The 1st International Conference
ICOPMAP 2021
on Pharmaceutical Sciences and Military Pharmacy
3-4 September 2021

ABSTRACT BOOK

PHARMACY COLLABORATION
in Achieving Health Resilience

In collaboration with:

[Logos of various institutions]
# CONTENT

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORAL PRESENTATION SCHEDULE</td>
<td>vii</td>
</tr>
<tr>
<td>PRESENTER PRESENTATION SCHEDULE</td>
<td>x</td>
</tr>
<tr>
<td>BIOLOGY PHARMACY</td>
<td>1</td>
</tr>
<tr>
<td>PHARMACEUTICAL CHEMISTRY</td>
<td>15</td>
</tr>
<tr>
<td>CLINICAL PHARMACY</td>
<td>37</td>
</tr>
<tr>
<td>MILITARY PHARMACY</td>
<td>65</td>
</tr>
<tr>
<td>PHARMACOLOGY &amp; BIOMEDICAL SCIENCES</td>
<td>79</td>
</tr>
<tr>
<td>PHARMACEUTICAL TECHNOLOGY</td>
<td>99</td>
</tr>
</tbody>
</table>
## ORAL PRESENTER SCHEDULE

**Room A: Pharmaceutical Chemistry**

<table>
<thead>
<tr>
<th>Topic</th>
<th>Presenter/Author</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influence Of Cyp2d6 Polymorphism On Tamoxifen Metabolism</td>
<td>Baitha Maggadani</td>
<td>12.30 – 14.10</td>
</tr>
<tr>
<td>Development and Validation Method for Quantification of Favipiravir in VAMs using High Performance Liquid Chromatography – Photodiode Array</td>
<td>Cahaya Azzahra Rahmadhani</td>
<td>12.30 – 14.10</td>
</tr>
<tr>
<td>Analysis of the Rate of Formation of 4-Hydroxycyclophosphamide in Dried Blood Spot of Indonesian Breast Cancer Patients after Administration of Cyclophosphamide</td>
<td>Devi Ramadhanti Nurhaliza</td>
<td>12.30 – 14.10</td>
</tr>
<tr>
<td>Validation of Rifampicin and Isoniazid Quantification Method in Dried Blood Spot by High Performance Liquid Chromatography - Photodiode Array</td>
<td>Edria Rasendriya</td>
<td>12.30 – 14.10</td>
</tr>
<tr>
<td>Pharmacokinetic Profile and Incurred Sample Stability of Hydroxychloroquine in Volumetric Absorptive Microsampling (VAMS) Using High-Performance Liquid Chromatography-Photodiode Array</td>
<td>Gregorio Fernando Hadi</td>
<td>12.30 – 14.10</td>
</tr>
<tr>
<td>Analysis of The Rate of Formation of 4-Hydroxycyclophosphamide in Volumetric Absorptive Microsampling of Breast Cancer Patients after Administration of Cyclophosphamide using LC-MS/MS</td>
<td>Hening Puspa Seruni</td>
<td>12.30 – 14.10</td>
</tr>
<tr>
<td>The Effect of Power on Synthesis of 4-(4-Methyl)Benzoiloksi-3-Metoxicynamate Acid Using Microwave Irradiation Method</td>
<td>Kholis Amalia Nofianti</td>
<td>12.30 – 14.10</td>
</tr>
<tr>
<td>Development And Validation Of Method For Analysis Of Favipiravir And Remdesivir In Volumetric Absorptive Microsampling With Ultra High Performance Liquid Chromatography Tandem Mass Spectrophotometry</td>
<td>Roesyta's Fitria Noer</td>
<td>12.30 – 14.10</td>
</tr>
<tr>
<td>ID</td>
<td>Title</td>
<td>Authors</td>
</tr>
<tr>
<td>--------------</td>
<td>---------------------------------------------------------------------------------------------</td>
<td>----------------------------------------------</td>
</tr>
<tr>
<td>(A-1625148891)</td>
<td>Comparison of Three Types of Biosampling on Matrix Effect and Recovery on Analysis of Tamoxifen and its Metabolites</td>
<td>Siska Silvany Br. Sormin</td>
</tr>
<tr>
<td>(A-1624366861)</td>
<td>Development and Validation of Quantification Method for Hydroxychloroquine in Volumetric Absorptive Microsampling (VAMS) Using High Performance Liquid Chromatography - Photodiode Array</td>
<td>Siti Ardyanti Rohadatul 'aisy</td>
</tr>
<tr>
<td>(A-1624865485)</td>
<td>Analysis 3-Hidroxy Propil Mercapturic Acid in Rat Urine on Cyclophosphamid Induced after Treatment Leucaena leucocephala (Lam.) de Wit Extract by Liquid Chromatography Tandem Mass Spectrometry</td>
<td>Sri Wardatun</td>
</tr>
<tr>
<td>(A-1624264873)</td>
<td>Development and Validation of Cyclophosphamide and 4-Hydroxy cyclophosphamide Quantification Method in Volumetric Absorptive Microsampling by Liquid Chromatography - Tandem Mass Spectrometry</td>
<td>Steven</td>
</tr>
</tbody>
</table>

