Free Access to the whole issue

# E3S Web of Conferences

## Volume 287 (2021)

## International Conference on Process Engineering and Advanced Materials 2020 (ICPEAM2020)

**Virtual Conference, July 13-15, 2021**

A. Nzihou, R. Boopathy, M. Nasef, S. Yusup, D.C.W. Tsang, N.A. Amran and B. Abdullah (Eds.)

Export the citation of the selected articles Export

Select all

Open Access

Statement of Peer review

Published online: 06 July 2021

PDF (498 KB)



Open Access

Preface 00001

Ange Nzihou, Ramaraj Boopathy, Mohamed Nasef, Suzana Yusup, Daniel C.W. Tsang, Nurul Aini Amran and Bawadi Abdullah

PDF (163.6 KB) | NASA ADS Abstract Service

Open Access

Opening Remarks 00002

Abdul Halim Shah Bin Maulud

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128700002

PDF (87.75 KB) | NASA ADS Abstract Service

## - *Advanced Kinetics and Thermodynamics*

Open Access

Effect of Monoethanolamine Concentration on $CO_2$ Removal using Continuous High Frequency Ultrasonic Reactor 01001

Siti Munirah Mhd Yusof, Azmi Mohd Sharif, Tay Wee Horng, Farhana Ajua Mustafa and Lau Kok Keong

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128701001

PDF (201.8 KB) | References | NASA ADS Abstract Service

Open Access

The influence of acoustic power on chemical absorption of $CO_2$ using Slow Kinetic Solvent 01002

Fatemeh Shokrollahi and Lau Kok Keong

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128701002

PDF (495.7 KB) | References | NASA ADS Abstract Service

## - *Green and Advanced Materials Engineering*

Open Access

HIC and SSC of Carbon Steel in High Partial Pressure $CO_2$ Environments with Elevated $H_2S$ 02001

Ahmad Zaki Abas, Azmi Mohammed Nor, Muhammad Firdaus Suhor, Ahmad Mustaza Ahmad Rusli and Mokhtar Che Ismail

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128702001

PDF (932.2 KB) | References | NASA ADS Abstract Service

Open Access

Khee Chung Hui, Nur Hafizah Zainal Abidin and Nonni Soraya Sambudi

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128702002



PDF (1.012 MB) | References | NASA ADS Abstract Service

---

Open Access

Screening of Metal Chloride Anion-based Ionic Liquids for Direct Conversion of Hydrogen Sulfide by COSMO-RS 02003

Muhammad Syahir Aminuddin, Zakaria Man, Mohamad Azmi Bustam Khalil and Bawadi Abdullah

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128702003

PDF (675.0 KB) | References | NASA ADS Abstract Service

---

Open Access

Optimization of Slow Pyrolysis of Bamboo for Biochar Production using Taguchi's L9 Orthogonal Array 02004

MNZ Moni, Suzana Yusuf, ASA Manaf and Waqiuddin Rahman

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128702004

PDF (342.6 KB) | References | NASA ADS Abstract Service

---

Open Access

Screening of gallate-based metal-organic frameworks for single-component $CO_2$ and $CH_4$ gas 02005

Marhaina Ismail, Mohamad Azmi Bustam and Nor Ernie Fatriyah Kari

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128702005

PDF (311.2 KB) | References | NASA ADS Abstract Service

---

Open Access

Synthesis and Characterization of Waste Eggshell-Based Montmorillonite Clay Catalyst for Biodiesel Production from Waste Cooking Oil 02006

Muhammad Ayoub, Suzana Yusuf, Abrar Inayat, Sami Ullah, Maliha Uroos, Mushtaq Ahmad, Muhammad Zafar and Zulqarnain

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128702006

PDF (583.9 KB) | References | NASA ADS Abstract Service

---

Open Access

Glycine 02007

Nur Farhana Ajua Mustafa, Azmi Mohd Shariff, WeeHorng Tay and Siti Munirah Mhd Yusof

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128702007

PDF (264.3 KB) | References | NASA ADS Abstract Service

---

Open Access

Preparation of Co-porphyrin catalyst encapsulated in cyclodextrin-based metal-organic framework for coupling reaction 02008

A Nagai, T Hontake, Y Abe, W Michida, H. Inokawa, M Sakuragi, T. Okobira, G Guan and K Kusakabe

