

A stylized human figure composed of white and yellow lines, with a green dot for a head and yellow leaves for hair. The figure is surrounded by a network of white and yellow lines, some ending in dots, suggesting a digital or networked environment. The background is a dark blue gradient with a faint network pattern.

EMBRACING SOCIETY 5.0 WITH HUMANITY

Editor: Diah Karmiyati

 Bildung

Copy right ©2022
All rights reserved

Embracing Society 5.0 with Humanity

Editor : Diah Karmiyati
Desain Sampul : Ruhtata
Lay out/tata letak Isi : Tim Redaksi Bildung

Perpustakaan Nasional: Katalog Dalam Terbitan (KDT)
Yogyakarta: CV. Bildung Nusantara, 2022

x + 1115 halaman; 15 x 23 cm
ISBN: 978-623-6225-67-7
Cetakan Pertama: Maret 2022

Penerbit:
BILDUNG
Jl. Raya Pleret KM 2
Banguntapan Bantul Yogyakarta 55791
Telepon: +6281227475754 (HP/WA)
Email: bildungpustakautama@gmail.com
Website: www.penerbitbildung.com Anggota IKAPI

Bekerja sama dengan Direktorat Program Pascasarjana
Universitas Muhammadiyah Malang

***Embracing Society 5.0
with Humanity***

Embracing Society 5.0 with Humanity

Society 5.0 is a concept presented by the Japanese as a core concept of their economic system. They believed that technology should not surpass the intelligent of men. As such, in society 5.0 the Japanese government would like to ensure that all technological things are designed to be a human-centered design. In fact, their ministry of education in 2018 has also been readily prepared the future generation through a change in their education system. For example, the minister explains that in Japan, or many parts of the world, university entrance are divided into two main concentrations, which are science and social science. The minister thought of changing the system, as society 5.0 is about creating a technology that is human centered. For instance, they gave an example on designer babies. If, people from hard science learn about philosophy, ethics, and humanities, they won't face such ethical concern when developing a product. This is what is being envision by the Japanese government for their younger generation. Collaboration between science and social science is necessary to build a better environment for our future children. Another example is the companies in Japan, such as Hitachi and Fujitsu has already been implementing this 5.0 by designing product that relied fully on technology but puts human at its center (Hitachi, 2017).

Likewise, it is currently a hot topic in Indonesia. Indonesia as a country with the 4th largest population in the world has not been implemented this concept. Our country is still on the industry 4.0. Yet, with the rising interest in AI, Blockchain, NFT, number of unicorn start-up. and all recent technological changes, our country are ready to compete with any other countries in Southeast Asia. Society 5.0 is coming, and we need to embrace it. To prepare with the society 5.0, It is not only the technological side. It is necessary for us to have a strong principle at hearts that based on our belief system. We, as an Indonesian have known to be religious that most of us believed in God. We also commonly practice our religion and tend to be kind to people because we know God would love our good deeds. I personally think that this will help us to move forward and live together with advanced technology.

Technology begets a very important leap in human's life journey. It is important to keep valued of the benefit but it's more important to look out for the human itself. As its purpose is smarter than us, to help us, it will be very ideal if we embrace the technology using our ability to be kind.

Malang, 21 Maret 2022

Diah Karmiyati

Daftar Isi

Market Potential of <i>Kafalah Bil Ujroh</i> Sharia Guaranteee Through E-Policy During the Covid-19 <i>A. Ifayani Haanurat, Ifadhila</i>	1
Development students character in 5.0 era through learning to write based on stories of the loves one <i>Abd. Rahman Rahim</i>	9
Higher Education and Human Resources Development for The Society 5.0 Era <i>Adri Efferi</i>	20
Pesticide Residual and Nutrition of Organic Cultivation Rice with Pumakkal and Conventional <i>Agus Sutanto, Hening Widowati, Achyani, Nendi Hendri, Feny Thresia, Eka Setyaningsih</i>	33
Social Capital in The Empowerment of Muslim Communities Face 5.0 Society <i>Agus Wahyu Triatmo</i>	40
Transformation Of Religiousity Of The Community At Wonolagi Gunung Kidul Yogyakarta <i>Ahmad Salim Novi Handayani</i>	49
Early Marriage Before and During Pandemic Covid-19 (Revolutionary Era of Society 5.0) <i>A'im Matun Nadhiroh</i>	57
E-Gov, Realization Of Anti Corruption Policy (long journey to Era Society 5.0) <i>Amalia Syauket</i>	66
Use of Voice Recognition of "Cake" Android-Based Application to Improve Student's Pronunciation <i>Amaluddin, Mutiah Nur Adzra, Siti Hajar Larekeng</i>	77

Combination of Curcumin and Honey as Supporting Therapy for Typhoid Fever in Children <i>Ami Febriza</i>	87
Employees Readiness Improvement Model to Face Changes in The Society 5.0 Era: Study On Indonesian Expatriates Abroad <i>Anggia Sari Lubis</i>	94
Features of Collaborative Writing in EFL Context <i>Ani Susanti</i>	103
The Hoax as Terror Communication: Threats and Challenges in Society 5.0 <i>Ari Sulistyanto, Hamida Syari Harahap, Wichitra Yasya</i>	112
Implementation of Human Resources in Sharia Capital Market Study Group During Covid-19 <i>Asri Jaya, A.Ifayani Haanurat, Nurlina, Nur'aeni</i>	121
Acts of Terrorism as a Crime Against Humanity Under International Law <i>Aulia Rosa Nasition</i>	127
Prophetic Legal Science Paradigm in The Era of Society 5.0 <i>Auliya Khasanofa</i>	137
IP Appraiser Role in The Implementation of Copyright as a Collateral in Indonesia <i>Cita Yustisia Serfiyani</i>	144
Indonesian Slangs in The Digital Communication <i>Dewi Kusumaningsih</i>	151
Students' Spatial Reasoning In Solving The Flat Shapes Problem <i>Dewi Risalah</i>	160
Industrial Revolution 4.0 and Society 5.0 Eras: From The Strategic Human Resource Management's Perspective <i>Dianawati Suryaningtyas</i>	165

The Online Learning Resources in Mastering Listening Comprehension: Students' and Teachers' Perspectives <i>Dodi Mulyadi</i>	173
Building Character Strengths through “new Islamic education” in Facing Era Society 5.0: Bibliometric reviews <i>Elihami, Kana Safrina, Riana Mashar, Hary Murcahyanto</i>	182
Ultraviolet Exposure To Energy Intake Synthesis Of Vitamin D <i>Emillia Devi Dwi Rianti</i>	194
Description Of Maternal-Fetal Attachment In Public Health Community Center Yogyakarta <i>Endang Koni Suryaningsih, Sri Subiyatun</i>	201
MSMEs Empowerment Strategy in Rural Areas Facing The Society ERA 5.0 <i>Endang Sungkawati</i>	208
Learning Assessment System in Islamic Higher Education <i>Enung Nugraha</i>	217
Midwifery Student Perception of Online Learning <i>Farida Kartini</i>	226
Implications of Constitutional Court Decision No. 91/PUU-XVIII/2020 on Working Relationship with PKWT Reviewed from Legal Certainty <i>Fithriatus Shalihah</i>	234
Dynamics Of The Digitalization Era For Women Umkm Activitiest <i>Hamida Syari H Ari Sulistyanto, Wichitra Yasa, Nita Komala Dewi</i>	243
Digital Marketing for Industrial Farming <i>Haris Hermawan</i>	252
Work Experience and Work Achievement Effect On Lecturer's Career <i>Hary Murcahyanto, Mohzana, Adri Efferi, Emilda Sulasmi, Koidah</i>	259

