass processing is still at its infancy stage when comparing with the utilization of DESs in other applications such as electroplating industry. To the best knowledge from these authors, it is found that the extraction of phenolic compounds from various biomass feedstocks was successfully achieved in a laboratory scale. Additionally, DESs could be used for other applications such as production of resin, sugar recovery from biomass, furanic derivatives, and biodiesel production other than for delignification process.

In order to increase the benefits of lignin in a biorefinery process, a detailed investigation on the characterization and sequential valorization of DESs extracted lignin are essential (Wang & Lee, 2021). As mentioned earlier, the extracted lignin could be used as a substitute element for the production resin. It is evidently proven that DESs derived lignin exhibits better performance in terms of thermal stability, strength from bonding, and duration involve in the sunshine gel (Hong et al., 2020; Lian et al., 2015). Tan et al. (2020) highlighted that the reactivity of the lignin depends on the phenolic hydroxyl group content. The improvement of the lignin reactivity usually takes place after the DESs treatment are implemented which will increase the yield of the hydroxyl content in the lignin (Tan et al., 2020). This observation was seen in the studies by Liu et al. (2016) from the developed lignin modification with DES (ChCl/oxalic acid) and Chen et al. (2019) from modified nickel oxide and DESs (ChCl/urea).

The extracted or modified lignin can be broadly applied in various applications such as plasticizer, binder from petroleum-based asphalt, phenolic compounds, wood adhesive, multi-purpose use nanocomposites and many more (Wang & Lee, 2021). It is said that the DESs in the phenolic compounds extraction process from biomass possess the capability to become a receiver and donor for both protons and electrons which could increase the possibility of hydrogen bond to be formed and also enhance the effectiveness of the dissolution to take place in the process (Bubalo et al., 2014). Table 6.4 summarized on the studies found in literature related to phenolic extraction via DESs. From this table, it is observed that chlorine chloride (ChCl) has been extensively used as DESs due to its outstanding extraction performance. This can be further explained on the strong hydrogen bonds formed with the selected compounds, which stop the continuation of the decomposition process to occur resulting to an increment in the yield of extraction and the production of stable extracts (Alam et al., 2021). In addition, the cost to synthesize the DESs would be cheaper compared to synthesize the IL by 80% (Xu et al., 2016). The individual compounds and molar selection play an important role in the DESs for phenolic compounds extraction (Loow et al., 2017; Wei et al., 2015). Despite lignin could potentially be used as a feedstock for aromatic compound production, however the production linked to benzene, toluene, and xylene are said to be limited due to the challenges encountered by lignin extraction that leads to unnecessary modification required on the lignin behavior and decomposition, and minimal yield produced (Tian et al., 2017). In addition, an in-depth understanding of the fundamental chemistry involved in the lignin extraction is still lacking and considered a necessity for the progression in a larger throughput for the lignin processing methods in the future (Melro et al., 2018; Xu et al., 2020).

The solvation ability of DESs was also exploited for extraction processes involving biomass feedstocks where it is versatilely applicable for both solid-liquid extraction and liquid-liquid

TABLE 6.4 Recent works for phenolic extraction with DESs from various lignocellulosic biomass.

Biomass feedstock	DESs	Initial pretreatment	Subsequent pretreatment	Extracted compound	Key findings	References
Wheat straw, corn stalk, and rapeseed	<ul style="list-style-type: none"> <li>• Acidic lactic- choline chloride</li> <li>• Alkaline K<sub>2</sub>CO<sub>3</sub>-glycerol (ChCl/K<sub>2</sub>CO<sub>3</sub>-G)</li> </ul>	<ul style="list-style-type: none"> <li>• 5 different DESs are evaluated:</li> <li>• Lactic acid (Lac): Choline chloride (Ch) = 2:1</li> <li>• Lactic acid (Lac5): Choline chloride = 5:1</li> <li>• Levulinic acid: Choline chloride = 2:1</li> <li>• Malic acid (Malic): Choline Chloride (Ch) =1:1</li> <li>• Glutaric acid (Glu): Choline Chloride (Ch) = 1:1</li> <li>• Glycerol (G): K<sub>2</sub>CO<sub>3</sub> =5:1</li> <li>• Temperature= 100°C</li> <li>• Time = 480 min</li> </ul>	None	Pre-treatment for phenolic compound	<ul style="list-style-type: none"> <li>• Highest delignification yields achieved from ChCl/K<sub>2</sub>CO<sub>3</sub>-G (11.8–5.7 wt-%).</li> <li>• Nanocellulose viscosity (555–1360 Pa.s)</li> <li>• Crystallinity index (38–54%)</li> </ul>	(Suopajarvi et al., 2020)
Onion ( <i>Allium cepa</i> L.)	ChCl/urea/H <sub>2</sub> O: 1:2:4	ChCl:urea = 1:1–1:3 Temperature = 50–90°C Time = 60–150 minutes	None	Total phenolic content	<ul style="list-style-type: none"> <li>• Major flavonoids (quercetin, kaempferol, and myricetin) were found.</li> <li>• Antiradical scavenging activity of 76.31% for ChCl/urea/H<sub>2</sub>O was obtained.</li> </ul>	Pal and Jadeja (2019)

(continued on next page)

Microalgae <i>Chlorella vulgaris</i>	ChCl/G/Ethylene glycol (EG)/1,3-propanediol (PDO)/1,4-butanediol (BDO)	<ul style="list-style-type: none"> <li>o Temperature = 60°C</li> <li>o Time = 100 minutes</li> <li>o Solvent to biomass ratio: 20:1</li> </ul>		Caffeic acid, Gallic acid, p-Coumaric acid	Optimum condition achieved at temperature (60°C), extraction time (10 min), and solvent to biomass ratio (20:1) to achieve 2-fold extraction efficiency with higher total polyphenolic content compared to conventional solvent.	Wan Mahmood et al. (2019)
Orange peel	ChCl/Levulinic acid (LeA)/N-methyl urea (1:1.2:0.8)	50	25	Total flavonoid	<ul style="list-style-type: none"> <li>• Highest extraction yield of total flavonoids from ChCl-LeA-N methyl urea.</li> <li>• Polymethoxylated flavonoids (PMFs) of 18.75 mg/g and glycosides of flavonoids (GOFs) of 47.07 mg/g achieved at the optimum conditions.</li> </ul>	Xu et al. (2019)
Orange peel waste	ChCl/EG (1:4)	60	100	Total phenolic	The total phenolic content of 3.61 mg gallic acid (GAE)/g orange peel (OP) and antioxidant potential of 30.6 µg/mL at the operating condition of water content (10wt%), temperature (333.15K), solid to liquid ratio (1:10), and extraction time (100 minutes).	Ozturk et al. (2018)
Empty fruit bunches	ChCl:Glycerol (G) (1:2)	Solid to liquid ratio = 10 Temperature = 120°C Time = 8 hours	None	–	<ul style="list-style-type: none"> <li>• The biopolymer removal in glucan, xylan, and lignin respectively are 31%, 15%, and 17%.</li> <li>• Solid yield produced is 96%.</li> </ul>	Tan et al. (2018)