**Room A: Military Pharmacy and Leadership**

<table>
<thead>
<tr>
<th>ID</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A-1626090341)</td>
<td>In Silico Study: Molecular Docking Targeting Kras Receptor in Lung Cancer</td>
<td>Arya Wijaya Harahap</td>
</tr>
<tr>
<td>(A-1625800218)</td>
<td>Military Pharmacy Education In Indonesia</td>
<td>Aliyah Nur Ariza</td>
</tr>
<tr>
<td>Time</td>
<td>Presentation</td>
<td></td>
</tr>
<tr>
<td>----------</td>
<td>------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>12.30 - 14.10</td>
<td>(A-1624797679) Agnes Frethernety The Green Extraction Technique Of Antioxidant Compounds From Seluang Belum Root's (Luvunga sarmentosa (Blume) Kurz.) Determined By The Abts Assay</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(A-1625924693) Angelina Deva Adella Putri Physalis angulata : Its Latest Compound And Biological Activities (a Review)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(A-1624636797) Annissa Primadiamanti Papaya Stem Ointment (Carica Papaya L.) And Its Activity As Wound Healer</td>
<td></td>
</tr>
<tr>
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</tbody>
</table>
## Room B: Clinical Pharmacy

<table>
<thead>
<tr>
<th>Time</th>
<th>Presentation Title</th>
<th>Author(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.40 – 16.00</td>
<td>Cost -Utility Analysis Of Treatment With Oseltamivir And Favipiravir On The Patient With Medium Degree Phase Of Covid-19 In Sentra Medika Hospital Cisalak Depok</td>
<td>(A-1624075501) Arif Rahmandani</td>
</tr>
<tr>
<td></td>
<td>The Effect Of Knowledge And Adherence To Clinical Outcome In Type 2 Diabetes Mellitus Patients In Several Health Centers In Bandar Lampung</td>
<td>(A-1626018272) Dirga</td>
</tr>
<tr>
<td></td>
<td>The Role Of Ursodeoxycholic Acid And Phenobarbitol In Children With Cholestasis: A Longitudinal Study</td>
<td>(A-1625390558) Harapan Parlindungan Ringoringo</td>
</tr>
<tr>
<td></td>
<td>Cost Effectiveness Analysis Of Antipsychotics In Schizophrenia Patients</td>
<td>(A-1624860863) Indah Kurnia Utami</td>
</tr>
<tr>
<td></td>
<td>The Effectiveness Of Favipiravir As An Antiviral Therapy In The Treatment Of Covid-19 In The Several Hospital In Blora.</td>
<td>(A-1625204328) Metrikana Novembrina</td>
</tr>
<tr>
<td></td>
<td>Potential Of Pharmacological And Herbal Medicines For Treatment Covid-19 Patients : A Narrative Review</td>
<td>(A-162658238) Syahrul Tuba</td>
</tr>
<tr>
<td></td>
<td>Lansoprazole-Induced Thrombocytopenia In Elderly: A Case Report</td>
<td>(A-1625466372) Widyati</td>
</tr>
<tr>
<td></td>
<td>Antioxidant and Antibacterial Activity of Various Fractions of Heterotrigna itama Propolis Found in Kutai Kartanagara</td>
<td>(A-1628044063) Paula Mariana Kustiawan</td>
</tr>
</tbody>
</table>

