ISBN 978-623-7054-43-6

PROCEEDINGS

The 4th International Conference on Sustainable Innovation (ICoSI) 2020

Cutting Edge Innovations for Sustainable Development Goals

Universitas Muhammadiyah Yogyakarta (Indonesia)
October 13 - 14 2020

https://icosi.umy.ac.id/

Focal Conferences

- **(ICPU)** The 2nd International Conference on Pharmaceutical Updates
- **(ICOMS)** The 6th International Conference on Management Sciences
- **(ICLAS)** The 9th International Conference on Law and Society
- **(ICMHS)** The 4th International Conference Medical and Health Sciences
- **(ICAF)** The 6th International Conference for Accounting and Finance
- **(ILEC)** The 2nd International Language and Education Conference
- **(ICONURS)** The 2nd International Conference on Nursing
- **(ICITAMEE)** The 1st International Conference on Information Technology, Advanced Mechanical and Electrical Engineering
- **(IConARD)** International Conference on Agribusiness and Rural Development
- **(ISHERSS)** The 2nd International Symposium on Social Humanities Education and Religious Sciences
- **(ICONPO)** The 10th International Conference on Public Organization
- **(DREAM)** The 5th Dental Research and Exhibition Meeting
- **(ICHA)** The 5th International Conference on Hospital Administration
- **(ICOSA)** The 3rd International Conference on Sustainable Agriculture

ISBN 978-623-7054-43-6

Proceedings

4th International Conference on Sustainable Innovation

2020

Publisher UMYPress

Lembaga Penelitian, Pengabdian, dan Pengembangan Masyarakat (LP3M)

Universitas Muhammadiyah Yogyakarta

Address

Gedung D Lantai 2

Universitas Muhammadiyah Yogyakarta

Jalan Brawijaya, Bantul,

55183 Indonesia

ISBN : 978-623-7054-43-6

ISBN 978-623-7054-43-6

The 4th ICoSI 2020 Commitees

Advisory Board

Dr. Ir. Gunawan Budiyanto, M.P, IPM
Prof. Dr. Ir. Sukamta, M.T., IPM
Prof. Dr. Nano Prawoto, S.E., M.Si
Dr. Suryo Pratolo, M.Si, Akt
Prof. Hilman Latief, MA., Ph.D
Prof. Dr. Achmad Nurmandi, M.Sc

Chairs

Dr. Yeni Rosilawati, S.IP., S.E., MM
Dr. Arie Paksi, S.IP., M.A
Dr. Dyah Dewanti

Secretariat

Abdul Rasyid Ghazali, M.Sc.
Mariska Intan Sari, S.S., M.A
Fitria Rahmawati, S.Pd. M.Hum.
Khanza Nabila Iftina, S.I.Kom
Qholiva Yuni Fadilla, S.I.Kom

Treasurer

Twediana Budi Hapsari, S.Sos., M.SI.,Ph.D
Safaroh Ivory Fananda, S.Sos

Scientific Committee

Prof. Agus Setyo Muntohar, S.T., M.Eng.Sc., Ph.D.(Eng.)
dr. Iman Permana, M.Kes., Ph.D
Dr. Sudarisman, M.T
Iwan Satriawan, Ph.D
Dr. Indira Prabasari, M.P
Eko Priyo Purnomo, S.IP., M.Si., M.Res., Ph.D
Dr Nuryakin, M.M
Prof. Dr. Achmad Nurmandi, M.Sc.
Rizal Yaya, S.E., M.Sc., Ph.D., Ak, CA
Dr. Mukti Fajar ND, SH., M.Hum

Proceedings and Journals

dr. Iman Permana, M.Kes., Ph.D
Dianita Sugiyo, S.Kep., Ns., MHID
Dr. Dyah Mutiarin, M.Si.

Program and Event

Hijriyah Oktaviani, S.IP, M.M
Krisna Mulawarman, S.Sos, M.Sn

ISBN 978-623-7054-43-6

IT Support

Miftahul Yaum
Winny Setyonugroho. S.Ked., M.T., Ph.D
Anhar Wahyu, S.E

Food and Beverages

Dr. Alni Rahmawati, M.M
Dr. Sri Handari Wahyuningsih, M.M
Siti Wijayanti
Dra. Luluk Chusniati