Development of Traditional Music Learning Media Using Macromedia Flash 8 <i>Hary Murcahyanto, Mohzana , Farida Sani</i>	273
Spices Removal Heavy Metal Pollutants, Increase CA and Protein in Foods <i>Hening Widowati, Agus Sutanto, Widya Sartika Sulistiani, Evita Anggereini, Maria Ulfah, Merri Sri Hartati, Asih Fitriana Dewi</i>	285
Teaching The Capita Selecta of Zoology Era 5.0 Based on the Surrounding Approach <i>Hening Widowati, Agus Sutanto, Widya Sartika Sulistiani, Evita Anggereini, Maria Ulfah, Merri Sri Hartati, Asih Fitriana Dewi</i>	307
Improved internal quality assurance system based on iso 9001:2008 with document management control (dmc) and web-based applications <i>Hermien Tridayanti Bayu Putra Airlangga</i>	325
Benefiting from Online Learning as a Shortcut to Address Society 5.0 Challenges: EFL Students' Perspective <i>Hersulastuti</i>	333
Bundes Services Can Improve the Community's Economy In Sharia Perspective <i>Heru Cahyono, Muh. Fahrurrozi, Nursaid</i>	344
Students' Critical Thinking In Solving Hots Problems: A Case Study In Gender Perspective <i>Ida Riskiana Dewi, Umy Zahroh</i>	359
Strengthening Pedagogical Competence of 21 st Century Teachers <i>Ifit Novita Sari</i>	368
Flipped Classroom Assisted by WhatsApp: Bridging Mathematics Learning During Pandemic and Era of Society 5.0 <i>Iis Holisin</i>	376
	387

Women Protection Against Sexual Violence Based On Human Security in The Era of 5.0 Society <i>Ika Dewi Sartika Saimima</i>	
A Mutualistic Talent Advantage In Teamwork Performance <i>Ika Nurul Qamari</i>	393
Corpus and Data-Driven Learning:Big Data for Language Teachers <i>Ikmi Nur Oktavianti</i>	402
Analysis of Leadership Style and Work Environment : The effect on employee Job Satisfaction <i>Irwan Idrus, Jumriani, Mutia Mursidiq Hasan</i>	413
The Architecture of <i>Banua tada</i> Buton, Southeast Sulawesi and its Challenges in the Future <i>Ishak Kadir, M. Husni Kotta</i>	420
Coping Strategy for the Defense of Persons with Disabilities During the Covid-19 Pandemic <i>Islamiyatur Rokhmah</i>	432
Prophets' Parenting Strategy Applied In The New Normal <i>Kana Safrina Rouzi</i>	436
Interconnection between Students' Cognitive Obstacles and Cognitive Load Theory in the Era of Society 5.0 <i>Kartinah</i>	447
From pandemics to business opportunities by young people: an opportunity and development <i>Kristina Sedyastuti</i>	456
Characteristics Of Lactic Acid Bacteria In Feces Of Mongoose (<i>Paradoxurus Hermaphroditus</i>) In District Jember <i>Kukuh Munandar</i>	463
Learning Geometry And Values From The Begalan Tradition: Ethnomatematic In Begalan Culture Of Banyumas, Indonesia <i>Kusno, Umy Zahrah, Reni Astuti, Muchtadi, Kusaeri, Triyono</i>	470

The Sustainability Of Maritime Eco-Lexicon Of Bungku Language In Morowali Regency <i>La Ino, Samsul and Maliudin</i>	483
Science And Interpretation Of The Qur'an In Indonesia Tracing The Scientific Interpretation Pattern In At-Tanwir Muhammadiyah's Tafsir <i>M Nurdin Zuhdi, M. Anwar Nawawi</i>	493
Locally Community Institutional Sustainability in Environmental Isolation Faced Pandemic becomes Endemic <i>Maharani, Marlinda Irwanti, Anita Ristianingrum</i>	501
Development of Teaching Materials Based On Mathematical Reasoning To Improve Mathematical Ability <i>Maifalinda Fatra, Lilis Marina Angraini</i>	522
Telenursing in Schizophrenia <i>Mamnuaah, Noorwahyu Trihidayati</i>	531
Practice speaking and social interaction for mentally retarded children through fantasy stories and role playing <i>Marwiah</i>	539
Antibiofilm Activity of Honey in Multispecies Pathogen <i>Masfufatun, Lusiani Tjandra, Budhi Setiawan</i>	562
Mother as Mother: Welcoming the Society Era of 5.0 <i>Mohd. Nasir</i>	576
Development of Audio Visual Media Based on Macro Media Flash 8 on Dayang-Dayang Dance Learning <i>Mohzana , Hary Murcahyanto , Linda Laili Harjuni</i>	584
Leadership And Principal Work Motivation Influence On School Operator Performance <i>Mohzana, Hary Murcahyanto, Adri Efferi, Emilda Sulasmi, Koidah</i>	596

Teacher Decision Making: Strategies to Give Examples Through Posing and Solving Mathematical Problems <i>Muchtadi</i>	613
Sharia Marketing Era of Industrial Revolution 4.0 in Improving Customer Loyalty <i>Muh. Fahrurrozi, Heru Cahyono, Nursaid</i>	623
Intelligent Transportation Management System (ITMS) in Indonesia Towards Society 5.0 <i>Muh. Nashir T</i>	634
Family Education during the Covid-19 Pandemic: Efforts to Build Parent-Child Attachment <i>Muhammad Abrar Parinduri</i>	643
Implementation of Digital Marketing as Integrated Marketing Strategy for Small and Medium Business Products in Palopo City <i>Muhammad Aqsa, M. Risal</i>	659
Sustainable Development 4.0 in Indonesia: eTOURISM, eMOBILITY, eCITIES and eDESA <i>Muhammad Ikhsan Setiawan, I Nyoman Sudapet, Agus Sukoco, Ronny Durrotun Nasihien, Che Zalina Zulkifli and Mohd Idrus Mohd Masirin</i>	668
Management of Science Learning in the Era of Society 5.0 in Indonesia <i>Muhammad Minan Chusni</i>	683
Culture Freedom to Learn Based on the Philosophy of the Indonesian Nation in Entrepreneurship Courses in the Era of Society 5.0 <i>Nanis Hairunisya</i>	690
Development of Children's Basic Movement Skills <i>Nevi Hardika</i>	699
Implementation of Quality-Based Islamic Worldviews Competitiveness in Industry 4.0 and Era of Society 5.0 <i>Novi Indriyani Sitepu</i>	708
	716