## Room B: Biology Pharmacy

<table>
<thead>
<tr>
<th>Time</th>
<th>Presentation Title</th>
<th>Author(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16.00 – 16.10</td>
<td>Antioxidant and Antibacterial Activity of Various Fractions of Heterotrigna itama Propolis Found in Kutai Kartanegara</td>
<td>(A-1628044063) Paula Mariana Kustiawan</td>
</tr>
<tr>
<td>Time</td>
<td>Room C: Pharmaceutical Technology</td>
<td>Room C: Pharmacology &amp; Biomedical Sciences</td>
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</tr>
<tr>
<td></td>
<td>(A-1626076124) Endang Wahyu Fitriani: Design Of Tea Tree Oil Loaded Nanostructured Lipid Carrier: Preparation And In-Vitro Antifungal Activity</td>
<td>(A-1628009542) Febriana Aquaresta: Comparison Between GenoType MTBDRsl VER 2.0 Assay and Phenotypic Method on Rifampicin Resistant Mycobacterium tuberculosis</td>
</tr>
<tr>
<td>Time</td>
<td>Speaker ID</td>
<td>Title</td>
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</tr>
<tr>
<td>15.30 – 16.00</td>
<td>(A-1626057961) Gilang Bhakti Nusantara</td>
<td>The Role Of Military Pharmacy In Medical Intelligence For State Defense With Sedative Agents</td>
</tr>
<tr>
<td></td>
<td>(A-1626108673) Riyas Muhammad Agung Kotta</td>
<td>Pharmacy As The Foundation Of The Nation: Indonesia's Preparedness In Facing Bioterrorism</td>
</tr>
<tr>
<td></td>
<td>(A-1626009002) Sionvhory Shvidarvy Sroyer</td>
<td>Optimization Therapy Using Combination Of Antiretroviral Therapy And Red Fruit Extract To Reduce Morbidity Of HIV/AIDS</td>
</tr>
</tbody>
</table>
## POSTER PRESENTER SCHEDULE

**September, 4th 2021**

**12.00 - 12.50**

### Room A: Pharmaceutical Chemistry and Military Pharmacy

<table>
<thead>
<tr>
<th>Code</th>
<th>Presenter</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A-1626658667)</td>
<td>Tesia Aisyah Rahmania</td>
<td>Synthesis And Antimicrobial Assay Of 3,5-Bis-(4'-Hydroxy-3',5'-Dichlorobenzyliden)-1-Methyl-4-Piperidone And 3,5-Bis-(4'-Hydroxy-3',5'-Dichlorobenzyliden)-4-Piperidone As Hexagamavunone-6 (HGV-6) Analogs</td>
</tr>
<tr>
<td>(A-1626101605)</td>
<td>Musadat Furqon Baihaki</td>
<td>Candidates Targeted Therapy Of EGFR For Lung Cancer: In Silico Study</td>
</tr>
<tr>
<td>(A-1626496351)</td>
<td>Ahmad Rofee Ramadhan</td>
<td>Management Dual Endemics Of Malaria And Covid 19 When A Tropical Cyclone Occurs In East Nusa Tenggara: A Narrative Review</td>
</tr>
<tr>
<td>(A-1626660972)</td>
<td>Yolanda Safitri</td>
<td>Potential of Ethanol Extract of <em>Ocimum americanum</em> L. as Hepatoprotector in Antituberculosis Drugs-Induced Hepatotoxicity</td>
</tr>
</tbody>
</table>

### Room B: Biology and Clinical Pharmacy

<table>
<thead>
<tr>
<th>Code</th>
<th>Presenter</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A-1626657975)</td>
<td>Editha Renesteen</td>
<td>Helminth Therapy As Potential Treatment For Multiple Sclerosis</td>
</tr>
<tr>
<td>(A-1626079685)</td>
<td>Fathku Rahman</td>
<td>Lactic Acidosis Associated With Metformin In Patients With Diabetic Kidney Disease: A Narrative Review</td>
</tr>
<tr>
<td>(A-162608874)</td>
<td>Yudha Aditya Pradana</td>
<td>Penicillins Vs Macrolides In Diphtheria Treatment In Indonesia</td>
</tr>
<tr>
<td>(A-1626013694)</td>
<td>A. Thafida Khalisa</td>
<td>Taken A Lesson In Pandemic Covid-19: Are Supplements And Vitamin Needed?</td>
</tr>
<tr>
<td>(A-1626054040)</td>
<td>Muhammad Rifly Aprianto</td>
<td>Effectivity Of Dexamethasone Threatening Severe Covid-19 Patients; Does Still Reliable Used For Covid-19?</td>
</tr>
<tr>
<td>(A-1626104820)</td>
<td>Muhammad Fajar Ridho Darussalam</td>
<td>Astrazeneca Covid-19 Vaccine Efficacy A Narrative Review</td>
</tr>
<tr>
<td>(A-162604630)</td>
<td>Savira Azhara Andavia</td>
<td>Level Of Community Knowledge And Behavior Regarding The Use Of Sunscreen Cosmetics</td>
</tr>
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</table>