Equipment, Facilities and Infrastructure

Bagus Subandono, ST, M. Eng
Aris Nuryanta, S.H
Galuh Sudarsono

Assets and Logistics

Eko Wahyudi, S.E
Noor Fajari
Suparno

ISBN 978-623-7054-43-6

Reviewers of 4th ICoSI 2020

Ahmad Zaki, Ph.D.
Al Afik, S.Kep., Ns., M.Kep.
Ali Awaludin, Ph.D.
Ana Majdawati
Angga Fajar Setiawan, S.T., M.Eng., Ph.D.
Anita Rahmawati, S.T., M.T.
Anugrah Ilahi, Ph.D.
apt. Aji Winanta, M.Sc
apt. Binar Asrining Dhiani, Ph.D
apt. Didik Setiawan, Ph.D
apt. Erza Genatrika, M.Sc
apt. Hari Widada, M.Sc
apt. Indah Hairunisa, S. Farm., M.Botech
apt. Ingenida Hadning, M.Sc
apt. Lusi Putri Dwita, M.Si
apt. Nurul Maziyyah, M.Sc
apt. Raditya Weka, M.Farm
apt. Rifki Febriansah, M.Sc
Assoc. Prof. Dr. Khairil Azmin Mokhtar
Asti Widuri
Azizah Khoiriyati, S.Kep., Ns., M.Kep
Cahyu Septiwii, M.Kep., Sp.Kep., MB., Ph.D.
Dedi Suryadi
Dina Wahyu Trisnawati, Ph.D.
Dr. Ahim Abdurahin M.Si., SAS., Ak., CA
Dr. Anas Puri, S.T., M.T.
Dr. Ani Hairani
Dr. apt. Bangunawati Rahajeng, M.Si
Dr. apt. Dwi Utami, M.Si
Dr. apt. Ika Yuni Astuti, M.Si
Dr. apt. Nurkhasanah, M.Si
Dr. apt. Siska, M.Farm
Dr. apt. Supandi, M.Si
Dr. Arni Surwanti,M.Si.
Dr. Astuti Masdar
Dr. Birgit C. P. Koch, PharmD, Ph.D
Dr. dr. Arlina Dewi,M.Kes., AAK
Dr. Dr. Nur Hidayah,M.M.
Dr. dr. Sri Sundari, M.Kes.
Dr. drg. Dwi Aji Nugroho MDSc
Dr. Drh. Sapto Yuliani, M.P
Dr. Edi Soesanto, S.Kp., M.Kes
Dr. Eko Hanudin
Dr. Elsye Maria Rosa, M.Kep.
Dr. Fadia Fitiyanti
Dr. Firman Pribadi, M.Si.
Dr. Firman Pribadi,SE.,MM.
Dr. Hosam Alden Riyadh A.Alazeez, M.S.A
Dr. Ihsan Nurkomar
Dr. Ika Nurul Qamari,SE.,M.Si
Dr. Indah Fatmawati,M.Si
Dr. Innaka Ageng Rineksane
Dr. Istianah ZA
Dr. Lis Noer Aini
Dr. Lisa Musharyanti, S.Kep., Ns., M.Med.Ed
Dr. Mahendro Prasetyo Kusumo
dr. Maria Ulfa, MMR.,Ph.D.
Dr. Muhammad Ichsan
Dr. Muria Indah Sokowati, M.Si
Dr. Ns. Umi Solikhah, S.Pd., M.Kep,
Dr. Nur Chayati, S.Kep., Ns., M.Kep
Dr. Nuryakin,MM.
Dr. Qurratul Aini, S.KG., M.Kes.
Dr. Seplika Yadi
Dr. Siti Nur Aisyah
Dr. Titih Huriah, M.Kep., Sp., Kom
Dr. Yeni Rosilawati
Dr.Eng. Rahmita Sari Rafdinal, S.ST., M.Eng.
Dr.Eng.Pinta Astuti, S.T., M.Eng.
Drg Arya Adiningrat PhD
Drg Atiek Driana R Sp.KGA
Drg Dian Yosi A MDSc PhD
Drg Dwi Suhartiningtyas MDSc
Drg Edwyn Saleh Sp.BMM
Drg Erlina Sih Mahanani
Drg Fahmi Yunisa Sp. Pros
Drg Hartanti Sp.Perio
Drg Iwan Dewanto MMR PhD
drg Sartika Puspita MDSc
Dr. Dyah Ekaari Sekar J
Eko Purwanti
Eko Purwanti, Ph.D
Ema Waliyanti, S.Kep., Ns., MPH
Endro Dwi Hatmanto
Erna Rochimawati, Ph.D
Erna Rochmawati
Etik Kresnawati, Dr., M.Si.
Evi Rahmawati, S.E., M.Acc., Ph.D., Ak., CA.
Evy Rahman Utami, S.E., M.Sc.
Fanny Monika, S.T., M.Eng.
Ferika Indarwati, S.Kep., Ns., M.Ng
Fitri Arofiati, S.Kep., Ns., MAN., Ph.D
Galuh Suryandari
Genesiska, S.Si., M.Sc.
Gina Puspita
Hafiez Sofyani, S.E., M.Sc.
Harjanti Widiastuti, Dr., S.E., M.Si., Ak.
Hendy Setiawan, Ph.D.
Hidayatul Kurniawati
Ida Faridah, S.Kp., M.Kes
Ietje Nazaruddin, Dr., M.Si., Ak., CA.
Ika Setyawati
Ikhlas Muhammad Jenie
Iman Permana
Imaniar Ranti
Inayati
Indira Prabasari, Ph.D.
Ir. Latif Budi Suparma, M.Sc., Ph.D
Iwan Satriawan, Ph.D
Jebul Suroso, Ns. M.Kep
Jenita Doli Tine Donsu, S.KM. M.Si
Lilis Suryani