Disease Perception And Its Relation To Quality Of Life Of Undergoing Haemodialysis Patients <i>Nur Chayati, Nur Aini Handayani</i>	
Reconstruction of agent-based model in predicting the risk of stock On Indonesian Stock Exchange (BEI) <i>Nursaid, Heru Cahyono, Muh. Fahrurrozi</i>	727
How to Increase Customer Satisfaction Based on Service Quality, Brand, And Trust in Cafe Customers? <i>Nurul Qomariah, Wekel Mega Wisesa</i>	739
Revitalization of Islamic Religious Education Readiness Facing Era 5.0 <i>Nurzannah</i>	758
Gender Digital Divide and Empowering Women in the Industrial Age 5.0 <i>Oktiva Anggraini</i>	768
Practicing Communication, Collaboration, Critical Thinking and Creative Thinking Skills in Learning <i>Peni Suharti</i>	777
Utilization Of <i>Canva</i> In Learning To Write Poetry As A Learning Source In The Era Society 5.0 <i>Purwati Zisca Diana</i>	786
Postmethod Era and Its Implication to Language Teacher's Education <i>Purwo Haryono</i>	796
The Existence of Religion, Scripture, and Islamic Thinkers in the Era 5.0 <i>Rafiudin</i>	804
Realization of Online Learning in the Perception of Junior High School Student <i>Rizka Harfiani</i>	812
Indonesia In Society 5.0 ; Impact On Legal Policy <i>Rizka</i>	822

The Implementation of the Teaching and Learning Model of the Value Clarification Technique in Society Era 5.0 <i>Ronggo Warsito, Dhiva Maulida Rizqi Nur'Aini</i>	832
Telepsychology: Alternative Digital Mental Health Services Towards The Society Era 5.0 <i>Rr. Setyawati</i>	841
Blended Learning in Islamic Education Learning: Moderate Learning Model in Society 5.0 Ruslan, Luthfiyah	853
Framing English Language Teacher in Facing Society 5.0: Challenges and Adaptive Strategy <i>Salasiah Ammade, Khairil</i>	861
Vocational High School Learning In Era 5.0 <i>Singgih Prastawa</i>	871
The contribution of science in building society 5.0 <i>Siti Patonah</i>	865
Building Student Character In Writing Poetry Based On Makassar Local Wisdom In The Era Of Society 5.0 <i>Siti Suwadah Rimang</i>	897
Early Detection Services Development For The Indonesian Ethnic Group Specified In The Community Era 5.0 <i>Sri Lestari Utami</i>	899
The Impacts Of Industry 4.0 And Society 5.0 To The Sovereignty Of States Based On International Law Perspective <i>Sri Wartini</i>	911
Strengthening Financing Reform For Msmes In The Society Era 5.0 <i>Sriyono</i>	921
Science Education: Its Role in Building Scientific Attitudes in The Context of Society 5.0 Era <i>Suciati</i>	931

The Implementation of Pop Culture as Teaching English Media in Society 5.0 <i>Sudiran</i>	941
Characteristics of Learning Facing the Era of Society 5.0 <i>Sulastri Rini Rindrayani</i>	949
Prevention and Control of Non-Communicable Diseases Era Society 5.0 <i>Sulistyaningsih</i>	958
Fuzzy Logic Optimization Implementation For Optimizing Motor Speed On Barrel Machine <i>Sumardi Sadi</i>	968
Agriculture Based on Biochemistry and Information Systems in Era 5.0 <i>Suryani</i>	982
<i>Problem Based Learning</i> Model Integrated With Islamic Values <i>Sutrisni Andayani</i>	994
Development of Mathematical Learning Media Integrated Qur'an <i>Syarifah Fadillah, Yadi Ardiawan, Rahman Haryadi</i>	1003
Literacy Program in Madrasah: Challenging Lagging <i>Taufiqur Rahman, Moh. Zamili</i>	1012
EFL Teaching Innovations in Indonesia <i>Tono Suwartono, Retno Ayu Cahyaningtyas</i>	1021
Blended Learning Strategy During the COVID-19 Pandemic in Plant Tissue Culture Course <i>Trianik Widyaningrum</i>	1036
The Approach to Stunting Problems in the Society 5.0 Era <i>Wa Ode Salma</i>	1044
Environment with Technology as Highly Important Element for The Wellbeing of the Elderly <i>Wantonoro, Moh Ali Imron</i>	1053

Social Media Use during the Covid-19 Pandemic and Beyond: A Uses and Gratifications Perspective <i>Wichitra Yasya, Nani Nurani Muksin</i>	1061
The Implication Of Project-Based Teaching On Undergraduate Students' Creativity <i>Wiwin Sri Hidayati</i>	1071
Implementation Of E-Learning In Integrated Islamic Junior High School Granada Tangerang City <i>Yessi Astriani, Asrori Mukhtarom</i>	1086
Bibliometric Analysis Of Digital Marketing And Halal Cosmetics <i>Yulist Rima Fiandari</i>	1092
The challenge of building critical thinking in Era 5.0 <i>Zahara Tussoleha Rony</i>	1101
Creative Industries in The New Normal Era: The Role of Digital Marketing <i>Zakiyah Zahara, Muslimin</i>	1109

Antibiofilm Activity of Honey in Multispecies Pathogen

Masfufatun, Lusiani Tjandra, Budhi Setiawan

Introduction

The invention of antimicrobial agents is an important contribution to the improvement of life-threatening communicable disease therapy. However, as a result of the widespread use of these useful drugs, a slew of new resistance mechanisms has developed and spread rapidly among bacteria that cause disease. Antibiotics resistance becomes more commonly found than before for instance bacteria strains that cannot be killed by Methicillin, Vancomycin, and Carbapenem [1], [2]. Besides mutations or gene resistance acquisition, this resistance could be caused by the ability of the microorganisms to form biofilms on the tissues or medical devices [2].

Microorganisms' biofilm is a complex protective mechanism structure in which microbes stick one to another to a surface. These aggregate cells are embedded within a slimy substance called extracellular polymeric substances (EPS) result in an increment of surface attachment ability, a higher population density, as well as pathogenicity improvement [3]. The protective effects of biofilm formation from antimicrobial agents include decreased penetration, drug molecules trap in the extracellular matrix and higher concentration microbial inactivation enzymes [4]. The Biofilm formation may cause microorganisms become more difficult to eradicate from the host due to higher tolerance to standard antimicrobial drugs and also resistance to phagocytosis [5]. Moreover, in the form of biofilms, particular fungi such as *Candida albicans* is able to produce 2.3 times higher concentration of carcinogenic compounds such as acetaldehyde [6]. To overcome this problem, it is necessary to find better alternative treatment strategies to prevent, mitigate and destroy biofilms.