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<table>
<thead>
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<th>ID</th>
<th>Title</th>
</tr>
</thead>
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<tr>
<td>(A-1626001998)</td>
<td>Level Of Public Knowledge Related To Covid-19 Supplementation</td>
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<tr>
<td>Jesicca Dwiyanti</td>
<td></td>
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<tr>
<td>(A-1624096399)</td>
<td>The Use of Lysozyme Toothpaste to Prevent Early Childhood Caries (EcC) in 24-Months Children (Based on <em>S. mutans</em> Colonization and Salivary Antibacterial)</td>
</tr>
<tr>
<td>Essie Octiara</td>
<td></td>
</tr>
<tr>
<td>Harapan Parlindungan Ringoringo</td>
<td></td>
</tr>
<tr>
<td>(A-1625314391)</td>
<td>The Role of Methylprednisolone in Children with Immune Thrombocytopenic Purpura: a Case Report</td>
</tr>
<tr>
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<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Room C: Pharmaceutical Technology and Pharmacology</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.20 – 12.40</td>
</tr>
<tr>
<td>(A-1626090987) Siti Maimunah</td>
</tr>
<tr>
<td>(A-1626058569) Nor Liliyana</td>
</tr>
<tr>
<td>(A-1626106757) Rahmah Elfiyani</td>
</tr>
<tr>
<td>(A-1626057614) Kurnia Sandy</td>
</tr>
<tr>
<td>(A-1626090393) Dewa Ayu Agung Puspita Dewi</td>
</tr>
<tr>
<td>(A-1626099348) Aliqbal Rajib Nohea</td>
</tr>
<tr>
<td>(A-1626081009) Ni Made Dwi Sandhiutami</td>
</tr>
</tbody>
</table>
## Abstracts

<table>
<thead>
<tr>
<th>Abstract ID</th>
<th>Name</th>
<th>Title</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A-1624797579)</td>
<td>Agnes Frethernety</td>
<td>The Green Extraction Technique Of Antioxidant Compounds From Seluang Belum Root's (Luvunga Sarmentosa (Blume) Kurz.) Determined By The Abs Assay</td>
<td>Oral Presenter</td>
</tr>
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</tr>
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</tr>
</tbody>
</table>
THE GREEN EXTRACTION TECHNIQUE OF ANTIOXIDANT COMPOUNDS FROM SELUANG BELUM ROOT’s (Luvunga sarmentosa (Blume) Kurz.) DETERMINED BY THE ABTS ASSAY

Elsa Trinovita*, Kadek Prayoga Zeolistrawan¹, Agnes Frethernety¹

¹Faculty of Medicine, University of Palangka Raya, Palangka Raya, Central Kalimantan, 73112, Indonesia

*Email: elsa3novita@gmail.com

ABSTRACT

An unhealthy lifestyle will usually cause free radical compounds that are reactive against cells and tissues of the body. Therefore free radical reactions in the body can be muted with antioxidants that can help protect the body from free radical attack and resist its negative impact. Synthetic antioxidants such as BHA and BHT can cause damage to the liver and carcinogenic. Some scientific studies worldwide identify compounds that have potential pharmacological activity as an antioxidant with low side effects. This study aims to determine the Potential of Seluang Belum Roots (Luvunga sarmentosa (Blume) Kurz.) have activity as an antioxidant using the ABTS method. Seluang belum root’s (Luvunga sarmentosa (Blume) Kurz.) is a traditional Kalimantan plant that contains chemical compounds that have the Potential of antioxidants that can inhibit free radicals. It extracted using the ultrasonic-assisted extraction (UAE) method with a 150 g sample/ 600 mL solvent ratio (1:4g/mL) and extraction time of 15 minutes. The test group was divided into five concentrations and vitamin C as a positive control. It was measured on an ultraviolet-visible (UV-Vis) spectrophotometer with a wavelength of 750 nm. The IC₅₀ value of Seluang Belum Root’s by 42.54 ppm. The Seluang Belum Root’s as a traditional plant from Kalimantan can be one alternative therapy made from the natural Potential to have very strong antioxidant activity.