ISBN 978-623-7054-43-6

M. Bahrul Ilmi, S.E., M.E.Sy
M. Endriyo Susila, Ph.D.
M. Syifa Amin Widigdo, Ph.D
Mahendro Prasetyo Kusumo
Matyana Dwi Cahyati, S.T., M.Eng.
Meika Kurnia Puji, RDA,M.Si.,Ph.D."
Muhammad Chairunsyah Riskyta Akbar
Muhammad Hazyar Arumbinang, S.H., LL.M
Muhammad Ibnu Syamsi, S.T., M.Eng.
Mundakir, S,Kep. Ns. M.Kep
Naim Abdul Majid
Nasrullah, S.H., S.Ag., MCL.
Naufal Bagus Pratama, S.H.
Noriko Kuwano
Nurvita Risdiana, S.Kep., Ns., M.Sc
Prof. Djoko Legono
Prof. Dr. Alan Lau, Pharm.D., FCCP
Prof. Dr. apt. Dyah Aryani Perwitasari S.Si., M.Si
Prof. Dr. Arthorn Riewpaiboon
Prof. Heru Kurnianto
Tjahjono,MM"
Prof. Hilman Latief, Ph.D.
Prof. Hironori Yasuda
Prof. Iman Satyarno
Prof. Ir. Mochamad Teguh, MSCE., Ph.D.
Prof. Jamsari
Prof. Keith Walters
Prof. Kriengsak Panuwatwanich
Prof. Maria Rosa Mosquera Losada
Prof. Maurice S. B. Ku
Prof. Michael Henry Boehme
Prof. Normah Mohd Noor
Punang Amaripuja,SE.,ST.,M.IT
Ratna Indriawati
Retno Widowati PA.,M.Si.,Ph.D.
Rizal Yaya, S.E., M.Sc., Ph.D., Ak., CA.
Rizka Fakhriani
Rofi Aulia Rahman, S.H., LL.M
sabtanti harimurti
Shanti Wardaningsih, Ph.D
Sherly Usman
SN Nurul Makiyah
Sri Atmaja P. Rosyidi, S.T., MSc.Eng., Ph.D., PE
Sri Rejeki M
Sri Sundari
Sudarisman
Suryanto
Suryo Pratolo, Dr., S.E., M.Si., Ak., CA., AAP-A.
Sutantri, Ns., M. Sc.,Ph.D
Talqis Nurdianto
Taufiq Hidayat, S.P., M.Sc.
Taufiqur Rahman, S.IP, M.A, Ph.D.
Titiek Hidayati
Tri Pitara
Tri Wulandari Kesetyaningsih
Tumin, Ph.D
Twediana Budi Hapsari, Ph.D
Wantoro, M.Kep., Ns., Sp.Kep., M.B., Ph.D
Warih Andan
Winny Setyonugroho,Ph.D.
Yanuar Fahrizal., S.Kep., Ns., M.Kep., Sp.Kep.J
Dr. Yoni Astuti
Yordan Gunawan, S.H., Int.MBA., M.H

ISBN 978-623-7054-43-6

Preface by the Chairperson of the 4th ICoSI 2020

Dr. Yeni Rosilawati, S.IP. S.E., MM.

Assalamu'alaikum Wr. Wb.

All praise is due to Allah, the Almighty, on whom we depend for sustenance and guidance. Prayers and peace be upon our Prophet, Muhammad SAW, his family and all of his companions.

On behalf of the organizing committee, it is my pleasure and privilege to welcome the honourable guests, distinguished keynote & invited speakers, and all the participants.

With the main theme of "Cutting-Edge Innovations on Sustainable Development Goals (SDGs)", the 4th International Conference on Sustainable Innovation (ICoSI) 2020 serves as a forum to facilitate scholars, policy makers, practitioners, and other interested parties at all levels from Indonesia and abroad to present their novel ideas, promote cutting-edge research, and to expand collaboration network. The conference has about 1373 participants participating from more than 8 countries 4 continents all over the world, making this conference a truly international conference in spirit.

This multidisciplinary conference was first held in 2012 and has undertaken various changes and adopted to the current technological trends of our education system. From having this conference with just 175 participants back in 2012 we have come a long way in making the conference a huge success with more than 1373 participants participating in this two-day conference.