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128702008

PDF (560.8 KB) | References | NASA ADS Abstract Service

---

Open Access

Layered double hydroxide supported cobalt nanocluster: size control and the effect in catalytic hydrogen generation 02009

Aishah Mahpudz, Siu Ling Lim, Hitoshi Inokawa, Katsuki Kusakabe and Ryuichi Tomoshige

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128702009

PDF (687.7 KB) | References | NASA ADS Abstract Service

---

Open Access

Evaluation of the antimicrobial performance of menthol and menthol-based deep eutectic solvents as potential future antibiotic 02010

Nor Azrini Nadiha Azmi, Amal Elgharbawy, Hamzah Mohd Salleh and Adeeb Hayyan

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128702010

PDF (324.1 KB) | References | NASA ADS Abstract Service

---

Open Access

Metal-Organic Frameworks: Screening M-MOF-74 (M = Co, Cr, Cu, Fe, Mg, Mn, Ni, Ti, and Zn) Based for Carbon Dioxide Adsorption 02011

N E Fatriyah Kari, M Azmi Bustam and Marhaina Ismail

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128702011

PDF (397.7 KB) | References | NASA ADS Abstract Service

---

Open Access

Yee Ho Chai, Suzana Yusup, Qiu Huan Seer, Muhammad Syafiq Hazwan Ruslan and Bridgid Lai Fui Chin
Published online: 06 July 2021
DOI: https://doi.org/10.1051/e3sconf/202128702012
PDF (436.7 KB) | References | NASA ADS Abstract Service

Open Access

Development of $\alpha Fe_2O_3$-$TiO_2$/$PPO_{dm}$ Mixed Matrix Membrane for $CO_2$/$CH_4$ Separation 02013
Yun Kee Yap, Pei Ching Oh and Evan Yew Jin Chin
Published online: 06 July 2021
DOI: https://doi.org/10.1051/e3sconf/202128702013
PDF (1.038 MB) | References | NASA ADS Abstract Service

Open Access

Conversion of palm oil to new sulfur-based polymer by inverse vulcanization 02014
Amin Abbasi, Mohamed Mahmoud Nasef, Wan Zaireen Nisa Yahya and Muhammad Moniruzzaman
Published online: 06 July 2021
DOI: https://doi.org/10.1051/e3sconf/202128702014
PDF (636.1 KB) | References | NASA ADS Abstract Service

Open Access

Viscosity and Ionic Conductivity of Imidazolium based Ionic Liquids bearing Triiodide Anion 02015
Ruwaida Asyikin Abu Talip, Wan Zaireen Nisa Yahya and Mohamad Azmi Bustam
Published online: 06 July 2021
DOI: https://doi.org/10.1051/e3sconf/202128702015
PDF (360.3 KB) | References | NASA ADS Abstract Service

Open Access

Computational studies of ionic liquids as co-catalyst for $CO_2$ electrochemical reduction to produce syngas using COSMO-RS 02016
Sulafa Abdalmageed Saadaldeen Mohammed, Wan Zaireen Nisa Yahya and Mohamad Azmi Bustam
Published online: 06 July 2021
DOI: https://doi.org/10.1051/e3sconf/202128702016
PDF (483.2 KB) | References | NASA ADS Abstract Service

Open Access

Nor Faizatulfitri Binti Salleh, Muhammad Syafiq Hazwan Bin Ruslan, Aysraf Hanim Ab Rahim, Lim Zu Jian, Fathin Nabilah Binti Azmee, Khafnini Khanafiah, Suzana Yusup and Pradip Chandra Mandal

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128702017

PDF (792.7 KB) | References | NASA ADS Abstract Service

---

Open Access

pH and electrical conductivity measurements of aqueous solutions of amino acid-based ionic 02018

Nur Khairunnisa Talib, Omar Nashed, Bhajan Lal and Ouahid Ben Ghanem

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128702018

PDF (367.0 KB) | References | NASA ADS Abstract Service

## *- Process Systems Engineering & Optimization*

Open Access

A View of Artificial Neural Network Models in Different Application Areas 03001

Kumaravel ArulRaj, Muthu Karthikeyan and Deenadayalan Narmatha

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128703001

PDF (504.0 KB) | References | NASA ADS Abstract Service

---

Open Access

Parametric Optimization of a Two Stage Vapor Compression Refrigeration System by Comparative Evolutionary Techniques 03002