extraction. For instance, recent studies indicated promising application of DESs as an extraction solvent to remove glycerol from biodiesel. Glycerol is a reaction by-product from biodiesel production which is highly undesirable due to the potential damages to modern diesel engines, hence must be eliminated through purification processes that are often costly. In particular, biodiesel purification by using DESs is a much cheaper alternative which exhibited outstanding performance with near complete removal of glycerin along with short residence time (Šalić et al., 2020). Apart from that, DESs also portrayed significance in the extraction of useful substrates from animal biomass such as crustacean shells. A study made use of DESs as an exfoliating agent to remove the outer surface of shrimp cells for the isolation of chitin substrates, in which DESs play simultaneous roles as demineralization, deproteinization, and chitin dissolution solvent (Bradić et al., 2020). Other instances include extraction of phenolic compounds, protein substrates, carbohydrate fractions, lignin oligomers, bioactive compounds, etc. that are either functional on their own or could be further processed into other value-added products.

Another notable involvement of DESs in biomass transformation can be linked to its role as catalysts. Catalysts have been acknowledged as an important asset to the chemical industry. In this context, catalysts can be regarded as the backbone to various industrial processes which lower the activation energy, increase the reaction rate, conversion, and yield, or as a prerequisite to certain chemical reactions. Various catalytic systems driven by DESs have been explored to produce upgraded biochemicals and value-added bioproducts, with the aim of harvesting the full chemical potential from biomass feedstocks. For instance, choline chloride-based DESs were used to catalyze the transformation of seaweed biomass into graphene which is a promising nanomaterial exhibiting exceptional mechanical, electrical, optical and thermal properties, with emerging applications including wearable electronics, membranes, biotechnology, energy storage, and much more (Mondal et al., 2016). Other studies also reported roles of DESs as catalysts in the conversion of biomass to sugars, protein-rich precipitates, biofuels, platform chemicals, etc. (Arslanoğlu & Sert, 2019; Bodachivskyi et al., 2019; Chen & Mu, 2019; Williamson et al., 2017). Catalytic DESs are renowned for its superiority compared to conventional solvents such that the concern over toxic by-products as typically seen in conventional catalysts are eliminated due to the environmentally friendly nature of DESs. On another note, DESs were found to be a viable alternative to precious metal-based catalysts and complex compounds for certain chemical reactions which is a far more sustainable option worth for further exploration.

Solvents are also typically used as reaction media for chemical synthesis wherein multiple studies reported enhanced performance by using DESs in place of conventional solvents across various applications. Chemical reactions are often carried out in a reaction media that are typically organic solvents or water which acts a medium for the feedstocks and reagents to dissolve and promote close, rapid contact at the molecular level. For example, improved yield of biodiesel compared to using ionic liquid as the reaction media was reported in a study (Merza et al., 2018). Additionally, existing works often employ DESs as the reaction media in various biomass transformation related studies to replace conventional solvents, especially ionic liquids that are analogous to DESs. Besides, material modification involving DESs is also commonly reported. For instance, DESs were used as a swelling agent that loosens the softwood biomass fibrous structure to enhance the efficiency for the production

of nonchemically modified cellulose nanofibers (Sirviö et al., 2021). However, it is essential to note that the exact function of DESs reported in existing research works is rather unclear since there is no clear boundary to that. The role as solvents, catalysts, reaction media, etc. could not be clearly distinguished as DESs may contribute a fraction to solvation, catalytic activity, or material modification simultaneously in a reaction. Hence, the high efficiency of DESs reported across various studies could be a synergistic effect of its multiple roles combined and further works that clears this ambiguity would be highly recommended.

## 6.5 Current constraints

---

The current progress of DESs synthesis and their industrial applications are still considered to be in their infancy. Despite the significant surge in the research interest related to DESs, most existing research works were in the form of case studies and focused on the application of DESs in various fields including but not limited to biomass pretreatment. The building principles, the mechanism, and kinetics of DESs in biomass dissolution and the subsequent conversion of biomass are not totally clear. Since fundamentals serve as the building block to profound knowledge, more advanced techniques and methods should be called for to explore these processes in order to clarify the ambiguity in the actual role of DESs in biomass pretreatment and the factors that are affecting the interactions at the molecular level.

Another major issue with regards to using DESs as the biomass pretreatment media is the lack of rapid and accurate tools for assessing and tracking the compatibility and effectiveness of DESs on varying biopolymer components and composition. Consequently, existing works typically adopt the “trial-and-error” approach in formulating DESs for specific applications due to the lack of theoretical understanding and robust modeling techniques that enable computer-aided design and development of DESs which will save tons of effort and time in research. On another note, it is worth mentioning that not every single combination of HBAs and HBDs at specific molar composition is compatible with each other or could result in a significant performance in biomass dissolution.

From the perspective of applicability, recycling and reusing DESs would be the ideal scenario that is highly favorable for low-cost and high-volume applications in the industry. Early studies have shown that DESs are considered to be readily recyclable because their synthesis and regeneration do not involve any chemical reactions but only the formation or dissociation of the hydrogen bonding network that binds their constituents together (Xu et al., 2017). Although it is broadly acknowledged that recycling DESs for multiple cycles is possible, more in-depth studies on the recovery and the chemistry beyond recycling DESs must be conducted to prove the potential in cost reduction and lower chemical uses with respect to biomass pretreatment efficiency. For instance, some studies pointed out the recovered DESs that were reused for the subsequent biomass pretreatment demonstrated lower pretreatment efficacy which can be attributed to the increase of impurities in the recovered solvents after each recycles (Kim et al., 2018).