Formerly, this conference consisted of only 9 (nine) focal conferences. This year, there are 14 focal conferences from various disciplines, namely: 1) The 2nd International Conference on Pharmaceutical Updates (ICPU), 2) The 6th International Conference on Management Sciences

ISBN 978-623-7054-43-6

(ICoMS), 3) The 9th International Conference on Law and Society (ICLAS), 4) The 4th International Conference Medical and Health Sciences (ICMHS), 5) The 6th International Conference for Accounting and Finance (ICAF), 6) The 2nd International Language and Education Conference (ILEC), 7) The 2nd International Conference on Nursing (ICONURS), 8) The International Conference on Information Technology, Advanced Mechanical and Electrical Engineering (ICITAMEE), 9) The 2nd International Conference of Agribusiness and Rural Development (IConARD), 10) The 10th International Conference on Public Organization (ICONPO), 11) The 2nd International Symposium on Social Humanities Education and Religious Sciences (ISHERSS), 12) The 5th Dental Research and Exhibition Meeting (DREAM), 13) The International Conference on Hospital Administration (ICHA), and 14) The 3rd International Conference on Sustainable Agriculture (ICoSA).

Accordingly, We are proud to announce that this year, the 4th ICoSI 2020 breaks the Museum Rekor-Dunia Indonesia (MURI) record as the Virtual Multidisciplinary Conference with the Largest Number of Area of Fields in Indonesia

In addition, this year, this conference holds special value since this is the first conference in the history of our university where the entire conference is taking place remotely on a digital platform through the use of advance technologies due to the Covid-19 Pandemic.

I would take this opportunity to express my highest respect to the Rector of Universitas Muhammadiyah Yogyakarta, Dr. Gunawan Budiyanto who gave approval and ensured the maximal support from all the faculty members of Universitas Muhammadiyah Yogyakarta (UMY) that made this event a big success. In addition, my appreciation goes to all the support teams who have provided their valuable support and advice from planning, designing and executing the program.

Let me conclude my speech by encouraging the delegates to participate with an increasing number in all the activities and discussions through the digital platforms for the next two days. I wish everyone a successful, safe, and fruitful conference.

Thank you!

Wassalamu'alaikum Wr. Wb.

Yogyakarta, Indonesia, 14 October 2020

ISBN 978-623-7054-43-6

Welcoming Remarks by the Rector of Universitas Muhammadiyah Yogyakarta

Assoc. Prof. Dr. Gunawan Budiyanto

Innovation is the beginning of the development of technology, and technology is a development machine that is expected to provide benefits to humans and provide the smallest possible impact on environmental quality. In the concept of sustainable development, development must improve the quality of human life without causing ecological damage and maintain the carrying capacity of natural resources.

International Conference on Sustainable Innovation (ICoSI) is an international conference which is an annual conference held by the University of Muhammadiyah Yogyakarta (UMY), Indonesia. In 2020 this raises the issue of "Cutting-Edge Innovations on Sustainable Development Goals." Therefore, on behalf of all UMY academics, I would like to congratulate you on joining the conference, hoping that during the Covid-19 Pandemic, we can still provide suggestions and frameworks for achieving sustainable development goals.

ISBN 978-623-7054-43-6

About The 4th International Conference on Sustainable Innovation (ICoSI) 2020

Cutting Edge Innovations for Sustainable Development Goals

The 2030 Agenda for Sustainable Development is enacted by the United Nations as a shared blueprint for peace and prosperity for people and the planet, now and into the future. It consists of strategies to improve health and education, reduce inequality, and spur economic growth while also conserving natures by 2030.

This year, however, at the first one-third of its timeline, the SDG Reports shows that the outbreak of COVID-19 did hinder the achievement, or at least decelerate the progress of achieving the 17 goals. In fact, according to the report, "some number of people suffering from food insecurity was on the rise and dramatic levels of inequality persisted in all regions. Change was still not happening at the speed or scale required", accordingly.

Therefore, in this event of pandemic, the quantity and quality of research, innovation, and more importantly multi-disciplinary collaboration are indispensable. Furthermore, there needs to be clear ends of those works. That is how those research are applicable and benefits directly to the society. That is how those research is incorporated as the drivers of policy making, and used practically in the society. Hence, the stakeholders especially the triple helix of higher education institution, government, and industry must be re-comprehended and supported to reach the common goal of the SGD.

International Conference on Sustainable Innovation (ICoSI) has been essentially attempting to strengthen this regard since its first establishment. One of the goals of ICoSI is to provide primarily a platform where scholars, practitioners, and government could grasp the development and trends of research. Hopefully, meeting these actors altogether would result in stronger collaboration, sophisticated and advantageous research, and brighter ideas for further research. Based on these reasoning, this year, the 4th ICoSI 2020 UMY is themed 'Cutting-edge Innovations for Sustainable Development Goals".