In the midst of various approaches that have been studied to control biofilm formation, the use of natural products has shown a promise. Honey has been known for its potential health benefits such as anti-inflammatory, anti-cancerous, antiviral, and anti-oxidant activities since 19th century [7]. In vitro and in vivo studies have shown honey exhibited a potential as a broad-spectrum antibiotic, antiviral and antifungal activities. [8]. Honey is a complex blend of many organic and inorganic compounds such as sugars, proteins,

minerals, vitamin, enzymes, phenolic acid, organic acids, pigments, minerals, phenolic acids, flavonoids and many other elements [9]. Honey's antimicrobial activity is determined by a number of bioactive substances, and one of them commonly studied such as hydrogen peroxide (H₂O₂). This substance is produced from the reaction between glucose and glucose oxidase activated when the honey is diluted. Hydrogen peroxide has been frequently suggested a major contributor for honey antimicrobial activities [10], [11].

A part from inhibition the growth of planktonic microorganism cells, honey also has demonstrated antibiofilm activity during in vitro studies. The antibacterial activities of honey on *Staphylococcus aureus*, *Pseudomonas aeruginosa* and other bacterial biofilms have been examined [12]–[15]. Honey also reduces the extracellular polysaccharide matrix production of microorganism thus results in mature biofilm integrity disturbance [16]. However, honey antibiofilm activity against fungi such as *Candida sp.* has not been widely explored. Therefore, this narrative review will discuss about phytochemicals, antimicrobial and antifungal properties as well as honey antibiofilm effect against bacteria and fungi.

Composition of honey

The composition of honey is very complex containing at least 181-200 different substances. In general, 100g of honey contains 82.4 g of total carbohydrates, consisting of Fructose 38.5 g, Glucose 31.28 g, Sucrose 1.31 g, Maltose 7.31. Total gluconic acid 0.57 g, Moisture content 17.1 g, Ash 0.169 g, Fiber 0.2 g, Amino acids / proteins 0.3 g, N 0.041 g, Iron 0.42 mg, Potassium 52 mg, Calcium 6.00 mg, Phosphorus 4.00 mg, Magnesium 2.00 mg, Copper 1–100 µg / g, Zinc 0.22 mg, Riboflavin 0.038 mg, Niacin 0.21 mg, Pantothenic acid 0.068 mg, Pyridoxine 0.024 mg, Folic acid 2 µg, Vitamin C 0.5 mg. Honey also contains enzymes namely invertase, diastase, catalase, glucose oxidase, phosphatase, and protease [17], [18], [19], [20].

Bioactive components and anti-microbial mechanism of honey

Hydrogen Peroxide is produced from the results of the glucose oxidase reaction where the enzymes in honey convert glucose into gluconolactone. Hydrogen Peroxide causes the death of microorganisms [21]. The antimicrobial activities in several types of honeys depend on the endogenous concentration hydrogen peroxide known as a disinfectant and a strong oxidizing agent. Honey also contains polyphenols, including Gallic acid, Ferulic acid, Chlorogenic

acid, Ellagic acid, Syringic acid and Caffeic acid and these bioactive compounds are also considered as antibacterial effect sources in honey [22]. There are more than 150 polyphenol compounds in honey. These polyphenolic compounds have function as antioxidants [23]. Honey antioxidant activity is mainly due to phenolic and flavonoid compounds. The level of honey antioxidant activity is proportional to the value of phenolic and flavonoid concentration [24].

Methylglyoxal (MGO) is a highly reactive dicarbonyl compound (1,2-dicarbonyl methylglyoxal) and it induces rapid and non-enzymatic modification of lysine and arginine residues of protein resulting generation of advanced glycation end products or AGEs [25]. Non-enzymatic conversion of dihydroxyacetone in Manuka honey is the source of MGO production. In Manuka honey stored for less than 1 year, the MGO level was from 0.102 to 0.793 mg / g, the level would increase to 1.541 mg / g when long-term storage or heat treatment [26]. At MGO levels above 0.15 mg / g, this is what causes the antibacterial properties of Manuka honey. Other types of honey have low MGO levels, ranging from 0.0004 to 0.0054 mg / g [27], [28].

Water is the main constituent of living things and honey only contains approximately 15% - 21% water. The water concentration in honey is low enough to allow bacteria or other microorganism growth and the activity of unbound water molecules ranges from 0.562 to 0.62 [29]. The high osmosis power of honey is because 84% of the components contained in honey consist of glucose and fructose). Osmolarity results in strong interactions between sugar molecules and water molecules and leaves very few water molecules. This osmotic pressure will cause the microorganisms to become dehydrated so that they cannot grow. Also, the high osmosis effect of honey inhibits bacterial growth [29], [30], [31]. The acidity level of honey has a pH of 3.2 - 4.5 and this characteristic will inhibit bacterial metabolism and cause bacteria to easily undergo lysis and bacteria to die [32]. The optimum pH for bacterial growth ranges from pH 7.2 to 7.4 [33].

Honey has the potential to inhibit the activity of many pathogenic bacteria including gram-negative and gram-positive bacteria [34], [35]. Manuka honey has activity bactericidal against planktonic cells and biofilms of *Pseudomonas aeruginosa* and *Staphylococcus aureus* honey and their antibiotic activity against *Pseudomonas aeruginosa* was higher than that of *Staphylococcus aureus* [36]. In addition, it was also reported that planktonic *S. aureus*

cells exposed to Manuka honey enlarged and had more septa [37]. Manuka honey interacts synergistically with vancomycin antibiotics in the formation of *S. aureus* biofilms and interacts additively with gentamicin antibiotics in the formation of *P. aeruginosa* biofilms [38]. Manuka and clover honey showed good activity against planktonic cells and biofilms from *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella spp.*, and *Proteus mirabilis* [39].

The mechanism of honey as an anti-fungal is still being debated, but several studies say that the mechanism is almost the same as honey as an antibacterial with active substances H₂O₂, flavonoids, methylglyoxal, as well as high sugar content that can affect fungal growth [40], [41], [42], [43].

Different types of honey anti-biofilm activity

Biofilms are a major mode of microbial growth and are essential to development of infection. Cell adhesion, microcolonies formation and biofilm maturation are important stages of biofilm growth. From these structures, bacteria can spread and develop colonies in new environments [44]. Biofilm can be identified using biopsy as a standard procedure of diagnosis in wounds. Often, staining of the biopsy samples is able to identify microcolonies, extracellular polysaccharide matrix, and inflammatory cells [45].

Not only bacteria, various clinically significant fungi also form biofilms such as *Candida*, *Aspergillus*, *Cryptococcus*, *Trichosporon*, *Coccidioides*, and *Pneumocystis* [46]. Even though *Candida albicans* is one of commonly studied fungi as biofilm producers but *Cryptococcus neoformans* and *Aspergillus fumigatus*, have been known also play significant role in biofilm-related infections. Adhesion, colonization, maturation and dispersal are the developmental stages of fungal biofilm formation which are controlled by complex molecular events [47].