Although biomass resources are indeed relatively cheap, the processing cost is often sufficiently high to the extent that utilizing biomass resources is greatly discouraged. Hence, the development of inexpensive and renewable green solvents is highly sought after. Although

most of these solvents were advertised and promoted as low-cost alternatives due to the starting materials being readily available and not exotic in nature, systematic methodologies such as life cycle assessment (LCA) or other technoeconomic analysis for using DESs as pretreatment media of biomass should be performed and properly documented. It is essential to note that a large fraction of the existing studies was using pure chemicals of analytical or reagent grade for their studies from which the costs of these pure chemicals are relatively high. To guarantee the economic feasibility of using DESs in the industry, these solvents need to attract a high market demand and be manufactured at an industrial scale in order to reach cost parity with existing technologies to finally qualify as low-cost green solvents. Similar to most established industrial processes, a possible key step toward maximizing the worth of DESs on an industrial scale could include finding or creating markets for the by-products generated from biomass pretreatment.

The stability of DESs is a very recent concern that was rarely discussed in previous works. In this context, the pretreatment of biomass by using DESs typically involves a thermo-chemical approach where the pretreatment condition usually exposes the DESs to harsh conditions such as elevated temperature or to be used in combination with ultrasound or microwave-assisted techniques to accelerate the speed of the pretreatment process and conversion of biomass. A recent study discovered and called for the concern over biomass pretreatment using choline chloride and carboxylic acid-based DESs due to the accelerated degradation of DESs during its application (Rodriguez Rodriguez et al., 2019). The degradation of DESs was attributed to the esterification side reaction that was accelerated at elevated temperature or even simply left at room condition for a prolonged period. Hence, it is evident that the stability of DESs must be revisited and feasible solutions should be properly addressed before progressing with industrial-wide implementation.

## 6.6 Conclusions and perspectives

Biomass pretreatment remains a key bottleneck in the valorization of biomass to produce biofuels and other value-added bioproducts. Although some of the existing pretreatment methods outstand the others, it is still unlikely that any specific method will become the ultimate choice for every biomass due to the varying composition in different biomass, at least not for all feedstocks. To relate, the existing pretreatment methods achieved great efficiency in biomass pretreatment and subsequently the conversion of biomass but there is always a drive to accommodate a wider range of possibilities and solutions in this sector. As the eye of the world shift toward acknowledging environmental sustainability as the new focus, many conventional pretreatment methods would no longer be in favor and could be phased out soon. Since the green chemistry metrics marked a significance toward sustainable development, biomass pretreatment strategies should make a transition to involve greener strategies despite the existing pretreatment methods being effective and well-established. The recent emergence of DESs is very much still in its infancy but early studies indicated promising results as a pretreatment media for biomass feedstocks. The traits of DESs are also ideal as a readily available, low cost, highly tunable, and environmentally friendly green solvent. Despite the current constraints faced in the development of DESs, this area of research outseen prospects for biomass valorization and left a large room yet to be explored. The key to

maximizing biomass potential may lie in the tons of questions regarding DESs that were left unanswered. Therefore, further works are highly recommended to contribute to the expanse of this research area and ultimately the commercialization of DESs in the biomass industry to upgrade the existing biomass utilization roadmap to a wider energy generation and chemical production sector.

## Acknowledgments

The authors would like to acknowledge the supports from Small Grant Scheme UNIMAS, F02/SGS/1992/2020 and Ministry of Higher Education Malaysia, Fundamental Research Grant Scheme, FRGS/1/2020/TK0/UNIMAS/03/2 with finance ID of 05-FA020700-0613-0017 and 05-FA020700-0708-0051, respectively.

## References

- Abbott AP, Capper G, Davies DL, Rasheed RK, Tambyrajah V: Novel solvent properties of choline chloride/urea mixtures, *Chem Commun*(1):70–71, 2003.
- Agbor VB, Cicek N, Sparling R, Berlin A, Levin DB: Biomass pretreatment: Fundamentals toward application, *Biotechnol Adv* 29(6):675–685, 2011.
- Alam MA, Muhammad G, Khan MN, Mofijur M, Lv Y, Xiong W, Xu J: Choline chloride-based deep eutectic solvents as green extractants for the isolation of phenolic compounds from biomass, *J Cleaner Prod* 309:127445, 2021.
- Anukam, A, Berghel, J, & Biomass pretreatment and characterization: A review. In Biomass, IntechOpen. 2020.
- Arslanoğlu A, Sert M: Direct conversion of biomass to platform chemicals, catalyzed using a deep eutectic solvent of N,N diethyl ethanol ammonium chloride-oxalic acid in a microwave reactor, *Fuel* 258:116142, 2019.
- Baruah J, Nath BK, Sharma R, Kumar S, Deka RC, Baruah DC, Kalita E: Recent trends in the pretreatment of lignocellulosic biomass for value-added products, *Frontiers in Energy Research* 6:141, 2018.
- Binod P, Pandey A: Introduction: In *Pretreatment of biomass: processes and technologies*, Amsterdam, Elsevier Inc, pp 3–6, 2015.
- Bodachivskiy I, Kuzhiumparambil U, Williams DBG: Catalytic valorization of native biomass in a deep eutectic solvent: A systematic approach toward high-yielding reactions of polysaccharides, *ACS Sustain Chem Eng* 8(1):678–685, 2019.
- Bradić B, Novak U, Likozar B: Crustacean shell bio-refining to chitin by natural deep eutectic solvents, *Green Processing and Synthesis* 9(1):13–25, 2020.
- Bubalo MC, Radosevic K, Redovnikovic IR, Halambek J, Srcek VG: A brief overview of the potential environmental hazards of ionic liquids, *Ecotoxicol Environ Saf* 99:1–12, 2014.
- Chen MQ, Sun QQ, Wang YS, Yang ZL, Wang Q, Cao Y, Wang J: Effect of DES-NiO system on modified lignin and synthesis of lignin-based epoxy resin, *J Cleaner Prod* 13(3):317328, 2019.
- Chen Y, Mu T: Application of deep eutectic solvents in biomass pretreatment and conversion, *Green Energy & Environment* 4:95–115, 2019.
- Chen Z, Ragauskas A, Wan C: Lignin extraction and upgrading using deep eutectic solvents, *Industrial Crops & Products* 147:112241, 2020.
- Cheng MH, Huang H, Dien BS, Singh V: The costs of sugar production from different feedstocks and processing technologies, *Biofuels, Bioprod Biorefin* 13(3):723–739, 2019.
- Fakayode OA, Akpabli-Tsigbe NDK, Wahia H, Tu S, Ren M, Zhou C, Ma H: Integrated bioprocess for bio-ethanol production from watermelon rind biomass: Ultrasound-assisted deep eutectic solvent pretreatment, enzymatic hydrolysis and fermentation, *Renewable Energy* 180:258–270, 2021.
- Fernandes C, Melro E, Magalhães S, Alves L, Craveiro R, Filipe A, Valente AJM, Martins G, Antunes FE, Romano A, Medronho B: New deep eutectic solvent assisted extraction of highly pure lignin from maritime pine sawdust (*Pinus pinaster* Ait.), *Int J Biol Macromol* 177:294–305, 2021.
- Francisco M, Van Den Bruinhorst A, Kroon MC: New natural and renewable low transition temperature mixtures (LTTMs): Screening as solvents for lignocellulosic biomass processing, *Green Chem* 14(8):2153–2157, 2012.
- Fu H, Wang X, Sang H, Hou Y, Chen X, Feng X: Dissolution behavior of microcrystalline cellulose in DBU-based deep eutectic solvents : Insights from spectroscopic investigation and quantum chemical calculations, *J Mol Liq* 299:112140, 2020.