Improving from last year conference which brought nine focal conference, this year ICoSI 2020 UMY brings 14 disciplines, from social sciences, natural sciences, and humanities. ICoSI 2020 received as much as 1005 papers. The paper works submitted in ICoSI 2020 UMY will be published in Atlantis Proceedings, IOP Proceedings, National/International Journals, and ICoSI ISBN-indexed Proceedings.

Nevertheless, ICoSI believes that publication is only the beginning of research dissemination. The publications will enhance the chance of the research known by wider audience, and then used, applied, and incorporated at either system, institutional, or personal level of human lives.

ISBN 978-623-7054-43-6

CONTENTS

ISBN 978-623-7054-43-6

ISBN 978-623-7054-43-6

ISBN 978-623-7054-43-6

ISBN 978-623-7054-43-6

TRACK ECONOMICS, LAW, EDUCATION, SOCIAL, AND HUMANITIES

ISBN 978-623-7054-43-6

Anti-Cancer Activity of Ants Nest Plant (*Myrmecodia Pendans Merr. & Perry*) on Protein Transduction Signal Resistance Complex CDK-2-Cyclin-E and NF-Kb: Silico Molecular Docking Study

Ana Medawati[1,*], Supriatno[2], Sofia Mubarika[3], Sitarina Widyarini[4]

[1]*Department Biomedical Science, Program Study of Dentistry, Faculty of Medicine and Health, Universitas Muhammadiyah Yogyakarta,Indonesia*
[2]*Department Oral Medicine, Associate Professor Faculty of Dentistry, Universitas Gadjah Mada, Yogyakarta, Indonesia*
[3]*Department of Histology and Cell Biology, Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta, Indonesia*
[4]*Department Pathology Anatomy, Associate Professor of Veterinary Science, Universitas Gadjah Mada, Yogyakarta, Indonesia*
** Corresponding Author. Email : medawati888@gmail.com*

ABSTRACT

Background: Efforts to inhibit cancer cells' growth in the oral cavity require effective strategies and potential. One of them uses the ant nest plant (Myrmecodia pendens Merr & Perry), a natural medicinal plant. It has been empirically and scientifically tested in its potential for antitumor. Herbal cancer treatment has advantages, i.e., minimal side effects than conventional therapies. Myrmecodia pendan Merr & Perry is a plant with the content of terpenoid, *procyanidin* B1, *rosmarinic acid*, alkaloid, flavonoid, and tocopherol compounds as anticancer compounds. Objective: To examine the anticancer activity of ant nest plants (Myrmecodia pendans Merr. & Perry) on the inhibition of signal transduction of the CDK-2-cyclin-E protein complex NF-kB in silico molecular docking'. Method: Using the main Auto DockVina application, in the silico molecular docking test. DS Visualizer was used to making and visualizing target proteins and test ligands. The molecular docking results measured root mean square atom position deviation (RMSD) values < 2.00Å. Results: The molecular docking test showed that in the ethyl acetate fraction compounds, terpenoid, procyanidin B1, rosmarinic acid, alkaloids, flavonoids, and tocopherols had docking scores with RMSD values < 2.00Å. Conclusion: Terpenoids, Procyanidin B1, rosmarinic acid, alkaloids, flavonoids, and tocopherols were active compounds in the M. Pendens fraction of ethyl acetate showing activity against its cancer. Ants Nest (*Myrmecodia pendans Merr. & Perry*) had anticancer activity in the protein complex CDD-2-cyclin-E and signal transduction barrier NF-kB: by the molecular docking test In Silico

Keywords : *anticancer, in silico, molecular docking, M*yrmecodia Pendens

1. INTRODUCTION

According to the National Center for Health Statistics in 2017, the data on mortality collected were 1.7 million new cancer cases and 600,920 mortalities due to cancer, projected to occur in the United States [1]. The number of new cancer cases globally reaches nearly 12.7 million and is expected to increase to 21.4 million by 2030 [2]. Cancer is a significant public health problem worldwide and is the second leading cause of death in the United States [1]. According to the 2013 Basic Health Research (Riskesdas) data, the prevalence of cancer in Indonesia was relatively high, namely 1.4 per 100 population or around 347,000 people [3].

The World Health Organization reports that cancer in the human body is a disease characterized by uncontrolled cell growth, and its development can spread to other organs, which can cause mortality [4]. Invasion, metastasis and therapeutic resistance are important phenomenon in the malignancy and progression of cancer cells. The abnormality of cell cycle regulation and the imbalance between dead cells and living cells is one of the triggers for the occurrence of malignancy and aggressiveness of cancer cells [5].