Keywords: Antioxidant, Luvunga sarmentosa (Blume) Kurz., UAE, ABTS
ABSTRACT

Physalis angulata is one of the famous herbal plants known for its efficacious compounds to treat several diseases, such as skin fibrosis, diuretic, asthma, infection, rheumatism, and liver problems. Though it has been widely researched, the study of its compounds identification and each biological activity has not been significantly classification yet. This review will provide information regarding the recent compounds of Physalis angulata and its biological activity. Based on research articles published since 2011 discussing Physalis angulata, several new compounds have been found, such as physalin XI, aminophysalin A, aromaphysalin B, and α – tocopherol. Those compounds have been analyzed in vivo or in vitro, even use a double-blind, randomized controlled trial method. The appropriate management therapy of Physalis angulata will be helpful, both as primary therapy and adjuvant.

Keywords: Physalis angulata, novel compounds, physalin, withanolides
Background: Papaya leaf and fruit had been known to have potency as wound healer. However, its stem had not been used as drugs. Objective: This research was conducted to observe activity of papaya stem ointment as wound healer. Materials and Methods: Papaya stem extract was made through maceration. Two types of formula were made. Animals were divided into six groups; (I) Control group which betadine ointment was given (II) Formula I (without extract) (III) Formula I (IV) Formula II (without extract) (V) Formula II (VI) No treatment group. Ointment was given on excised wound daily. Diameter size (mm) of the wound in all treatment group were measured on every 2 days. Results: Formula II group hydrocarbon base extract experienced wound closure on day 7, formula I group hydrophilic base extract experienced wound closure on day 9. This explained that formula II had shorter duration than formula I in wound healing. However, in formula I (group III), it could not be concluded that extract had its effectiveness because similar result was also obtained in group II (formula I without extract); that wound healing effect was not the result of the extract. Conclusion: It concluded that papaya stem ointment with hydrocarbon base could heal wound within 7 days.

Keywords: papaya stem, ointment, wound healer.
POTENTIAL OF Rhinachanthus nasutus (L.) KURZ LEAVES EXTRACT AS ANTIOXIDANT AND INHIBITOR OF ALPHA-GLUCOSIDASE ACTIVITY

Candra Irawan¹², Berna Elya*, Muhammad Hanafi³, and Fadlina Chany Saputri¹

¹Faculty of Pharmacy Universitas Indonesia, Depok, West Java, Indonesia
²Department of Chemical Analysis, Politeknik AKABogor, Bogor, West Java, Indonesia
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ABSTRACT

Background: Rhinachanthus nasutus (L.) Kurz is a plant that has long been used by people in Southeast Asia, India, and China as traditional medicine. The leaf preparations of R. nasutus have been used in traditional medicine to treat diabetes. Objective: This study aims to obtain a leaves extract of R. nasutus through the application of ultrasound-assisted extraction (UAE), reveals the total phenolic content in the extract; Methods: The extract's potential as an antioxidant with copper-reducing strength parameters and its potential as an antidiabetic by inhibiting its alpha-glucosidase activity. Results: The crude ethanol extract of R. nasutus leaves obtained from the UAE process was 5.8520 g with a yield of 8.36%. The total phenolic content of the leaves extract was 607.05 ± 0.18 mg GAE / g sample. The antioxidant activity test using the CUPRAC method gave an IC₅₀ value of 19.07 ± 0.10 mg / L. In addition, leaves ethanol extract had a high ability to inhibit alpha-glucosidase activity with an IC₅₀ value of 81.31 ± 2.59 mg/L. Conclusion: From this study, we can conclude that the ethanol extract of the leaves of R. nasutus from UAE can potentially be a source of antioxidants and antidiabetic.