- Häkkinen R, Abbott AP: Solvation of carbohydrates in five choline chloride-based deep eutectic solvents and the implication for cellulose solubility, *Green Chem* 21(17):4673–4682, 2019.
- Hansen BB, Spittle S, Chen B, Poe D, Zhang Y, Klein JM, Sangoro JR: Deep eutectic solvents: A review of fundamentals and applications, *Chem Rev* 121(3):1232–1285, 2021.
- Hong S, Sun X, Lian HL, Pojman JA, Mota-Morales JD: Zinc chloride/acetamide deep eutectic solvent-mediated fractionation of lignin produces high- and low-molecular-weight fillers for phenol-formaldehyde resins, *J Appl Polym Sci* 137:48385, 2020.
- Hou XD, Feng GJ, Ye M, Huang CM, Zhang Y: Significantly enhanced enzymatic hydrolysis of rice straw via a high-performance two-stage deep eutectic solvents synergistic pretreatment, *Bioresour Technol* 238:139–146, 2017.
- Ji Q, Yu X, Yagoub AEA, Chen L, Mustapha AT, Zhou C: Enhancement of lignin removal and enzymolysis of sugarcane bagasse by ultrasound-assisted ethanol synergized deep eutectic solvent pretreatment, *Renewable Energy* 172:304–316, 2021.
- Ji Q, Yu X, Yagoub AEA, Chen L, Zhou C: Efficient removal of lignin from vegetable wastes by ultrasonic and microwave-assisted treatment with ternary deep eutectic solvent, *Industrial Crops & Products* 149:112357, 2020.
- Kim KH, Dutta T, Sun J, Simmons B, Singh S: Biomass pretreatment using deep eutectic solvents from lignin derived phenols, *Green Chem* 20(4):809–815, 2018.
- Li C, Huang C, Zhao Y, Zheng C, Su H, Zhang L, Luo W, Zhao H, Wang S, Huang LJ: Effect of choline-based deep eutectic solvent pretreatment on the structure of cellulose and lignin in Bagasse, *Processes* 9(384):1–14, 2021.
- Li P, Zhang Q, Zhang X, Pan X, Xu F: Subcellular dissolution of xylan and lignin for enhancing enzymatic hydrolysis of microwave assisted deep eutectic solvent pretreated *Pinus bungeana* Zucc, *Bioresour Technol* 288:121475, 2019.
- Lian H, Hong S, Carranza A, Mota-Morales JD, Pojman JA: Processing of lignin in urea-zinc chloride deep-eutectic solvent and its use as a filler in a phenol-formaldehyde resin, *RSC Adv* 5(36):28778–28785, 2015.
- Liu J, Wang J, Fu Y, Chang J: Synthesis and characterization of phenol-furfural resins using lignin modified by a low transition temperature mixture, *RSC Adv* 6(97):94588–94594, 2016.
- Liu X, Li T, Wu S, Ma H, Yin Y: Structural characterization and comparison of enzymatic and deep eutectic solvents isolated lignin from various green processes: Toward lignin valorization, *Bioresour Technol* 310:123460, 2020.
- Liu Y, Friesen JB, McAlpine JB, Lankin DC, Chen S-N, Pauli GF: Natural deep eutectic solvents: Properties, applications, and perspectives, *J Nat Prod* 81(3):679–690, 2018.
- Loow YL, New EK, Yang GH, Ang LY, Foo LYW, Wu TY: Potential use of deep eutectic solvents to facilitate lignocellulosic biomass utilization and conversion, *Cellulose* 24(9):3591–3618, 2017.
- Loow YL, Wu TY, Yang GH, Ang LY, New EK, Siow LF, Md Jahim J, Mohammad AW, Teoh WH: Deep eutectic solvent and inorganic salt pretreatment of lignocellulosic biomass for improving xylose recovery, *Bioresour Technol* 249:818–825, 2018.
- Lynam JG, Kumar N, Wong MJ: Deep eutectic solvents' ability to solubilize lignin, cellulose, and hemicellulose; thermal stability; and density, *Bioresour Technol* 238:684–689, 2017.
- Ma CY, Gao X, Peng XP, Gao YF, Liu J, Wen JL, Yuan TQ: Microwave-assisted deep eutectic solvents (DES) pretreatment of control and transgenic poplars for boosting the lignin valorization and cellulose bioconversion, *Industrial Crops & Products* 164:113415, 2021.
- Malaeke H, Housaindokht MR, Monhemi H, Izadyar M: Deep eutectic solvent as an efficient molecular liquid for lignin solubilization and wood delignification, *J Mol Liq* 263:193–199, 2018.
- Melro E, Alves L, Antunes FE, Medronho B: A brief overview on lignin dissolution, *J Mol Liq* 265:578–584, 2018.
- Merza F, Fawzy A, AlNashef I, Al-Zuhair S, Taher H: Effectiveness of using deep eutectic solvents as an alternative to conventional solvents in enzymatic biodiesel production from waste oils, *Energy Reports* 4:77–83, 2018.
- Mondal D, Sharma M, Wang CH, Lin YC, Huang HC, Saha A, Nataraj SK, Prasad K: Deep eutectic solvent promoted one step sustainable conversion of fresh seaweed biomass to functionalized graphene as a potential electrocatalyst, *Green Chem* 18(9):2819–2826, 2016.
- Nauman Aftab M, Iqbal I, Riaz F, Karadag A, Tabatabaei M: *Biomass for bioenergy - Recent trends and future challenges*. Different pretreatment methods of lignocellulosic biomass for use in biofuel production, London, IntechOpen, 2019.
- Oh Y, Park S, Jung D, Oh KK, Lee SH: Effect of hydrogen bond donor on the choline chloride-based deep eutectic solvent-mediated extraction of lignin from pine wood, *Int J Biol Macromol* 165(Part A):187–197, 2020.
- Ong VZ, Wu TY, Lee CBTL, Cheong NWR, Shak KPY: Sequential ultrasonication and deep eutectic solvent pretreatment to remove lignin and recover xylose from oil palm fronds, *Ultrason Sonochem* 58:104598, 2019.