Shuhaimi Mahadzir and Rasel Ahmed

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128703002

PDF (428.9 KB) | References | NASA ADS Abstract Service

---

Open Access

Crude Oil Fouling in Heat Exchangers: A Study on Effects of Influencing Forces 03003

Sampath Emani, M. Ramasamy and Ku Zilati Ku Shaari

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128703003

PDF (1.203 MB) | References | NASA ADS Abstract Service

---

Open Access

Mohamad Hafizi Zakria, Mohd Ghazali Mohd Nawawi and Mohd Rizal Abdul Rahman
Published online: 06 July 2021
DOI: https://doi.org/10.1051/e3sconf/202128703004
PDF (557.2 KB) | References | NASA ADS Abstract Service

---

Open Access
Simulation Comparison Between Equilibrium and Rate-Based Approach for $CO_2$ Removal Via Promoted $K_2CO_3$ with Glycine 03005
Faezah Isa, Haslinda Zabiri, Noorlisa Harun, Azmi Muhammad Shariff, Nur Kamarul Syaabah Ng and Muhammad Afif Asyraf Afian
Published online: 06 July 2021
DOI: https://doi.org/10.1051/e3sconf/202128703005
PDF (638.9 KB) | References | NASA ADS Abstract Service

---

Open Access
Combined Effect of Dispersion Pressure and Concentration on Minimum Ignition Temperature of Corn Dust using Response Surface Methodology – Preliminary Investigation 03006
Ushtar Arshad, Azizul Buang and Khafnini Khanafiah
Published online: 06 July 2021
DOI: https://doi.org/10.1051/e3sconf/202128703006
PDF (863.7 KB) | References | NASA ADS Abstract Service

---

Open Access
Conceptual Framework for the Conservation of Natural Environment from Toxic Ionic Liquids by QSAR Model 03007
Muhammad Ishaq Khan, Dzulkarnain Zaini and Azmi Mohd Shariff
Published online: 06 July 2021
DOI: https://doi.org/10.1051/e3sconf/202128703007
PDF (336.0 KB) | References | NASA ADS Abstract Service

---

Open Access
Bayesian Network for Probability Risk Analysis of Biomass Boiler in Renewable Energy Plant 03008
Nurul Ain Syhadah Mohammad Khorri and Nurul Sa'aadah Sulaiman
Published online: 06 July 2021
DOI: https://doi.org/10.1051/e3sconf/202128703008
PDF (640.5 KB) | References | NASA ADS Abstract Service

Optimization of MDEA-PZ Ratio and Concentration for $CO_2$ Removal in Semi-Lean Membrane Contactor Process 03009

Syafiqa Saleh, Armansyah Razali, Rashid Hanafiah, Athirah Tamidi and Zhe Phak Chan

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128703009

PDF (733.6 KB) | References | NASA ADS Abstract Service

---

Open Access

Heat Transfer Performance of Different Fluids During Natural Convection in Enclosures with Varying Aspect Ratios 03010

Rajashekhar Pendyala, Suhaib Umer Ilyas and Yean Sang Wong

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128703010

PDF (1.742 MB) | References | NASA ADS Abstract Service

---

Open Access

Multiscale fault classification framework using kernel principal component analysis and k-nearest neighbors for chemical process system 03011

Muhammad Nawaz, Abdulhalim Shah Maulud and Haslinda Zabiri

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128703011

PDF (343.1 KB) | References | NASA ADS Abstract Service

---

Open Access

Control valve stiction detection by use of AlexNet and transfer learning 03012

Y. Y. S. Henry, C. Aldrich and H. Zabiri

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128703012

PDF (1.399 MB) | References | NASA ADS Abstract Service

---

Open Access

Propylene Yield from Olefin Plant Utilizing Box-Cox Transformation in Regression Analysis 03013

Mohamad Hafizi Zakria, Mohd Ghazali Mohd Nawawi and Mohd Rizal Abdul Rahman

Published online: 06 July 2021

DOI: https://doi.org/10.1051/e3sconf/202128703013

PDF (475.8 KB) | References | NASA ADS Abstract Service

---

Open Access

## *- Sustainable Process Development*

Rajapandian Rajagopal, Masaharu Komiyama and Azry Borhan
Published online: 06 July 2021
DOI: https://doi.org/10.1051/e3sconf/202128704007
PDF (786.6 KB) | References | NASA ADS Abstract Service