A biofilm is a complex structure made of aggregate of microbial cells and extracellular polymeric substances (EPS) on any surface [48], which can prevent the healing process [49]. A biofilm formation may create a physical barrier that can inhibit infiltration of antibiotics and decrease the chance of wound disinfection [50]. Antibiotic resistance of bacteria in the existence of biofilm has significant contribution to the chronicity of infections. While the exact cause the resistance remains uncertain, several studies have shown that it might be multimodal strategies [51], [52]. Bacterial biofilms may lead to chronic infections due to the increment of tolerance to

antibacterial agents and chemical disinfectant, and phagocytosis prevention. It might be associated also with an increased level of mutations as well as with quorum-sensing pathways. Other factors such as common mechanisms of resistance, efflux pumps upregulation and antibiotic target molecules mutations in bacteria may also promote to the formation of biofilms [53]. It has been suggested that over 75% of microbial infections in the human body is characterized by biofilm-related infections [54].

It has been shown by studies that systemic infection is initiated by biofilm dispersal since start from this point, the bacteria exit from biofilm structure and disseminates inside of the host [55], [56]. The release of singular cells and/or multicellular aggregates of bacteria controlled by an active phenotype change involving the sensing of environmental signals and their transduction via complex regulatory networks to final effectors [57]. Similar to the ability to form biofilms, the dispersion of microorganism seems to be a common property shared by most bacteria that cause them suitable for colonization of new niches [58].

It is well established that chronic wounds such as diabetic foot ulcers, pressure ulcers, and venous leg ulcers are difficult to treat and the evidence of bacterial biofilm was abundantly found in specimens from chronic wounds [59]. Evidence from studies suggests that the formation of polymicrobial biofilm in skin and wound infections could be a risk factor for relapse and the treatment become more challenging because of antibiotic resistance [60]. Risk of infection and chronic inflammation increase since biofilm may prolong and prevent healing in both acute and chronic wounds [45]. Mechanical debridement followed by topical antimicrobial agents are crucial to mitigate biofilm reformation because of commercially available antimicrobials and wound dressings are often ineffective in managing biofilm [61]. Efficacious novel antibiofilm agents' development become an area of interest in wound care. The multimodal anti-biofilm mechanism of different types honey and their efficacy against multidrug-resistant bacteria would make it an exciting prospect for forthcoming study [62].

Antibacterial properties of honey have been associated to various bioactive ingredients and mechanisms. These properties include methylglyoxal (MGO), hydrogen peroxide, defensin-1, flavonoids, bee peptides, dehydration of the wound and a low pH and high osmotic pressure [63]–[66]. Specific mechanism might be predominantly involved for particular microorganism for instance the

osmotic effect of honey demonstrates significant antibacterial effect for *Helicobacter pylori*, while hydrogen peroxide only exhibits a minor contribution [63]. On the other hand, Egyptian honeys have mostly show antimicrobial activity against *Escherichia coli* mainly by hydrogen peroxide production [67]. Furthermore, the antibacterial efficacy of Manuka honey towards *Escherichia coli* and *Staphylococcus aureus* was found directly to the presence of methylglyoxal [68]. However, the bactericidal activity of Manuka honey is still effective on *Escherichia coli* even after neutralization of its methylglyoxal component due to several unknown factors [69]. Methylglyoxal has demonstrated the antibacterial activity of manuka honey against *Bacillus subtilis* and *Staphylococcus aureus* and but not against *Pseudomonas aeruginosa* and *Escherichia coli* [69]. Among the aforementioned antibacterial mechanism of actions, Methylglyoxal (MGO) appeared to be associated to Manuka honey's efficacy to prevent biofilm formation. Moreover, Manuka honey has shown "significant partial detachment" at 50% concentration of *Proteus mirabilis* biofilms after 24 hours [70]. However, though Manuka honey can infiltrate the biofilm and kills bacterial cells but MGO administration alone is not responsible for this effect, highlighting the importance of other bioactive substances in honey's antibacterial activity, especially on *Staphylococcus aureus* and *Pseudomonas aeruginosa* strains [71], [72].

Even though in vitro studies have demonstrated prospective anti-biofilm efficacy of different types of honey [14] but current randomized controlled trial (RCT) has found no superiority of honey in preventing biofilm on infections when compared with standard care in some settings [73]. Perhaps, antibiofilm activity reported by in vitro assay studies might have inadequate clinical relevance [71], [72]. A recent review study found that there is evidence with limited quality of honey's beneficial effect for partial thickness burns healing. However, inconclusive evidence regarding the use of honey for other wound-related indications. For partial thickness burns, treatment with honey may heal faster compared to conventional dressing [74].

Conclusion

Honey exhibits antibacterial activity against a wide variety of gram-positive and gram-negative bacteria, antibiotic-resistant as well as antibiotic-sensitive bacteria. Several honey bioactive components may contribute not only to the antibacterial efficacy but also antifungal effect. These bioactive substances provide a synergy that

result in modulation of the resistance to antimicrobial drugs. Honey demonstrates activities against both planktonic and biofilm phenotype states of microorganisms. Microorganism's planktonic and biofilm states play important role in delaying healing of wounds. There is a very large variation in terms of the anti-microorganism's potency of different types of honey. Manuka is one of the most studied honey which has in vitro activity against both planktonic and biofilm microorganisms. It is clinically important, particularly since most traditional antibiotics or antifungal lack activity against biofilms. However, further clinical studies are required to test the efficacy of the prospective anti-biofilm efficacy of honey as a treatment for wounds and other health conditions.

References

- [1] World Health Organization, *Antimicrobial resistance: global report on surveillance*, World Health Organization, 2014.
- [2] G. M. Rossolini, F. Arena, P. Pecile, and S. Pollini, "Update on the antibiotic resistance crisis," *Current Opinion in Pharmacology*, vol. 18, pp. 56–60, 2014, doi: 10.1016/J.COPH.2014.09.006.
- [3] F. Nazzaro *et al.*, "Anti-Biofilm Properties Exhibited by Different Types of Monofloral Honey," *Proceedings 2020, Vol. 66, Page 16*, vol. 66, no. 1, p. 16, Jan. 2021, doi: 10.3390/PROCEEDINGS2020066016.
- [4] N. Høiby, T. Bjarnsholt, M. Givskov, S. Molin, and O. Ciofu, "Antibiotic resistance of bacterial biofilms," *International Journal of Antimicrobial Agents*, vol. 35, no. 4, pp. 322–332, 2010, doi: 10.1016/j.ijantimicag.2009.12.011.
- [5] K. Lewis, "Riddle of biofilm resistance," *Antimicrobial Agents and Chemotherapy*, vol. 45, no. 4, pp. 999–1007, 2001, doi: 10.1128/AAC.45.4.999-1007.2001.
- [6] Masfufatun *et al.*, "serum acetaldehyde as a potential biomarker for the detection of pathogenic biofilm formation by *Candida albicans*," *Journal of Chemical Technology and Metallurgy*, vol. 52, no. 6, pp. 1032–1038, 2017.
- [7] M. Küçük, S. Kolayli, Ş. Karaoğlu, E. Ulusoy, C. Baltacı, and F. Candan, "Biological activities and chemical composition of three honeys of different types from Anatolia," *Food Chemistry*, vol. 100, no. 2, pp. 526–534, 2007, doi: 10.1016/j.foodchem.2005.10.010.
- [8] N. S. Al-Waili, F. S. Al-Waili, M. Akmal, A. Ali, K. Y. Salom, and A. A. Al Ghamdi, "Effects of natural honey on polymicrobial culture of