- Owhe EO, Kumar N, Lynam JG: Lignin extraction from waste biomass with deep eutectic solvents: Molecular weight and heating value, *Biocatalysis and Agricultural Biotechnology* 32:101949, 2021.
- Ozturk B, Parkinson C, Gonzalez-Miquel M: Extraction of polyphenolic antioxidants from orange peel waste using deep eutectic solvents, *Sep Purif Technol* 206:1–13, 2018.
- Paiva A, Craveiro R, Aroso I, Martins M, Reis RL, Duarte ARC: Natural deep eutectic solvents – Solvents for the 21st century, *ACS Sustain Chem Eng* 2(5):1063–1071, 2014.
- Pal CBT, Jadeja GC: Deep eutectic solvent-based extraction of polyphenolic antioxidants from onion (*Allium cepa* L.) peel, *J Sci Food Agric* 99(4):1969–1979, 2019.
- Perna FM, Vitale P, Capriati V: Deep eutectic solvents and their applications as green solvents, *Current Opinion in Green and Sustainable Chemistry* 21:27–33, 2020.
- Ren H, Chen C, Guo S, Zhao D, Wang Q: Synthesis of a novel allyl-functionalized deep eutectic solvent to promote dissolution of cellulose, *BioResources* 11(4):8457–8469, 2016a.
- Ren H, Chen C, Wang Q, Zhao D, Guo S: The properties of choline chloride-based deep eutectic solvents and their performance in the dissolution of cellulose, *BioResources* 11(2):5435–5451, 2016b.
- Rodriguez Rodriguez N, Van Den Bruinhorst A, Kollau LJBM, Kroon MC, Binnemans K: Degradation of deep-eutectic solvents based on choline chloride and carboxylic acids, *ACS Sustain Chem Eng* 7(13):11521–11528, 2019.
- Šalić A, Jurinjak Tušek A, Gojun M, Zelić B: Biodiesel purification in microextractors: Choline chloride based deep eutectic solvents vs water, *Sep Purif Technol* 242:116783, 2020.
- Sharma G, Takahashi K, Kuroda K: Polar zwitterion/saccharide-based deep eutectic solvents for cellulose processing, *Carbohydr Polym* 267:118171, 2021.
- Sharma M, Mukesh C, Mondal D, Prasad K: Dissolution of  $\alpha$ -chitin in deep eutectic solvents, *RSC Adv* 3(39):18149–18155, 2013.
- Sirviö JA, Isokoski E, Kantola AM, Komulainen S, Ämmälä A: Mechanochemical and thermal succinylation of softwood sawdust in presence of deep eutectic solvent to produce lignin-containing wood nanofibers, *Cellulose* 28(11):6881–6898, 2021.
- Song Y, Ji H, Shi X, Yang X, Zhang X: Successive organic solvent fractionation and structural characterization of lignin extracted from hybrid poplar by deep eutectic solvent for improving the homogeneity and isolating narrow fractions, *Renewable Energy* 157:1025–1034, 2020.
- Sun S, Sun S, Cao X, Sun R: The role of pretreatment in improving the enzymatic hydrolysis of lignocellulosic materials, *Bioresour Technol* 199:49–58, 2016.
- Suopajarvi T, Ricci P, Karvonen V, Ottolina G, Liimatainen H: Acidic and alkaline deep eutectic solvents in delignification and nanofibrillation of corn stalk, wheat straw, and rapeseed stem residues, *Industrial Crops and Products* 145:111956, 2020.
- Tan YT, Chua ASM, Ngho GC: Deep eutectic solvent for lignocellulosic biomass fractionation and the subsequent conversion to bio-based products - A review, *Bioresour Technol* 297:122522, 2020.
- Tan YY, Ngho GC, Chua ASM: Evaluation of fractionation and delignification efficiencies of deep eutectic solvents on oil palm empty fruit bunch, *Ind Crops Prod* 123:271–277, 2018.
- Tian D, Chandra RP, Lee JS, Lu CH, Saddler JN: A comparison of various lignin-extraction methods to enhance the accessibility and ease of enzymatic hydrolysis of the cellulosic component of steam-pretreated poplar, *Biotechnol Biofuels* 10(157):1–10, 2017.
- Tomé LIN, Baião V, da Silva W, Brett CMA: Deep eutectic solvents for the production and application of new materials, *Applied Materials Today* 10:30–50, 2018.
- Tong Z, Meng J, Liu S, Liu Y, Zeng S, Wang L, Xia Q, Yu H: Room temperature dissolving cellulose with a metal salt hydrate-based deep eutectic solvent, *Carbohydr Polym* 272:118473, 2021.
- Wan Mahmood WMA, Lorwirachsutee A, Theodoropoulos C, Gonzalez-Miquel M: Polyol-based deep eutectic solvents for extraction of natural polyphenolic antioxidants from *Chlorella vulgaris*, *ACS Sustain Chem Eng* 7(5):5018–5026, 2019.
- Wang W, Lee DJ: Lignocellulosic biomass pretreatment by deep eutectic solvents on lignin extraction and saccharification enhancement: A review, *Bioresour Technol* 339:125587, 2021.
- Wei Z, Qi X, Li T, Luo M, Wang W, Zu Y, Fu Y: Application of natural deep eutectic solvents for extraction and determination of phenolics in *Cajanus cajan* leaves by ultra performance liquid chromatography, *Sep Purif Technol* 149:237–244, 2015.