Keywords: Rhinachanthus nasutus (L.) Kurz, Ultrasound-Assisted Extraction, Antioxidant, Total Phenolics Content, Antidiabetic, Alpha-Glucosidase Enzyme.
POSSIBILITY OF PASAK BUMI (E. longifolia JACK) ROOT AS ANTI PROSTATE CANCER THROUGH ANTI PROLIFERATION MECHANISM ON ADENOCARCINOMA PROSTATE CELLS PC3

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ABSTRACT

Background: The active compound of Pasak Bumi root has a cytotoxic effect on various types of cancer such as colon cancer, breast cancer, lung cancer, skin cancer and ovarian cancer. Is it also cytotoxic in prostate cancer?

Objective: This study aimed to know the potential of Pasak Bumi root as an anticancer of the prostate by inhibiting proliferation of PC3 cells.

Method: The active compound of the roots of Pasak Bum E. longifolia was obtained by extraction using ethanol as the solvent. Prostate cancer PC-3 cell culture was obtained from independent androgen prostate adenocarcinoma that had bone metastases as the research subject. This study was an in vitro experimental study with a post-test control group design. Analysis of PC3 cell viability used the MTT assay method.

Result: Anova test results showed that p-value (Sig.) at 0.011 and smaller than α = 0.05. Therefore, it can be concluded that there is a significant difference in the viability of Adenocarcinoma cells in the administration of ethanol extract Pasak Bumi root with different concentrations.

Conclusion: Ethanol extract of Pasak Bumi root could inhibit the proliferation of PC-3 prostate cancer cells. The higher the ethanol extract concentration of the Pasak bumi root, the lower the viability of PC-3 cells. The ethanol extract of Pasak Bumi root has the potential as an anticancer of the prostate through a proliferation inhibition mechanism.

Keyword: Pasak Bumi, Anti prostate cancer, antiproliferation, PC3 cell
ABSTRACT

Background: Ultrasonic-Assisted Extraction (UAE) technology is an effective method for the extraction of chemical constituents from plant materials. The antioxidant activity found in *Musa balbisiana* Colla may be related to antigout activity, where there is a role for antioxidants in the inhibition of xanthine oxidase activity. **Objective:** This research aims to gain ethanolic extract from the unripe of *Musa balbisiana* Colla pulp using the UAE method and obtain information about secondary metabolites and their bioactivity as antioxidant and antigout. **Methods:** Ethanolic extract was obtained by the UAE method, total phenolic content was determined by the Folin-Ciocalteu method, antioxidant activity was measured using DPPH and FRAP method, then the uric acid level was measured using uric acid test kit. **Results:** The results showed that antioxidant activity test using the DPPH and FRAP methods gave IC50 values of 411.59 ± 0.1336 mg/L and 98.03 ± 0.2926 mg/L, respectively. The total phenolic content value of 823.95 ± 3.9806 mg GAE/g ethanolic extract is thought to have a role in high antioxidant activity. Furthermore, ethanolic extract with a concentration of 50 mg/L has activity in reducing uric acid levels by around 10%. **Conclusion:** It can be concluded that the ethanolic extract produced by UAE has potential as a source of antioxidants and antigout.

**Keywords:** Anti-gout, Antioxidant, *Musa balbisiana* Colla, Phenolic Content, Ultrasonic-Assisted Extraction
ENZYMATIC PRODUCTION OF PROTEIN HYDROLYSATE FROM Nannochloropsis sp.

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ABSTRACT

Background: Nannochloropsis sp. is considered a promising microalga for biopharmaceutical application, since its bioactive peptides have potential biological activities, such as antioxidant, angiotensin-converting enzyme (ACE) inhibitor, and antiaging. Protein hydrolysate is a complex mixture of several peptides and free amino acids, which have better effectiveness than free amino acids or intact proteins.

Objective: This study aimed to produce a protein hydrolysate from microalgae of Nannochloropsis sp. by enzymatic method for pharmaceutical application. Materials and Methods: Dried Nannochloropsis sp. Microalgae was hydrolyzed by Alcalase at pH 9.0 and 50°C for 1 hour, then the hydrolysate was heated at 95°C for 10 minutes. The obtained Nannochloropsis sp. protein hydrolysate (NPH) was analyzed for protein content using the Kjeldahl method. Furthermore, the degree of hydrolysis (DH) was measured by trichloroacetic acid (TCA) method.