---

Open Access

Cohydrothermal carbonization of waste polyvinyl chloride and wood chip for dechlorination 04008
K Kusakabe, T Steven, JY Ong, Y Uemura and K Ikenaga
Published online: 06 July 2021
DOI: https://doi.org/10.1051/e3sconf/202128704008
PDF (519.8 KB) | References | NASA ADS Abstract Service

---

Open Access

Purification of Anthocyanin Extract from Roselle by Progressive Freezing: Effect of coolant temperature and stirring rate 04009
Aisyah Nur Hanis Azhar, Muhammad Athir Mohamed Anuar, Siti Nor Adibah Mustapha and Nurul Aini Amran
Published online: 06 July 2021
DOI: https://doi.org/10.1051/e3sconf/202128704009
PDF (265.0 KB) | References | NASA ADS Abstract Service

---

Open Access

Modeling of reaction kinetics in generation of hydrogen from wastewater by microbial electrolysis 04010
Ujwal Shreenag Meda, Lourdu Antony Raj Molayan Amritanatan and Kruthika Parappa
Published online: 06 July 2021
DOI: https://doi.org/10.1051/e3sconf/202128704010
PDF (435.5 KB) | References | NASA ADS Abstract Service

---

Open Access

A review on sustainability and quality of biochar production from oil palm biomass in Malaysia using thermal conversion technology 04011
Mustakimah Mohamed and Suzana Yusup
Published online: 06 July 2021
DOI: https://doi.org/10.1051/e3sconf/202128704011
PDF (489.1 KB) | References | NASA ADS Abstract Service

---

Open Access

Standard methods used for mercury analysis in the oil and gas industry 04012

E3S Web of Conferences
eISSN: 2267-1242

https://doi.org/10.1051/e3sconf/202128702010

# Evaluation of the antimicrobial performance of menthol and menthol-based deep eutectic solvents as potential future antibiotic

*Nor Azrini Nadiha* Azmi[1], *Amal* Elgharbawy[*], *Hamzah* Mohd Salleh[1*], and *Adeeb* Hayyan[2]

[1]International Institute for Halal Research and Training (INHART), International Islamic University Malaysia, P.O. Box 10, 50278 Kuala Lumpur, Malaysia

[2]Department of Chemical Engineering, Faculty of Engineering, Universiti Malaya, 50603 Kuala Lumpur, Malaysia

**Abstract.** Triggered by the strong antimicrobial activities of menthol and various fatty acids, eutectic mixtures based on the components are developed, producing new solvents that have possibilities to become a new antibiotic. This study aims to provide an insight into the antimicrobial activities of the new deep eutectic solvents (DESs) developed. Menthol-based DES combined with fatty acids, namely propionic acid, butanoic acid, hexanoic acid, octanoic acid, decanoic acid, and levulinic acid, were successfully obtained and their thermal profile was analyzed. The antimicrobial potential of DES systems was evaluated against both Gram positive and Gram negative bacteria. Owing to the activities of the start-up components, the results are considered promising, and this illustrates the potential of the newly obtained DESs as a new antimicrobial agent in various fields such as food, cosmetics as well as pharmaceutical.

## 1 Introduction

A novel solvent that fulfills the criteria of Green Chemistry has long become a dispute in the chemistry field. Abbott et al. [1] firstly pioneered deep eutectic solvent, a new type of solvents which interestingly appears to become alternatives to the conventional organic solvents. DESs defied most of the conventional solvents' characteristics. Different from the latter solvents, DESs exhibit excellent properties such as biodegradable, low costs, sustainable, non-volatile, non-toxic, and also easy and simple preparation [2].

DES is described as a mixture of two or more components, when at a certain molar ratio, significant reduction of the melting point is demonstrated, resulting in a liquid state at room temperature [3]; [4]. This combination is usually associated and characterized by a decreased freezing point than the individual compound [5]**.** This phenomenon appears as it is because of the formation of hydrogen bonding interactions between the compounds, namely hydrogen bond donor and another one as hydrogen bond acceptor [5].

The possibilities of the formation of DES are endless, accounting for possibly $10^6$ individual mixture. Thus, making DES flexible and tunable for many applications in various fields [6]. Due to the versatility, variety of DESs had been used in applications such as extraction media for bioactive natural component [7]; [8]; [9], electrochemical processes [10] , and also molecular sensing [11]. Other than that, DES had been used in various research in the biomedical field in terms of enhancing the performance of biological materials and improving active pharmaceutical ingredients (APIs). Several studies recently have also focused on DES with antibacterial properties, which indicate the potential of DES as a wide-spectrum antiseptic agent for therapeutic and also preventive applications.