- Williamson ST, Shahbaz K, Mjalli FS, AlNashef IM, Farid MM: Application of deep eutectic solvents as catalysts for the esterification of oleic acid with glycerol, *Renewable Energy* 114:480–488, 2017.
- Xie J, Chen J, Cheng Z, Zhu S, Xu J: Pretreatment of pine lignocelluloses by recyclable deep eutectic solvent for elevated enzymatic saccharification and lignin nanoparticles extraction, *Carbohydr Polym* 269:118321, 2021.
- Xu GC, Ding JC, Han RZ, Dong JJ, Ni Y: Enhancing cellulose accessibility of corn stover by deep eutectic solvent pretreatment for butanol fermentation, *Bioresour Technol* 203:364–369, 2016.
- Xu H, Peng J, Kong Y, Liu Y, Su Z, Li B, Song X, Liu S, Tian W: Key process parameters for deep eutectic solvents pretreatment of lignocellulosic biomass materials: A review, *Bioresour Technol* 310:123416, 2020.
- Xu M, Ran L, Chen N, Fan X, Ren D, Yi L: Polarity-dependent extraction of flavonoids from citrus peel waste using a tailor-made deep eutectic solvent, *Food Chem* 297:124970, 2019.
- Xu P, Zheng GW, Zong MH, Li N, Lou WY: Recent progress on deep eutectic solvents in biocatalysis, *Bioresources and Bioprocessing* 4(1):34, 2017.
- Yu Q, Qin L, Liu Y, Sun Y, Xu H, Wang Z, Yuan Z: In situ deep eutectic solvent pretreatment to improve lignin removal from garden wastes and enhance production of bio-methane and microbial lipids, *Bioresour Technol* 271:210–217, 2019.
- Zhang CW, Xia SQ, Ma PS: Facile pretreatment of lignocellulosic biomass using deep eutectic solvents, *Bioresour Technol* 219:1–5, 2016.
- Zhang H, Lang J, Lan P, Yang H, Lu J, Wang Z: Study on the dissolution mechanism of cellulose by ChCl-based deep eutectic solvents, *Materials* 13(2):1–12, 2020.
- Zhang Q, Benoit M, De Oliveira Vigier K, Barrault J, Jérôme F: Green and inexpensive choline-derived solvents for cellulose decrystallization, *Chem Eur J* 18(4):1043–1046, 2012.
- Zhang Q, Ma R, Ma L, Zhang L, Fan Y, Wang Z: Contribution of lignin in esterified lignocellulose nanofibers (LCNFs) prepared by deep eutectic solvent treatment to the interface compatibility of LCNF/PLA composites, *Industrial Crops & Products* 166:113460, 2021.
- Zhou X, Huang T, Liu J, Gao H, Bian H, Wang R, Huang C, Sha J, Dai H: Recyclable deep eutectic solvent coupling sodium hydroxide post-treatment for boosting woody/herbaceous biomass conversion at mild condition, *Bioresour Technol* 320:124327, 2021.

# Index

---

Page numbers followed by “*f*” and “*t*” indicate, figures and tables respectively.

## A

Absorbance probes, 91  
Acetone-butanol-ethanol (ABE) fermentation, 206  
Active pharmaceutical ingredient (API), 4, 283  
Adsorption methods, 206  
Adsorptive desulfurization, 356  
Aerobic oxidative desulfurization (AODS), 353  
Aprotic ionic liquids (AIL), 109  
Aqueous two-phase system (ATPS), 93  
Arrhenius equation, 9  
Aspen database, 212  
Atom economy, 232  
Atomic force microscopy (AFM), 191  
Average charge distribution, 194

## B

Benign alternative solvent systems, 2  
Biginelli reactions, 95  
Biocatalytic processes  
  ab initio molecular studies, 169  
  biocatalytic performance, 171  
  biotransformation, 175  
  cellulosic biofuels, 171  
  commercially relevant biocatalytic processes, 171  
  compatible biocatalysts, 165  
  evolution, 162  
  hydrolases, 167  
  lipid-base biofuels, 174  
  molecular mechanics calculations, 170  
  natural, 164  
  natural product extraction, 175  
  oxidoreductases, 167  
  perspectives, 176  
  process optimization, 168  
  pulp and paper, 174  
  simulation techniques, 170  
  types, 162  
  whole cells, 167  
Biologically aerobic oxidation (BAO), 355  
Biomass pretreatment  
  biological pretreatment, 141  
  chemical pretreatment, 141  
  physical pretreatment, 140

  status, 140  
Biomass transformation, 150  
Biopharmaceutical Classification System (BCS), 283  
Biopolymers solubility, 143  
Bipyridine ligands, 260  
Boric acid, 350  
Buchwald–Hartwig type C–N coupling reaction, 268

## C

Canadian Environmental Protection Act (CEPA), 377  
Candida antarctica Lipase B (CAL-B), 167  
Candida rugosa lipase (CRL), 167  
Carbene ligands, 259  
Carbon-nitrogen cross-coupling reactions, 264  
  Buchwald–Hartwig type C–N coupling reaction, 268  
  external catalyst, 267  
  Goldberg-type C–N coupling reaction, 269  
  heterogeneous catalyst, 264  
  homogeneous catalyst, 267  
Carbon-oxygen cross-coupling reactions, 270  
Carbon-sulfur cross-coupling reactions, 270  
Cellulosic biofuels, 171  
Chemical industry, 223  
Choline, 84  
Choline chloride-based THEDES, 306,  
  *see also* Deep eutectic solvents (DES)  
Choline-chloride (ChCl)-urea mixtures, 182  
Cluster model (CM), 169  
CO<sub>2</sub> capture, deep eutectic solvents, 78  
  amine based, 80  
  ammonium/phosphonium-functionalized, 79  
  azolide-based, 81  
  hydrophobic, 82  
  imidazolium-derived, 80  
  miscellaneous methods, 82  
  superbase-added, 81  
Conventional heating, 194

## D

Deep eutectic solvents (DESs), 85, 1, 3, 4, 9, 12, 15, 187,  
  206, 224, 240, 241, 407  
  ability, 12, 13  
  ab initio molecular studies, 169