Results: The results showed that NPH was produced with a yield of 28.01% (w/w) and the DH value of 36.73%. Moreover, the protein content of NPH was 8.98% (w/w), which was much higher than that dried Nannochloropsis sp. In addition, the contents of ash, fat, and water in NPH was much lower than that dried Nannochloropsis sp. microalgae. Conclusion: NPH was successfully produced from dried Nannochloropsis sp. with high yield value and higher protein content compared to dried Nannochloropsis sp. Protein hydrolysate can be valuable bio-ingredient with pharmaceutical and nutraceutical application potentials.

Keywords: microalgae, Nannochloropsis sp., enzymatic hydrolysis, protein hydrolysate.
ABSTRACT

Prostate transmembrane protein androgen-induced 1 (PMEPA1) or Transmembrane prostate androgen-induced protein (TMEPAI) is a type 1b transmembrane protein that is reported to be highly expressed in various cancers, including breast cancer. Previous studies reported that knockdown and knockout of TMEPAI in breast cancer cells decreased their tumorigenic activity. However, how TMEPAI promotes tumorigenesis is still poorly understood. Elucidating the molecular functions of TMEPAI through its essential motifs might help to better understand how TMEPAI promotes tumorigenesis. Here, we generated CRISPR/Cas9-mediated TMEPAI knockout (KO) breast cancer cell lines and used a lentiviral system to complement each of TMEPAI isoform and TMEPAI mutant individually. As a result, there were no clear functional differences between isoforms, while interestingly double PPxY (PY) motifs and a Smad-interaction motif (SIM) of TMEPAI which commonly located on all TMEPAI isoform’s intracellular region, were both essential for colony and sphere formation. Collectively, our finding revealed that coordination between double PY motifs and a SIM of TMEPAI are essential for TMEPAI tumorigenic functions in breast cancer cells.
HMG-COA REDUCTASE INHIBITORY ACTIVITY OF EXTRACT AND CATECHIN ISOLATE FROM Uncaria gambir AS A TREATMENT FOR HYPERCHOLESTEROLEMIA

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ABSTRACT

Background: The enzyme 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase is the key enzyme of the mevalonate pathway that produces cholesterol. Inhibition of HMG-CoA reductase reduces cholesterol biosynthesis in the liver. Synthetic drugs, statins, are commonly used for the treatment of hypercholesterolemia. Catechin as the main compounds in Uncaria gambir A. have potential for the treatment of hypercholesterolemia. Objective: This study aims to determine the inhibitory effect of extract and catechin isolate of Uncaria gambir. Methods: Extraction gambir leaf with water. Isolation of catechin gambier has been done by maceration using ethyl acetate-hexane. Phytochemical analysis of a extract and catechin isolat using UHPLC. The inhibitory activity of HMG CoA enzymes was carried out enzymatically using HMG-CoA Reductase assay kit by ELISA as well as simvastatin as the standard drug. Result: The results showed that the catechin contents in extract and catechin isolate were 68.32% and 96.74%. The in-vitro assessment of HMG -CoA reductase activity indicated a 78.12; 97.46% and 85.74% inhibition by the extract, catechin isolate and simvastatin. Conclusion: Catechin isolate from Uncaria gambir showed strong HMG-CoA reductase activity. The result showed a correlation that the higher catechin content, the higher inhibitory of HMG CoA reductase respectively.

Keyword: HMG COA Reductase, Uncaria gambir, catechin, hypercholesterolemia
THE MOLECULAR MODELING OF rpoB GENE MUTATION IN ACTIVE PULMONARY TUBERCULOSIS PATIENTS

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ABSTRACT

Background: Rifampicin resistance cases of pulmonary tuberculosis in Indonesia increased. Rifampicin is the most potential drug in the first-line anti-tuberculosis treatment. Objective: To find out the role and molecular modeling of rpoB gene mutation in RRDR of Mycobacterium tuberculosis in the clinical isolates. Materials and Methods: One hundred and ten of pulmonary tuberculosis patient isolates from Indonesia were collected from July 2017 - October 2018. All of the samples were examined by the molecular methods using specific gene amplification and sequencing for identification of rpoB gene mutation in the Mycobacterium isolates. Results: There were 13.6% mutation in the RRDR of rpoB gene from pulmonary tuberculosis patient isolates. The dominant mutation appeared in the codon 450, with changes amino acid of Serine to Leucine. Conclusion: The mutation indicated to rifampicin resistance were confirmed by molecular modeling.