Cancer treatment's success is still low, and treatments such as chemotherapy are expensive, so it is necessary to find new anticancer agents by exploring natural medicinal plants. One of them is using ant nest plants (Myrmecodia Pendens Merr & Perry), which have antitumor potential tested empirically and scientifically. Ant nest plant or Myrmecodia Pendens Merr. & Perry is an epiphytic plant from Papua from hydnophytinae (Rubiaceae), which can be in symbiosis with ants and is said to be epiphytic as it attaches to other plants, but does not live parasitically against its host [6].

Myrmecophytes (Myrmecodia pendans, literally "ant-plant") originates from the Papua Islands, located in Indonesia's eastern part. This plant can also be found in the Malay Peninsula, the Philippines, Cambodia, Sumatera, Java, Cape York, and the Solomon Islands. M. pendan belongs to the Rubiaceae family, which contains five genera, and only two of these genera are associated with ants, Myrmecodia (45 species) and Hydnophytum (26 species). Out of all these species, only H. formicarium, M. pendans, and M. bulbosa are

ISBN 978-623-7054-43-6

frequently used as natural remedies. M. pendans, known by the Papuans as a medicinal plant, can be used to treat various diseases, such as cancer, tumors, gout, diarrhea, and fever [7]. Therefore, many studies have been conducted on the use of natural compounds for the prevention of disease.

Ant nest plants contain active compounds of flavonoids, polyphenols, and tannins, which function as antioxidants that can prevent the growth of various types of human cancer cells and effectively suppress carcinogens. Ant nests also contain tocopherol and alpha-tocopherol, substances with high activity that can inhibit free radicals [7]. The content of the metabolite compound Myrmecodia Pendens is believed to increase human immunity and can treat various infectious and degenerative diseases [8]. Cytotoxic test results showed that Myrmecodia extract was toxic to several cancer cells in humans, including uterine cancer cells (HeLa) and breast cancer cells or MCM-B2 [7], as well as oral carcinoma cells (KB) [9].

NF-κB is a transcription factor that controls the expression of genes involved in immune response, apoptosis, and the cell cycle. The high regulation of the NF-κB protein can cause inflammation and autoimmunity, viral infections, and cancer [10]. It underlies the in silico test using molecular docking to prove the active compounds in the ethyl acetate fraction of Myrmecodia Pendens having anti-cancer activity so that further research can be carried out related to the inhibition activity of the protein complex CDK-2-cyclin-E and NF. -κB.

2. METHODS

The optimization structure of the active compound ethyl acetate fraction was as independent variables and the protein structure of the CDK2-Cyclin E and NF-κB complex as control variables, while the dependent variable was the docking score.

This study used a computer to download the Autodock Vina application and other supporting applications such as DS Visualizer, AutoDock Tools, Python, YASARA, and Open Babel. Each application had a function in the molecular docking process. The main application used was Autodock Vina. DS Visualizer was used for the preparation and visualization of target proteins and test ligands. Meanwhile, AutodockTools was used to process target proteins and test ligands. AutodockTools could be run by first activating the Python application. The results of the molecular docking were measured by the RMSD value using YASARA. Meanwhile, the application was used to convert the docking results into PDB extensions so that Open Babel could be visualized.

The structure of the VEGF, HER-2, and COX-2 target proteins was downloaded via the Protein Data Bank (PDB) according to PDB ID. The changed structures were structures, ligands, sequences, and active sites. The test ligand structure could be made by describing the nobiletin compound's 2D structure using Marvin Sketch 6.0.0 software. To save the ligand structure in 3D, a .cml to .pdb conversion was performed.

The target protein molecule was opened in the AutoDock Vina application and added with polar hydrogen using the Edit> Hydrogens> Add> Polar Only tool. Then the structure was converted to a .pdbqt extension. These changes could be done with the Grid tool. The grid size used for the docking process was determined. After the target protein was ready, only ligand files (without protein) were prepared. A selection was then made for the bonds that could be rotated by clicking the Ligan tools> Torsion Tree> Choose Torsion. Just like the target protein, the ligands were stored in .pdbqt extension.

Docking was carried out by opening a command prompt and typing the command cd Nama_Dirdir \ Nama_Sub_Dirdir. Thus, after a while, the results of the running of the docking appeared in the form of affinity and RMSD values. The results of the docking were observed for the bond interaction with the DS Visualizer application. Files that could be viewed through this application must be in the .pdb extension. They must be converted from .pdbqt to .pdb using Indonesia's Babel application. Furthermore, DS Visualizer could identify ligands and proteins' position and a 3-dimensional (3D) picture of their interactions.

3. RESULT AND DISCUSSION

The in silico molecular docking test used a cyclin-dependent kinase-2 (CDK-2) complex. The results of docking ligands from the CDK-2 receptor can be seen in Table 1.