- in adsorptive desulfurization, 356
- aerobic oxidative desulfurization, 353
- amine based, 80
- ammonium/phosphonium-functionalized, 79
- antibacterial, 286
- anticancer, 295
- antifungal, 293
- antiviral, 294
- application, 285*f*
- applications, 93, 97, 11, 408*f*
- azolide-based, 81
- based drug delivery, 308
- based processes, 232
- for biocatalysis, 166*f*
- biocatalytic performance, 171
- biodegradability, 413
- biomass/biofuel, 390
- biomass pretreatment and transformation, 145
- biomass transformation, 150
- biopolymers solubility, 143
- biotransformation, 175
- bipyridine ligands, 260
- carbene ligands, 259
- carbon-carbon cross-coupling reactions, 257
- carbon-oxygen cross-coupling reactions, 270
- cellulosic biofuels, 171
- challenges in development and applications, 14
- choline chloride-based THEDES, 306
- commercially relevant biocatalytic processes, 171
- compatible biocatalysts, 165
- components, 6*f*
- compound selection and processing, 395
- constraints, 155
- cross-coupling reactions, 252
- current development, 375
- cytotoxicity behavior of, 411*f*
- definition and classification, 142
- in desulfurization, 346, 360
- developments, 4
- drawbacks, 387
- drug applications, 286
- drug formulations for permeation and bioavailability, 308
- for drug solubilization, 297
- electrochemical applications, 11
- emergence, 13
- environmental impact, 413
- environmental impacts, 411
- evolution, 162
- extractive catalytic oxidative desulfurization, 352
- in extractive desulfurization, 347
- extractive oxidative desulfurization, 352
- food industry, 389
- gas capture, 392
- gas separation applications, 192
- general formula, 163
- growth, 11
- HBD components, 416*f*
- health and safety risk measures, 397
- hybrid ChCl-resorcinol-glycerol, 192
- hydrogen bonding network, 195
- hydrolases, 167
- hydrophobic, 82
- ibuprofen-based eutectic mixtures, 304
- imidazolium-derived, 80
- for improving drug bioavailability, 304
- inherent safety assessment of, 414
- involving process, 233
- ligand-free cross-coupling reactions, 254
- lipid-base biofuels, 174
- low vapor pressure and low toxicity, 412
- macroscopic physical properties, 88
- mechanisms, 362
- membrane matrix, 412
- membranes as polymer electrolytes, 418
- membranes in water filtration applications, 418
- miscellaneous methods, 82
- molecular mechanics calculations, 170
- molecular modeling, 364
- natural product extraction, 175
- oxidative desulfurization, 351
- oxidoreductases, 167
- perspectives, 156, 176, 312
- pharmaceutical, 387
- phosphine ligands, 257
- physical properties of, 87
- physicochemical properties, 5
- polymerization in, 95
- possessing drug-like properties, 286
- post-usage risks, 393
- potential and reality, 91
- preparation, 285
- pretreatment media, 145
- problems, 379
- process optimization, 168
- pulp and paper, 174
- reactivity, 87
- regulation, 376, 378
- regulation of solvents, 376
- regulatory aspects, 393
- regulatory body, 394
- response surface methodology, 359
- safety consideration of, 414*f*
- schematic representation of structural changes, 98
- simulation techniques, 170
- socialization, 395
- standard limit usage and residue, 396
- sugar-based, 7

superbase-added, 81  
synthesis, 4, 5, 7f  
technical properties assessments, 396  
temperature dependence of physical properties of, 230f  
terpene-based eutectic mixture, 305  
timeline of, 5f  
toxicity, 242, 408, 412f  
toxicological profile, 310  
types, 111f, 162  
unavailability, 379  
viscosity, 10f  
whole cells, 167  
Density functional theory (DFT), 169, 186, 187, 190  
Diels–Alder reactions, 94  
Diethanolamine, 77  
Diglycolamine, 77  
Distribution coefficient, 207, 208

## E

Economics and equipment sizing, 216f  
E-factor, 190  
Electrochemical techniques, 42  
Electrodeposition, 11  
Electropolishing, 12  
Energy, 205  
Energy consumption, 86  
Environmentally-benign and sustainable systems, 1  
Environmental Protection and Management Act (EPMA), 377  
Environment, health and safety (EHS) method, 233  
Evaporation methods, 206  
Exothermic reaction, 95  
Extraction methods, 206  
Extractive catalytic oxidative desulfurization (ECODS), 352  
Extractive desulfurization (EDS), deep eutectic solvents, 347  
Extractive oxidative desulfurization (EODS), 352

## F

Fluorescence probes, 91  
Food industry, deep eutectic solvents, 389  
Fossil fuels, combustion of, 195  
Functional deep eutectic solvent (FDES), 198

## G

Gas capture, 14  
  computational models, 14  
  multifacet potentials, 14  
Gas stripping methods, 206  
Goldberg-type C–N coupling reaction, 269  
G-quadruplexes, 14

Green chemistry, 181  
Green chemistry metrics (GCM), 227  
Green chemistry movement, 232  
Greenhouse gases (GHG), 77  
Greenhouse gases (GHGs), 181  
Green solvents, 142  
Green solvents synthesis, 181

## H

Hartree–Fock (HF) method, 169  
High-vacuum scanning electron microscopy, 191  
Hybrid extraction-distillation system, 208, 211, 215  
  flow sheet, 215f, 217f  
Hydrated metal salts, 183  
Hydrodesulfurization (HDS), 346  
Hydrogen bond acceptors (HBAs), 3, 78, 108, 142, 162, 182, 410  
Hydrogen bond donors (HBDs), 3, 78, 108, 142, 162, 182, 187, 206, 242, 407  
Hydrolases, 167  
Hydrophobic DESs, 183, 184, 191  
Hydrophobic ionic liquids (ILs), 206  
Hydrophobicity and hydrophilicity, 416

## I

Ibuprofen-based eutectic mixtures, 304,  
  *see also* Deep eutectic solvents (DES)  
Infinite dilution limit using AIMD simulations, 192  
Inherent Safety Index (ISI), 418  
Inorganic extractions, 93  
Intergovernmental Panel on Climate Change (IPCC), 77  
Ion exchange chromatography, 86  
Ionic conductivity, 11  
Ionic liquids (ILs), 2, 107, 407  
  biodegradability, 119  
  classification, 109  
  combustion and flammability, 413  
  definition, 107  
  density and excess volume, 112  
  physicochemical properties, 112  
  solvatochromic parameters, 116  
  toxicity, 117  
  viscosity, 113  
Isobaric thermal expansion coefficients, 8

## K

Kamlet-Taft (KT) multiparameter scale, 116

## L

Life-cycle assessment (LCA), 233  
Ligand-free cross-coupling reactions, in DES, 254  
Lignin–carbohydrates complexes (LCC), 150