- various human pathogens," *Archives of Medical Science*, vol. 10, no. 2, pp. 246–250, 2014, doi: 10.5114/aoms.2012.28603.
- [9] S. Wyndham Lewis, "Eva Crane: Honey, 'A Comprehensive Survey,'" *Bee World*, vol. 98, no. 3, pp. 105–105, Jul. 2021, doi: 10.1080/0005772X.2020.1865626.
- [10] J. W. White, M. H. Subers, and A. I. Schepartz, "The identification of inihibine, the antibacterial factor in honey, as hydrogen peroxide and its origin in a honey glucose-oxidase system," *BBA - Biochimica et Biophysica Acta*, vol. 73, no. 1, pp. 57–70, 1963, doi: 10.1016/0006-3002(63)90359-7.
- [11] L. M. Bang, C. Bunting, and P. Molan, "Peroxide production in honey & its implications," *Journal of Alternative & Complementary Medicine*, vol. 9, no. 2, pp. 267–273, 2003.
- [12] T. Alandejani *et al.*, "Effectiveness of honey on Staphylococcus aureus and Pseudomonas aeruginosa biofilms," *Otolaryngology - Head and Neck Surgery*, vol. 141, no. 1, pp. 114–118, 2009, doi: 10.1016/j.otohns.2009.01.005.
- [13] P. Merckoll *et al.*, "Bacteria, biofilm and honey: A study of the effects of honey on 'planktonic' and biofilm-embedded chronic wound bacteria," *Scandinavian Journal of Infectious Diseases*, vol. 41, no. 5, pp. 341–347, 2009, doi: 10.1080/00365540902849383.
- [14] R. Cooper, L. Jenkins, and S. Hooper, "Inhibition of biofilms of Pseudomonas aeruginosa by Medihoney in vitro," *Journal of Wound Care*, vol. 23, no. 3, pp. 93–104, 2014, doi: 10.12968/JOWC.2014.23.3.93.
- [15] N. HM, L. M, G. RL, H. M. Nassar, M. Li, and R. L. Gregory, "Effect of honey on Streptococcus mutans growth and biofilm formation," *Applied and Environmental Microbiology*, vol. 78, no. 2, pp. 536–540, 2012, doi: 10.1128/AEM.05538-11.
- [16] O. A. Okhiria, "The role of biofilm in wounds," no. May, 2010.
- [17] L. Vorlová and A. Pridal, "Invertase and diastase activity in honeys of Czech provenience," vol. 5, no. 2002, pp. 57–66, 2010.
- [18] I. C. F. R. Ferreira, E. Aires, J. C. M. Barreira, and L. M. Estevinho, "Antioxidant activity of Portuguese honey samples: Different contributions of the entire honey and phenolic extract," *Food Chemistry*, vol. 114, no. 4, pp. 1438–1443, 2009, doi: 10.1016/j.foodchem.2008.11.028.
- [19] I. I. Fatma, S. Haryanti, and S. W. A. Suedy, "Uji kualitas madu pada beberapa wilayah budidaya lebah madu di Kabupaten Pati," *Jurnal Akademika Biologi*, vol. 6, no. 2, pp. 58–65, 2017.

- [20] S. Ahmed *et al.*, "Honey as a Potential Natural Antioxidant Medicine: An Insight into Its Molecular Mechanisms of Action," *Oxidative Medicine and Cellular Longevity*, vol. 2018, 2018, doi: 10.1155/2018/8367846.
- [21] P. B. Olaitan, O. E. Adeleke, and I. O. Ola, "Honey: A reservoir for microorganisms and an inhibitory agent for microbes," *African Health Sciences*, vol. 7, no. 3, pp. 159–165, 2007, doi: 10.5555/afhs.2007.7.3.159.
- [22] S. Almasaudi and A. Saad, "The Antibacterial Activities of Honey," *Saudi Journal of Biological Sciences*, 2020, doi: 10.1016/j.sjbs.2020.10.017.
- [23] I. C. F. R. Ferreira, E. Aires, J. C. M. Barreira, and L. M. Estevinho, "Antioxidant activity of Portuguese honey samples: Different contributions of the entire honey and phenolic extract," *Food Chemistry*, vol. 114, no. 4, pp. 1438–1443, 2009, doi: 10.1016/j.foodchem.2008.11.028.
- [24] Ustadi, L. E. Radiati, and I. Thohari, "Komponen Bioaktif pada Madu Karet (*Hevea brasiliensis*) Madu Kaliandra (*Calliandra calothyrsus*) dan Madu Randu (*Ceiba pentandra*)," *Jurnal Ilmu dan Teknologi Hasil Ternak*, vol. 12, no. 2, pp. 97–102, 2017.
- [25] J. Majtan *et al.*, "Methylglyoxal-induced modifications of significant honeybee proteinous components in manuka honey: Possible therapeutic implications," *Fitoterapia*, vol. 83, no. 4, pp. 671–677, 2012, doi: 10.1016/j.fitote.2012.02.002.
- [26] J. M. Stephens *et al.*, "Phenolic compounds and methylglyoxal in some New Zealand manuka and kanuka honeys," *Food Chemistry*, vol. 120, no. 1, pp. 78–86, 2010, doi: 10.1016/j.foodchem.2009.09.074.
- [27] J. Atrott and T. Henle, "Methylglyoxal in manuka honey - correlation with antibacterial properties," *Czech Journal of Food Sciences*, vol. 27, no. SPEC. ISS., pp. 2008–2010, 2009, doi: 10.17221/911-cjfs.
- [28] K. U. Weigel, T. Opitz, and T. Henle, "Studies on the occurrence and formation of 1,2-dicarbonyls in honey," *European Food Research and Technology*, vol. 218, no. 2, pp. 147–151, 2004, doi: 10.1007/s00217-003-0814-0.
- [29] P. C. Molan, "The role of honey in the management of wounds," *Journal of wound care*, vol. 8, no. 8, pp. 415–418, 1999, doi: 10.12968/jowc.1999.8.8.25904.
- [30] N. F. Nadhilla, "the activity of antibacterial agent of honey against *Staphylococcus aureus*," *J Majority*, vol. 3, no. 7, pp. 94–101, 2014.