Original ligand docking score of the CDK-2 receptor

Compound	Intervention	Protein	RMSD (<2.00 Å)	Docking Score
Native Ligand	*Auto-dock Vina*	CDK-2 (Code Protein: 1PYE)	0.458	-9.1
Terpenoid			1.190	-7.5
Procyanidin B1			1.556	-7.6
Rosmarinic acid			1.680	-7.6
Alkaloid			1.531	-7.0
Flavonoid			1.108	-7.8
Tocopherol			1.846	-6.3

Based on Table 1, the results of the three ligand tests with CDK-2 protein showed terpenoids (docking score: -7.5), procyanidin B1 (docking score: -7.6), and rosmarinic acid (docking score: -7.6) at the 2nd conformation. The best compound detected was flavonoids as it had a docking score of -7.8 and was the closest to the original ligand docking score (-9.1).

Furthermore, the results of visualization using the DS Visualizer application showed that the ligand docking score of the cyclin-dependent kinase 2 (CDK-2) receptor was -9.1, with a root mean square deviation of atomic position (RMSD) value of 0.458 (<2.00Å) located at the 2nd amino acid conformation. The visualization results showed that the ligands bind to several residues of the target protein, as shown in Figure 1 below.

ISBN 978-623-7054-43-6

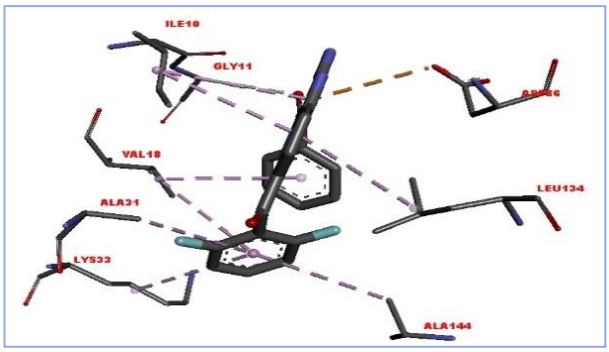

Figure 5. Visualization of the original ligand with the CDK-2 protein

The result of ligand docking from the cyclin-E receptor showed that all active M. Pendens compounds had a docking score with an RMSD value of <2.00Å. The compound that was best detected to have the strongest bond was flavonoids with the smallest docking score of -7.8. Based on these results, it was confirmed that the compounds in the active fraction of M. Pendens had a cell cycle of inhibition effect through the reduction of cyclin-E regulation that can be seen in Table 2 below.

TABLE I. THE ORIGINAL LIGAND DOCKING SCORE OF THE CYCLIN-E RECEPTOR

Compound	Intervention	Protein	RMSD (<2.00 Å)	*Docking Score*	Conformation of amino acid Amino
Terpenoid	*Auto-dock Vina*	Cyclin E (Code Protein: 1W98)	1.088	-7.4	3
Procyanidin B1			1.433	-7.1	3
Rosmarinic acid			1.935	-7.4	2
Alkaloid			1.983	-6.3	6
Flavonoid			1.280	-7.8	3
Tocopherol			1.365	-7.5	6
Terpenoid			1.088	-7.4	3

The original ligand docking results of the NF-κB receptor showed the ligand docking score of the NF-κB receptor was -4.2 with an RMSD value of 1.688 or <2.00Å, located at the 5th conformation. The compounds were best detected in alkaloids and tocopherols as they were closest to the original ligand docking score (-4.2). Based on these results, it was confirmed that the compounds in the active fraction of M. Pendens had a cell cycle of inhibition effect through the reduction of NF-κB regulation, which can be seen in Table 3 below.

The original ligand docking score of the NF-κB receptor

Compound	Intervention	Protein	RMSD (<2.00 Å)	*Docking Score*
Native Ligand	*Auto-dock Vina*	NF-κB (Code Protein: 1LB5)	1.688	-4.2
Terpenoid			1.635	-5.4
Procyanidin B1			1.421	-5.4
Rosmarinic acid			1.967	-5.8
Alkaloid			1.537	-5.2
Flavonoid			1.573	-2.9
Native Ligand			1.688	-4.2

Based on the inhibition test study for the complex protein CDK-2-cyclin-E and NF-κB against Burkitt's lymphoma oral cells treated with the ethyl acetate fraction Myrmecodia Pendens, it showed a decrease in the activity of complex proteins CDK-2-cyclin-E and NF-κB according to increasing concentrations. It suggested that the ethyl acetate fraction of Myrmecodia Pendens was shown to inhibit Burkitt's lymphoma oral cells' growth through the mechanism of signal transduction inhibition of the protein complexes CDK-2-cyclin-E and NF-κB. It is known that the CDK-2 protein inhibition test results in Burkitt's lymphoma oral cells treated with ethyl acetate Myrmecodia Pendens fraction at a concentration of 300 µg / mL showed CDK-2 inhibition of 49%. Meanwhile, the cyclin-E protein inhibition test results in Burkitt's lymphoma oral cells treated with ethyl acetate Myrmecodia Pendens fraction at a concentration of 300 µg / mL showed a cyclin-E inhibition of 54% [11].