- Lignocellulosic biomass valorization, 121  
  biomass fractionation, 124  
  cellulose dissolution, 122  
  lignin dissolution, 123
- Lipid-base biofuels, 174
- Liquid-liquid equilibria, 205, 206
- Liquid-liquid extraction technique, 207, 211
- Low transition temperature mixtures (LTTMs), 195
- Lydersen-Joback-Reid (LJR), 212
- M**
- Membrane-based separation process, 181
- Membrane distillation process, 183
- Membrane morphology and porosity, 191
- Membrane separation  
  methods, 206  
  processes, 181  
  technology, 191, 182, 413  
  technology processing, 191
- Metabolic processes, 84
- Metal-organic frameworks (MOFs), 184
- Metal reduction methods, 12
- Metal salt and hydrogen bond donor
- Methyldiethanolamine (MDEA), 77
- Methyl urea, 191
- Microwave-assisted DES extraction, 196
- Microwave-assisted synthesis, 198
- Microwave extraction technique, 197
- Microwave heating, 194
- Microwave irradiation, 194
- Modern commercial microwave, 192
- Molecular docking, 170
- Molecular dynamics simulation, 196
- Molecular mechanics calculations, 170
- Multicriteria decision analysis algorithms (MCDA), 417
- N**
- Natural deep eutectic solvents (NADESs), 85, 109, 162, 164, 185
- Natural product extraction, 175
- N-heterocyclic carbene (NHC) ligands, 259
- Nonflammable chemical, 412
- O**
- Organic reactions, 94
- Organic salts  
  hydrogen bond donor, 190  
  metal salts hydrates, 189
- Organic solvents, 93
- Organisation for Economic Co-operation and Development (OECD), 233
- Oxidative desulfurization (ODS), 360
- Oxidative desulfurization, deep eutectic solvents, 351
- Oxidoreductases, 167
- P**
- Persistent compounds, 236
- Persistent organic pollutants (POPs), 236
- Pervaporation techniques, 417
- Phenolic DESs extraction, 196
- Planetary boundaries (PB), 224f, 237
- Polar antioxidants, 42
- Polarity, 88
- Polarizability, 88
- Polyesters, 95
- Polyethylene glycol (PEG), 143
- Polymerized ionic liquids (PYIL), 111
- Pressure swing adsorption (PSA), 182
- Protein separation methods, 93
- Protic ionic liquids (PIL), 109
- Purification methods, 93
- Pyridiniophosphine ligand, 258
- Q**
- Quantitative Safety Health Environmental Index, 414, 415f
- Quantum mechanics calculations, 169
- Quaternary ammonium salt (QAS), 408
- Quaternary phosphonium salts, 242
- R**
- Radial distribution functions (RDFs), 184
- Refractive index, 87
- Response surface methodology (RSM), 359
- Room-temperature IL (RTIL), 111
- S**
- Selectivity and distribution coefficients, 211f
- Solid-state electrolytes, 96
- Solution-based syntheses, 232
- Solution chemistry, 2
- Solvatochromic probes, 92, 90
- Solvents  
  definition, 2  
  developments, 2  
  extraction technique, 206, 207  
  interactions, 90  
  polarity, 88  
  recycling, 126  
  screening setup, 79
- Strecker synthesis, 242
- Supercritical fluids (SCF), 77
- Supported liquid membrane (SLM), 413
- Surface tension, 88, 10
- Sustainable chemicals, 240
- Suzuki–Miyaura reaction, 254

**T**

Task-specific ionic liquids (TSIL), 111

Terpene-based eutectic mixture, 305,  
*see also* Deep eutectic solvents (DES)

Therapeutic deep eutectic solvents, 4

Triethanolamine, 77

**U**

Ullmann reactions

external catalyst, 267

heterogeneous, 264

homogeneous, 267

Ultrasound-assisted technique, 199

**V**

Viscosity, 9

measurement, 191

Volatile organic compounds (VOCs), 181

**Z**

Zeolites, 182



# Current Developments in Biotechnology and Bioengineering

## Deep Eutectic Solvents: Fundamentals and Emerging Applications

*Series Editor*  
**Ashok Pandey**

### About the editors

**Dr. Ashish Pandey** is a Scientist at the Centre for Energy and Environmental Sustainability, Lucknow, India.

**Dr. Bhagyashree Tiwari** is MITACS-ELEVATE researcher in Institut national de la recherche Scientifique - Eau, terre, et environnement, Université du Québec, Canada.

**Prof. Ashok Pandey** is a Distinguished Scientist at the Centre for Innovation and Translational Research, CSIR-Indian Institute of Toxicology Research, Lucknow, India & Distinguished Professor, Sustainability Cluster, School of Engineering, University of Petroleum and Energy Studies, Dehradun, India.

**Ir. Dr. Suzana Yusup** is the Head of Section and Principal Researcher of TNBResearch Sdn Bhd, Department of Generation and Environment, Selangor, Malaysia.

*Deep Eutectic Solvents: Fundamentals and Emerging Applications* provides detailed insights on these neoteric solvents, their synthesis methods, types, physicochemical properties, and sustainable applications in emerging scientific areas. Deep eutectic solvents represent the newest addition among all other nonconventional and alternate solvent systems. Providing a detailed account on the development of deep eutectic solvents with a special focus on their green credentials, and differences from ionic liquids, this book follows a mechanistic approach to the understanding of the role of deep eutectic solvents in gas capture, biomass transformation, biocatalytic process design, membrane-based separation processes, in cross-coupling reactions, and as templates for drug delivery. Including coverage on the use of deep eutectic solvents in emerging areas, such as in CO<sub>2</sub> mitigation, decontaminants, pharmaceuticals, drug discovery, and fuel oil desulphurisation, this book offers a springboard for encouraging vital discussions and inspiring further innovations in the field of environmentally benign eutectic solvent systems. The book also emphasizes the regulatory aspects of DESs use along with their impact on health, safety, and the environment.

### Key Features

- Describes the experimental and theoretical outlook on the physical and chemical properties of deep eutectic solvents.
- Discusses the toxicity profiling of deep eutectic solvents and their importance in designing biocatalytic routes.
- Covers the use of deep eutectic solvents in CO<sub>2</sub> capture, biomass transformations, and organic reactions.



ELSEVIER

[elsevier.com/books-and-journals](http://elsevier.com/books-and-journals)

ISBN 978-0-323-99905-2



9 780323 999052