- [31] S. P. Fitriyaningsih, A. Khairat, and R. Choestrina, "Aktivitas antibakteri madu Pahit dan Madu Hitam manis terhadap *Escherichia coli* dan *Staphylococcus aureus*," *Jurnal farmasi Galenika*, vol. 1, no. 2, pp. 32–37, 2014.
- [32] B. Pieper, "Honey-based dressings and wound care: An option for care in the United States," *Journal of Wound, Ostomy and Continence Nursing*, vol. 36, no. 1, pp. 60–66, Jan. 2009, doi: 10.1097/01.WON.0000345177.58740.7D.
- [33] G. D. Aggad H, "Honey Antibacterial Activity," *Medicinal & Aromatic Plants*, vol. 03, no. 02, pp. 3–4, 2014, doi: 10.4172/2167-0412.1000152.
- [34] J. Lu *et al.*, "Manuka-type honeys can eradicate biofilms produced by *Staphylococcus aureus* strains with different biofilm-forming abilities," *PeerJ*, vol. 2014, no. 1, pp. 1–25, 2014, doi: 10.7717/peerj.326.
- [35] J. J. Veloz, N. Saavedra, A. Lillo, M. Alvear, L. Barrientos, and L. A. Salazar, "Antibiofilm Activity of Chilean Propolis on *Streptococcus mutans* Is Influenced by the Year of Collection," *BioMed Research International*, vol. 2015, 2015, doi: 10.1155/2015/291351.
- [36] I. D. Iliev *et al.*, "Interactions between commensal fungi and the C-type lectin receptor Dectin-1 influence colitis," *Science (New York, N.Y.)*, vol. 336, no. 6086, pp. 1314–1317, Jun. 2012, doi: 10.1126/SCIENCE.1221789.
- [37] R. Jenkins, A. Roberts, and H. L. Brown, "On the antibacterial effects of manuka honey: mechanistic insights," *Research and Reports in Biology*, p. 215, 2015, doi: 10.2147/rrb.s75754.
- [38] M. E. M. Campeau and R. Patel, "Antibiofilm Activity of Manuka Honey in Combination with Antibiotics," *International Journal of Bacteriology*, vol. 2014, pp. 1–7, 2014, doi: 10.1155/2014/795281.
- [39] Abbas, Hisham A. "Comparative antibacterial and antibiofilm activities of manuka honey and Egyptian clover honey." *Asian Journal of Applied Sciences*, vol. 2, no. 2, 2014.
- [40] S. Anand, M. Deighton, G. Livanos, E. C. K. Pang, and N. Mantri, "Agastache honey has superior antifungal activity in comparison with important commercial honeys," *Scientific Reports*, vol. 9, no. 1, pp. 1–14, 2019, doi: 10.1038/s41598-019-54679-w.
- [41] M. Candiracci, B. Citterio, G. Diamantini, M. Blasa, A. Accorsi, and E. Piatti, "Honey flavonoids, natural antifungal agents against *Candida albicans*," *International Journal of Food Properties*, vol.

- 14, no. 4, pp. 799–808, 2011, doi: 10.1080/10942910903453355.
- [42] L. Fernandes *et al.*, “Portuguese honeys as antimicrobial agents against *Candida* species,” *Journal of Traditional and Complementary Medicine*, vol. 11, no. xxxx, pp. 130–136, Mar. 2020, doi: 10.1016/j.jtcme.2020.02.007.
- [43] P. H. S. Kwakman *et al.*, “Medical-grade honey kills antibiotic-resistant bacteria in vitro and eradicates skin colonization,” *Clinical Infectious Diseases*, vol. 46, no. 11, pp. 1677–1682, 2008, doi: 10.1086/587892.
- [44] C. Guilhen *et al.*, “Transcriptional profiling of *Klebsiella pneumoniae* defines signatures for planktonic, sessile and biofilm-dispersed cells,” *BMC genomics*, vol. 17, no. 1, 2016, doi: 10.1186/S12864-016-2557-X.
- [45] S. L. Percival, “Importance of biofilm formation in surgical infection,” *The British journal of surgery*, vol. 104, no. 2, pp. e85–e94, Jan. 2017, doi: 10.1002/BJS.10433.
- [46] S. Fanning and A. P. Mitchell, “Fungal Biofilms,” *PLOS Pathogens*, vol. 8, no. 4, p. e1002585, 2012, doi: 10.1371/JOURNAL.PPAT.1002585.
- [47] G. Ramage, E. Mowat, B. Jones, C. Williams, and J. Lopez-Ribot, “Our Current Understanding of Fungal Biofilms,” <https://doi.org/10.3109/10408410903241436>, vol. 35, no. 4, pp. 340–355, Nov. 2009, doi: 10.3109/10408410903241436.
- [48] M. A. Jabra-Rizk, W. A. Falkler, and T. F. Meiller, “Fungal Biofilms and Drug Resistance,” *Emerging Infectious Diseases*, vol. 10, no. 1, p. 14, 2004, doi: 10.3201/EID1001.030119.
- [49] R. Edwards and K. G. Harding, “Bacteria and wound healing,” *Current opinion in infectious diseases*, vol. 17, no. 2, pp. 91–96, Apr. 2004, doi: 10.1097/00001432-200404000-00004.
- [50] M. v. Ranall, M. S. Butler, M. A. Blaskovich, and M. A. Cooper, “Resolving Biofilm Infections: Current Therapy and Drug Discovery Strategies,” *Current Drug Targets*, vol. 13, no. 11, pp. 1375–1385, Oct. 2012, doi: 10.2174/138945012803530251.
- [51] P. S. Stewart and J. W. Costerton, “Antibiotic resistance of bacteria in biofilms,” *The Lancet*, vol. 358, no. 9276, pp. 135–138, Jul. 2001, doi: 10.1016/S0140-6736(01)05321-1.
- [52] A. Bridier, R. Briandet, V. Thomas, and F. Dubois-Brissonnet, “Resistance of bacterial biofilms to disinfectants: a review,” <http://dx.doi.org/10.1080/08927014.2011.626899>, vol. 27, no. 9,