The active compound in the ethyl acetate fraction of M. Pendens showed anticancer activity through molecular docking tests. Ethyl acetate fraction from the plant Myrmecodia Pendens was shown to inhibit Burkitt's lymphoma oral cells' growth through the mechanism of signal transduction inhibition of NF-κB and the protein complex CDK-2-cyclin-E. It was reported that NF-κB activation would inhibit apoptosis [12].

When it was activated, NF-κB would suppress apoptosis and disruption of proliferation (Putra, 2011). It is evidenced by the research results on the inhibition of protein NF-κB on Burkitt's lymphoma oral cells treated with ethyl acetate fraction at a concentration of 300 µg / ml showing a protein barrier of 28% [11].

Based on the results of the docking test, it can be seen that all active compounds, including terpenoids, procyanidin B1, rosmarinic acid, alkaloids, flavonoids, and tocopherols in ant nest plants (Myrmecodia Pendens) showed anti-cancer activity. It was proven in the validation process using the AutoDock Vina application that all test compounds had an RMSD value <2.00 Å so that the Molecular Docking process could be carried out.

4. CONCLUSION

Terpenoids, Procyanidin B1, rosmarinic acid, alkaloids, flavonoids, and tocopherols were active compounds in the M. Pendens fraction of ethyl acetate showing activity against its cancer. Ants Nest (Myrmecodia pendans Merr. & Perry) had anticancer activity in the protein complex CDD-2-cyclin-E and signal transduction barrier NF-kB: by the molecular docking test In Silico

DECLARATION OF INTEREST

The authors report no conflict of interest

REFERENCES

[1] R.L. Siegel, K.D. Miller, and A. Jemal, "Cancer Statistics", A Cancer J for Clinicians, vol. 67, pp. 7–30, 2017.

[2] World Health Organization, "Cancer : Fact Sheet", WHO, 2017.

[3] Riset Kesehatan Dasar (Riskesdas), "Badan Penelitian dan Pengembangan Kesehatan Kementerian RI tahun 2013," 2013.

[4] World Health Organization (WHO), "The GLOBOCAN Project," *Cancer Fact Sheets*, 2015.

ISBN 978-623-7054-43-6

[5] Supriatno, Harada K, Yoshida H, Sato M. Basic investigation on the development of molecular targeting therapy against cyclin- dependent kinase inhibitor p27Kip1 in head and neck cancer cells. Int J Oncol 2005; 27:627-35.

[6] *F. Crisnaningtyas and A.T. Rachmadi, "Pemanfaatan Sarang Semut* Myrmecodia pendens asal Kalimantan Selatan sebagai Antibakteri, JRIHH, vol. 2, 2010.

[7] A. Soeksmanto, M.A. Soebroto, H. Wijaya, and P. Simanjuntak, "Anticancer activity for extracts of Sarang Semut plant (Myrmecodia pendens) to HeLa and MCM-B2 cells," Pakistan J Biol Sci, vol. 13, pp.148-51, 2010.

[8] Supriatno, "Antitumor Activity of Papua's Myrmecodia pendans in Human OralTongueSquamous Cell Carcinoma Cell Line Through Induction of CyclinDependent Kinase Inhibitor p27Kip1 and Suppression of CyclinE," J of Cancer Research and Therapy, vol. 2, pp. 48-53, 2018.

[9] S.E. Yuletnawati and Supriatno, "Antitumor Activity Of Chronic Heart Failure Drug Quinolinone Derivate-Vesnarinone On An Oral Malignant Burkitt's Lymphoma Cell (Study on proliferation, chemotactic migration and cell apoptosis)," J Int Dent Med Res, vol. 11, pp. 834-839, 2018.

[10] Z. Bibi, J. Achmad, A. Ali, A. Siddiqa, S. Shahzad, S. HK. Tareen, H.A. Janjua, and S. Khusro, "On the modeling and analysis of the biological regulatory network of NF-$_{\kappa}$B activation in HIV-1 infection," vol. 4, pp. 1-18, 2016.

[11] A. Medawati, Supriatno, S. Mubarika, and S. Widyarini, "Ethyl Acetate Fraction of Papua Ant Nest Plant (Myrmecodia pendans Merr & Perry) Induce Cell Cycle Arrest and Apoptosis of an Oral Malignant Burkitt lymphoma Cell through down Regulationof cyclin-E-CDK-2 Complex Mechanism," Indian J of Public Health Research Development, vol. 11, pp. 884-889, 2020.

[12] D. Hanahan and R.A. Weinberg, "Hallmarks of cancer: the next generation," Cell, vol.144, pp. 646-74, 2011.