In this study, menthol was selected as a hydrogen bond acceptor, and various fatty acids act as hydrogen bond donor. Menthol is chosen for the activities it possessed. The biological properties of menthol include antibacterial, analgesic, anaesthetic, antifungal, and penetration-enhancing effects in addition to chemopreventive and immunomodulating actions [12]. Menthol had also emerged as both hydrogen bond donor and hydrogen bond acceptor in the formation of DESs [5,13]. Long-chain fatty acids were being used in this study as they exhibit antibacterial activity and are the key ingredients of antimicrobial food additives and some antibacterial herbs.

The aim was to reveal the potential of menthol and fatty acids as antimicrobial agents in DES form due to the possible synergistic effects among their counterparts. An insight into the antibacterial activity of the DESs formed from menthol, and different fatty acids with different chain size length are expected from this research.

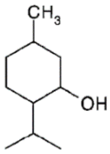
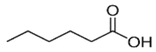
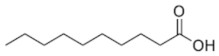
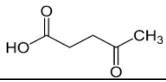
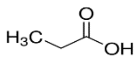
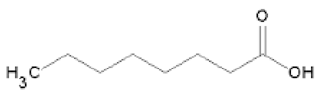
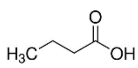
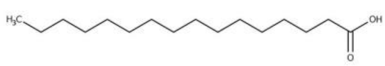
[*] Corresponding author: hamzah@iium.edu.my

# 2 Experimental section

## 2.1 Preparation of DESs

The DESs were prepared by mixing menthol and various fatty acids such as propionic acid (R&M, ≥99%), butanoic acid (R&M, AR grade), hexanoic acid (Sigma Aldrich, ≥96%), octanoic acid (Sigma Aldrich, ≥98%), decanoic acid (R&M, ≥99%), levulinic acid (Nacalai Tesque, ≥97%), palmitic acid (Sigma Aldrich, ≥98%), and dodecanoic acid (R&M, ≥99%) in the desired amounts, to obtain molar ratios of 1:1. The molar ratio is chosen as the reported procedure by [14]. For each mixture, the constituents were transferred into a completely sealed glass flask and heated to 70 °C, for four hours without stirring for all the mixtures to ensure the formation of a homogenous, transparent liquid. The mixture was allowed to cool naturally to room temperature. For the mixtures which did not form a liquid, the process was considered concluded after 16 h [3]. Table 1 lists hydrogen bond acceptor and hydrogen bond donors used in the study.

Table 1. Hydrogen bond acceptor and hydrogen bond donor utilized in the study

| Hydrogen bond acceptor and structure | Hydrogen bond donor and structure |
|---|---|
| **Menthol**  | Hexanoic acid  |
| | Decanoic acid  |
| | Levulinic acid  |
| | Propionic acid  |
| | Octanoic acid  |
| | Butanoic acid  |
| | Palmitic acid  |
| | Dodecanoic acid  |

## 2.2 Thermal analysis

Differential scanning calorimetry (DSC) measurements were performed in aluminium cells at a heating rate of 10 °C/min (Mettler Toledo DSC 1, USA). Approximately 10–15 mg of DES samples were weighed into the aluminium liquid pan. Samples were scanned from -30 °C to 500 °C. The experiments were performed under a nitrogen atmosphere (50 ml/min). The procedures followed [3].

## 2.3 Assessment of antimicrobial activity

Two Gram positive (*Staphylococcus aureus* ATCC 12600 and *Bacillus subtilis* ATCC11774) and one Gram negative bacteria (*Escherichia coli* ATCC 1129) were pre-cultured by transferring loopful of cells into 10 ml of already autoclaved LB broth and allowed to incubate at 37 °C for 24 h. The standard cells were spread on the plates by using a sterile cotton bud. For the disc diffusion assay, a sterile 6 mm diameter filter paper (Whatman No. 1) was soaked with different concentration DES solutions and allowed to equilibrate before placing on the seeded plates and allowed to stand before incubation. The plates were then incubated at 37 °C for 24 h before the diameters of zones of inhibition were then measured. These were repeated in three replicates for each of the tested organisms. Tetracycline at 5 mg/ml and 100% dimethyl sulfoxide (DMSO) were used as positive and negative controls, respectively [6];[15].