- pp. 1017–1032, Oct. 2011, doi: 10.1080/08927014.2011.626899.
- [53] N. Høiby, T. Bjarnsholt, M. Givskov, S. Molin, and O. Ciofu, “Antibiotic resistance of bacterial biofilms,” *International Journal of Antimicrobial Agents*, vol. 35, no. 4, pp. 322–332, 2010, doi: 10.1016/j.ijantimicag.2009.12.011.
- [54] D. Davies, “Understanding biofilm resistance to antibacterial agents,” *Nature reviews. Drug discovery*, vol. 2, no. 2, pp. 114–122, Feb. 2003, doi: 10.1038/NRD1008.
- [55] R. Wang *et al.*, “Staphylococcus epidermidis surfactant peptides promote biofilm maturation and dissemination of biofilm-associated infection in mice,” *The Journal of Clinical Investigation*, vol. 121, no. 1, pp. 238–248, Jan. 2011, doi: 10.1172/JCI42520.
- [56] L. R. Marks, B. A. Davidson, P. R. Knight, and A. P. Hakansson, “Interkingdom signaling induces *Streptococcus pneumoniae* biofilm dispersion and transition from asymptomatic colonization to disease,” *mBio*, vol. 4, no. 4, Jul. 2013, doi: 10.1128/MBIO.00438-13.
- [57] O. E. Petrova and K. Sauer, “Escaping the biofilm in more than one way: desorption, detachment or dispersion,” *Current Opinion in Microbiology*, vol. 30, pp. 67–78, Apr. 2016, doi: 10.1016/J.MIB.2016.01.004.
- [58] C. Guilhen, C. Forestier, and D. Balestrino, “Biofilm dispersal: multiple elaborate strategies for dissemination of bacteria with unique properties,” *Molecular Microbiology*, vol. 105, no. 2, pp. 188–210, Jul. 2017, doi: 10.1111/MMI.13698.
- [59] G. A. James *et al.*, “Biofilms in chronic wounds,” *Wound Repair and Regeneration*, vol. 16, no. 1, pp. 37–44, Jan. 2008, doi: 10.1111/J.1524-475X.2007.00321.X.
- [60] K. S. Akers *et al.*, “Biofilms and persistent wound infections in United States military trauma patients: a case-control analysis,” *BMC infectious diseases*, vol. 14, no. 1, Apr. 2014, doi: 10.1186/1471-2334-14-190.
- [61] C. E. Black and J. W. Costerton, “Current concepts regarding the effect of wound microbial ecology and biofilms on wound healing,” *The Surgical clinics of North America*, vol. 90, no. 6, pp. 1147–1160, Dec. 2010, doi: 10.1016/J.SUC.2010.08.009.
- [62] V. C. Nolan, J. Harrison, and J. A. G. Cox, “Dissecting the Antimicrobial Composition of Honey,” *Antibiotics*, vol. 8, no. 4, p. 251, 2019, doi: 10.3390/antibiotics8040251.

- [63] M. S. Osato, S. G. Reddy, and D. Y. Graham, "Osmotic effect of honey on growth and viability of *Helicobacter pylori*," *Digestive diseases and sciences*, vol. 44, no. 3, pp. 462–464, 1999, doi: 10.1023/A:1026676517213.
- [64] P. Sowa, D. Grabek-Lejko, M. Wesołowska, S. Swacha, and M. Dżugan, "Hydrogen peroxide-dependent antibacterial action of *Melilotus albus* honey," *Letters in applied microbiology*, vol. 65, no. 1, pp. 82–89, Jul. 2017, doi: 10.1111/LAM.12749.
- [65] N. N. Cokcetin *et al.*, "The Antibacterial Activity of Australian *Leptospermum* Honey Correlates with Methylglyoxal Levels," *PloS one*, vol. 11, no. 12, Dec. 2016, doi: 10.1371/JOURNAL.PONE.0167780.
- [66] Z. H. Israili, "Antimicrobial properties of honey," *American Journal of Therapeutics*, vol. 21, no. 4, pp. 304–323, 2014, doi: 10.1097/MJT.0b013e318293b09b.
- [67] R. Wasfi, W. F. Elkhatib, and A. S. Khairalla, "Effects of Selected Egyptian honeys on the cellular ultrastructure and the gene expression profile of *Escherichia coli*," *PloS one*, vol. 11, no. 3, Mar. 2016, doi: 10.1371/JOURNAL.PONE.0150984.
- [68] E. Mavric, S. Wittmann, G. Barth, and T. Henle, "Identification and quantification of methylglyoxal as the dominant antibacterial constituent of Manuka (*Leptospermum scoparium*) honeys from New Zealand," *Molecular nutrition & food research*, vol. 52, no. 4, pp. 483–489, Apr. 2008, doi: 10.1002/MNFR.200700282.
- [69] P. H. S. S. Kwakman and S. A. J. J. Zaat, "Antibacterial components of honey," *IUBMB Life*, vol. 64, no. 1, pp. 48–55, 2012, doi: 10.1002/iub.578.
- [70] J. Majtan, "Honey: An immunomodulator in wound healing," *Wound Repair and Regeneration*, vol. 22, no. 2, pp. 187–192, 2014, doi: 10.1111/wrr.12117.
- [71] J. Lu *et al.*, "Honey can inhibit and eliminate biofilms produced by *Pseudomonas aeruginosa*," *Scientific reports*, vol. 9, no. 1, Dec. 2019, doi: 10.1038/S41598-019-54576-2.
- [72] J. Lu *et al.*, "Manuka-type honeys can eradicate biofilms produced by *Staphylococcus aureus* strains with different biofilm-forming abilities," *PeerJ*, vol. 2, no. 1, 2014, doi: 10.7717/PEERJ.326.
- [73] L. Zhang *et al.*, "The Effect of Exit-Site Antibacterial Honey Versus Nasal Mupirocin Prophylaxis on the Microbiology and Outcomes of Peritoneal Dialysis-Associated Peritonitis and Exit-Site Infections: A Sub-Study of the HoneyPot Trial," *Peritoneal dialysis international: journal of the International Society for Peritoneal*

Dialysis, vol. 35, no. 7, pp. 712–721, Dec. 2015, doi: 10.3747/PDI.2014.00206.

- [74] A. B. Jull, N. Walker, and S. Deshpande, “Honey as a topical treatment for wounds,” *The Cochrane database of systematic reviews*, vol. 2013, no. 2, Feb. 2013, doi: 10.1002/14651858.CD005083.PUB3.



EMBRACING SOCIETY 5.0 WITH HUMANITY

Society 5.0 is a concept presented by the Japanese as a core concept of their economic system. They believed that technology should not surpass the intelligent of men. As such, in society 5.0 the Japanese government would like to ensure that all technological things are designed to be a human-centered design. In fact, their ministry of education in 2018 has also been readily prepared the future generation through a change in their education system. For example, the minister explains that in Japan, or many parts of the world, university entrance are divided into two main concentrations, which are science and social science. The minister thought of changing the system, as society 5.0 is about creating a technology that is human centered. For instance, they gave an example on designer babies. If, people from hard science learn about philosophy, ethics, and humanities, they won't face such ethical concern when developing a product. This is what is being envision by the Japanese government for their younger generation. Collaboration between science and social science is necessary to build a better environment for our future children. Another example is the companies in Japan, such as Hitachi and Fujitsu has already been implementing this 5.0 by designing product that relied fully on technology but puts human at its center (Hitachi, 2017).

Likewise, it is currently a hot topic in Indonesia. Indonesia as a country with the 4th largest population in the world has not been implemented this concept. Our country is still on the industry 4.0. Yet, with the rising interest in AI, Blockchain, NFT, number of unicorn start-up, and all recent technological changes, our country are ready to compete with any other countries in Southeast Asia. Society 5.0 is coming, and we need to embrace it. To prepare with the society 5.0, It is not only the technological side. It is necessary for us to have a strong principle at hearts that based on our belief system. We, as an Indonesian have known to be religious that most of us believed in God. We also commonly practice our religion and tend to be kind to people because we know God would love our good deeds. I personally think that this will help us to move forward and live together with advanced technology.

Technology begets a very important leap in human's life journey. It is important to keep valued of the benefit but it's more important to look out for the human itself. As its purpose is smarter than us, to help us, it will be very ideal if we embrace the technology using our ability to be kind.



+6281227475754
Bildung
@sahabatbildung
bildungpustakautama@gmail.com
www.penerbitbildung.com