# 3 Results and discussion

## 3.1 Preparation of DESs and visual aspect

Eight samples of DESs were prepared using menthol as hydrogen bond donor and various fatty acids as hydrogen bond acceptor. The formation of the DESs, along with their designations as well as the visual aspect of the mixture are listed in Table 2.

Table 2. Components of the DESs, molar ratio used, and the visual aspects

| **Designa-tion** | **Compo-nent 1** | **Compo-nent 2** | **Molar ratio** | **Visual aspect** |
|---|---|---|---|---|
| DES 1 | Menthol | Propionic acid | 1:1 | Transparent liquid |
| DES 2 | | Butanoic acid | | Transparent liquid |
| DES 3 | | Hexanoic acid | | Transparent liquid |
| DES 4 | | Octanoic acid | | Transparent liquid |
| DES 5 | | Decanoic acid | | Transparent liquid |
| DES 6 | | Levulinic acid | | Transparent liquid |
| DES 7 | | Palmitic acid | | White, Solid |
| DES 8 | | Dodecanoic acid | | White, Solid |

During the preparation process, throughout heating, the mixtures of menthol with all fatty acids gradually obtained the liquid aspect. However, upon cooling, only DES 1,2,3,4,5 and 6 retain as liquid such as illustrated in Figure 1. DES 7 and DES 8 were discarded from further characterization as both of the compounds are not successfully mixed and the products after cooling were in white solid form. The reason DES 7 and DES 8 are in solid phase after mixing and heating is most probably because the amount of menthol was not enough to build hydrogen bonding with the palmitic acid and dodecanoic acid. This results in a saturation of acid in the mixture and no further decrease in freezing point was achieved. The high concentration of hydrogen bond donor compared to hydrogen bond acceptor makes the mixture heterogeneous and even after a long time of shaking under high temperature, upon cooling, the mixture still becomes solid. This can also be seen in a study conducted by Hayyan et al. [16] that confront the same situation when the amount of glucose as hydrogen bond donor exceeds the amount of choline chloride which acts as hydrogen bond acceptor.

Figure 1. Successful DES 2 obtained when menthol and butanoic acid are combined with 1:1 molar ratio.

### 3.2 Thermal analysis

Differential scanning calorimetry is one of the most used methods for thermal analysis, measuring the temperature and energy associated with a range of thermal events, including melting, crystallization, and glass transitions. Many studies have been using this method to analyze the thermal events happening in the DESs. The melting point of the menthol and their eutectic mixtures are also presented in Table 3.

Table 3. Melting temperatures of menthol and DES obtained in the study

| Component/Mixture | $T_m$ (°C) |
|---|---|
| Menthol | 38.00 |
| DES 1 | 41.34 |
| DES 2 | 195.89 |
| DES 3 | 158.68 |
| DES 4 | 160.07 |
| DES 5 | 95.95 |
| DES 6 | 59.59 |

From Table 3, D,L-menthol shows melting point at 38 °C. (Alhadid et al., [17] decribed L-menthol had low value of melting enthalpy, thus making L-menthol a good candidate for designing deep eutectic systems. It can be seen clearly that in all cases, the melting temperature of the mixture is different than those of the pure starting components, which confirms that these DES are supramolecular complexes in the liquid state over a wide temperature range. Consequently, less pure compounds will exhibit a broadened melting peak that begins at a lower temperature than a pure compound as shown in Figure 2 exhibiting the thermal profile of DES 4. In all the DESs, a depression of the melting point occurs. Figure 2 shows the DSG thermogram for DES 4, where all the peaks are endothermic suggesting fusion process is occurring. Endothermic process is a thermal event of a material where energy is absorbed by the material which appears to occur in this case. This is similar to all DSC analysis of the DES in this study.

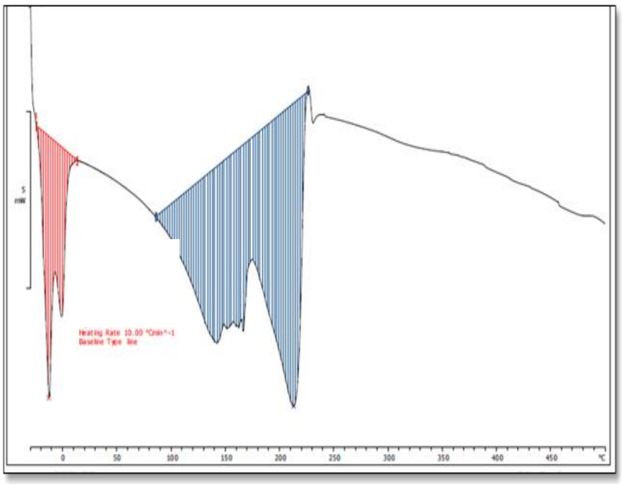



Figure 2. The thermal profile of DES 4 (Menthol: Octanoic acid with 1 to 1 ratio).

### 3.3 Antimicrobial properties evaluation

The antimicrobial potential of the various DES formulations was evaluated using disk diffusion assay, which was carried out using different selected microbial strains. From Table 2, it can be seen that all the DESs exhibit antimicrobial properties against all microbes tested. The results for Gram positive bacteria, *B. subtilis* and *S. aureus* is supported by a similar study [6], which shows good inhibition of the DESs to the tested microbes. The largest inhibition zone for *B. subtilis* is obtained when using DES 2, and the smallest is with DES 4. DES 2 also showed the largest inhibition zone for *S. aureus*, while DES 1 has the smallest inhibition zone. The results are comparable to the study by (Huang et al. [18], which stated that short and medium-chain fatty acids possessed antibacterial activity. The reason for this is thought to be attributed to the cell wall of Gram positive bacteria which readily absorbs fatty acids allowing their passage into the inner membrane, thus interact with intracellular sites critical for antibacterial activity [19]. However, our results for Gram negative bacteria, *E. coli* is very different from their study. In this study, DES 3 showed the largest inhibition zone, while the smallest was exhibited by DES 4. Piran et al. [19] stated that Gram negative bacteria are usually resistant to the antibacterial activity of fatty acids because of more complex membrane structure. Desbois and Smith [20] reported that the presence of lipopolysaccharides on the cell wall prevents the fatty acids from reaching cell membrane and exerting its effect. However, our results showed different trends and this could be due to the presence of menthol. Menthol possessed strong antibacterial activity towards Gram negative bacteria [21]. Figure 3 (a) and (b) show the inhibition zones of the DES on microbes tested.

Table 4. Inhibition measurements (diameter (mm)±SD) for the various DES formulations. Results are presented by formulation for each microbial strain tested. Tetracycline is positive control and DMSO is the negative control.

| DESs | *B. subtilis* | *S. aureus* | *E. coli* |
|---|---|---|---|
| DES 1 | 10.33± 0.57 | 6.33± 0.94 | 6.00± 0.47 |
| DES 2 | 14.67± 0.47 | 11.67± 0.82 | 4.33± 0.57 |
| DES 3 | 12.67± 1.15 | 8.67± 0.57 | 8.67± 1.52 |
| DES 4 | 6.33± 1.52 | 8.67± 0.58 | 1.33± 0.57 |
| DES 5 | 8.67± 1.52 | 7.67± 0.57 | 2.33± 0.82 |
| DES 6 | 10.33± 0.47 | 7.00± 1.00 | 8.00± 1.15 |
| DMSO | 0.00± 0.00 | 0.00± 0.00 | 0.00± 0.00 |
| Tetracycline | 35.67± 0.33 | 38.50± 0.41 | 24.33± 0.94 |

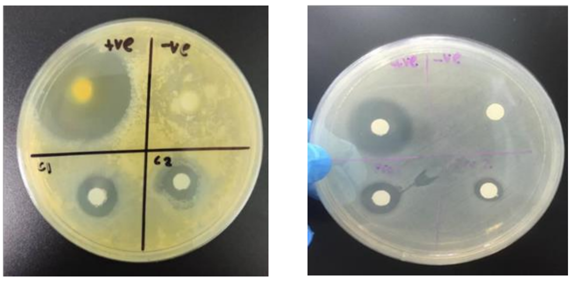



Figure 3. (a) shows the inhibition zone of DES 5 on *B. subtilis* and (b) shows the inhibition zone of DES 3 on *E. coli*.

## 4 Conclusion

Due to the renowned antimicrobial properties of fatty acids and menthol, this study presented new green solvents based on eutectic mixtures. This study provides an insight into the antimicrobial activity of menthol based DESs. Antimicrobial activity of different DESs was assessed against three types of microbes. From the results obtained, one of the promising DES was DES 2 (menthol: butanoic acid at 1:1 molar ratio) which had the largest inhibition zone against both Gram positive bacteria tested. DES 3 (menthol: hexanoic acid at 1:1 molar ratio) possessed the highest antimicrobial activity against *E. coli* which is a Gram negative bacteria. A more thorough study on antimicrobial activity of DESs should be carried out ton a wider array of microbes. These DESs might be one of the components to produce antimicrobial agents in food, cosmetics, or even pharmaceutical area as it consists of natural constituents.

**Acknowledgement**

This research was funded by the Fundamental Research Grant Scheme, MoHE-Malaysia [FRGS19-027-0635] (Hamzah Mohd Salleh), and Research Management Centre, IIUM [RMCG20-021-0021] (Amal A. M. Elgharbawy).

### References

1. Abbott, A.P.; Capper, G.; Davies, D.L.; Rasheed, R.K.; Tambyrajah, V. *Chem. Commun.* 70–71, (2003).
2. Dai, Y.; Witkamp, G.; Verpoorte, R.; Hae, Y. *FOOD Chem.* **187**, 14–19, (2015).
3. Aroso, I.M.; Paiva, A.; Reis, R.L.; Duarte, A.R.C. *J. Mol. Liq.*, **241**, 654–661, (2017).
4. Hayyan, A.; Mjalli, F.S.; AlNashef, I.M.; Al-Wahaibi, T.; Al-Wahaibi, Y.M.; Hashim, M.A. *Thermochim. Acta*, **541**, 70–75, (2012).
5. Ribeiro, B.D.; Florindo, C.; Coelho, M.A.Z.; Marrucho, I.M. (2015).
6. Silva, J.M.; Silva, E.; Reis, R.L.; Duarte, A.R.C. *Sustain. Chem. Pharm.* **14**, 100192, (2019).
7. Ahmad, I.; Pertiwi, A.S.; Kembaren, Y.H.; Rahman, A.; Mun'im, A. *J. Appl. Pharm. Sci.*, **8**, 138–143, (2018).
8. Dai, Y.; Witkamp, G.J.; Verpoorte, R.; Choi, Y.H. *Anal. Chem.*, **85**, 6272–6278, (2013).
9. Saravana, P.S.; Ho, T.C.; Chae, S.J.; Cho, Y.J.; Park, J.S.; Lee, H.J.; Chun, B.S. *Carbohydr. Polym.*, **195**, 622–630, (2018).
10. Baby, J.N.; Sriram, B.; Wang, S.F.; George, M. *ACS Sustain. Chem. Eng.*, **8**, 1479–1486, (2020).
11. Krishnan, S.K.; Chipatecua Godoy, Y. *ACS Omega*, **5**, 1384–1393, (2020).
12. A. Farco, J.; Grundmann, O. *Mini Rev. Med. Chem.*, **13**, 124–131, (2012).
13. Pereira, C. V.; Silva, J.M.; Rodrigues, L.; Reis, R.L.; Paiva, A.; Duarte, A.R.C.; Matias, A. *Sci. Rep.*, **9**, 1–11, (2019).
14. Tang, W.; Dai, Y.; Row, K.H. *Anal. Bioanal. Chem.*, **410**, 7325–7336, (2018).
15. Hayyan, M.; Hashim, M.A.; Al-Saadi, M.A.; Hayyan, A.; AlNashef, I.M.; Mirghani, M.E.S. *Chemosphere*, **93**, 455–459, (2013).
16. Hayyan, A.; Mjalli, F.S.; AlNashef, I.M.; Al-Wahaibi, Y.M.; Al-Wahaibi, T.; Hashim, M.A. *J. Mol. Liq.*, **178**, 137–141, (2013).
17. Alhadid, A.; Mokrushina, L.; Minceva, M. *Molecules*, **25**, 1–11, (2020).
18. Huang, C.B.; Alimova, Y.; Myers, T.M.; Ebersole, J.L. *Arch. Oral Biol.*, **56**, 650–654, (2011).
19. Piran, P.; Kafil, H.S.; Ghanbarzadeh, S.; Safdari, R.; Hamishehkar, H. *Adv. Pharm. Bull.*, **7**, 261–268, (2017).

20. Desbois, A.P.; Smith, V.J. *Appl. Microbiol. Biotechnol.*, **85**, 1629–1642, (2010).
21. Pľuchtová, M.; Gervasi, T.; Benameur, Q.; Pellizzeri, V.; Gruľová, D.; Campone, L.; Sedlák, V.; Cicero, N. *Nat. Prod. Commun.* **13**, 1051–1054(2018).