Keywords: Isolates, sequencing, pulmonary tuberculosis, mutation
ANTIOXIDANT AND ANTIBACTERIAL ACTIVITY OF VARIOUS FRACTIONS OF *Heterotrigona itama* PROPOLIS FOUND IN KUTAI KARTANEGARA

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ABSTRACT

**Background**: In the current pandemic era, people are trying to find additional income, such as stingless bee cultivation. Especially, bee species of *Heterotrigona itama*, because the selling value of stingless bee honey for maintaining health is quite high. However, the potential of other bee products such as propolis is still underutilized. In this study, the antioxidant and antibacterial activity of propolis from various fractions was investigated. **Materials and Methods**: *H. itama* propolis was extracted with 96% ethanol to obtain Ethanol Extract Propolis (EEP). Then it was used for liquid-liquid partition with different polarity (n-hexane and ethyl acetate) to obtain the n-hexane fraction (HF) and ethyl acetate fraction (EAF). These fractions were tested for antioxidants using the DPPH method and antibacterial against bacteria *Propionibacterium acne*, *Staphylococcus aureus* and *Escherichia coli* using the agar diffusion method. Vitamin C was used as a positive control in the antioxidant test and Thiamphenicol was used in the bacterial test. **Results**: The ethyl acetate fraction had better antioxidant activity (IC\(_{50}\) 128.46 ug/mL) than the ethanol extract (IC\(_{50}\) 205.86 ug/mL) and n-hexane fraction (IC\(_{50}\) 350.01 g/mL). Antibacterial activity of EEP at 200 ug/mL against *P. acne* was 6±1.5 mm which categorised as medium inhibition, while the other fractions were classified as weak. **Conclusion**: EAF had the highest antioxidant activity meanwhile EEP is the most potent on antibacterial activity. The results obtained are influenced by the environment where the sample is taken which is less varied in plant sources and the time of sample collection.

**Keywords**: Antioxidant, Antibacterial, Fractions, Propolis, *Heterotrigona itama*
HELMINTH THERAPY AS POTENTIAL TREATMENT FOR MULTIPLE SCLEROSIS

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ABSTRACT

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS) which is characterized by the recruitment of T cells into the CNS, leading to demyelination and axonal damage. Currently, there are limited options for MS therapy, thus researchers start to use helminths therapy as a new therapeutic agent. Helminths are promising organisms to treat autoimmune diseases like MS by interfering the host's immune responses. Several helminths, including *Trichinella spiralis*, *Trichuis suis*, *Fasciola hepatica*, *Schistosoma japonicum* and *Schistosoma mansoni* are under investigation in animal models for MS, experimental autoimmune encephalitis (EAE). Furthermore, *Trichuis suis*, *Fasciola hepatica* and *Schistosoma mansoni* are being examined in patients. This narrative review outlines basic insight of MS, immunoregulation mechanisms induced by helminths, current helminths therapy for MS as well as helminths therapy for MS application in the future. Likewise, several factors like issues relating to in vivo stability and pharmacodynamics of helminth-derived molecules as well as delivery method to patients need to be studied to develop new therapeutic products.

Keywords: multiple sclerosis, helminth therapy, immunoregulation, immune system, autoimmunity
PHARMACEUTICAL CHEMISTRY
<table>
<thead>
<tr>
<th>Abstract ID</th>
<th>Name</th>
<th>Title</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A-1624003261)</td>
<td>Baitha Maggadani</td>
<td>Influence Of Cyp2d6 Polymorphism On Tamoxifen Metabolism</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1623141322)</td>
<td>Devi Ramadhanti Nurhaliza</td>
<td>Analysis of the Rate of Formation of 4-Hydroxycyclophosphamide in Dried Blood Spot of Indonesian Breast Cancer Patients after Administration of Cyclophosphamide</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1625148558)</td>
<td>Edria Rasendriya</td>
<td>Validation of Rifampicin and Isoniazid Quantification Method in Dried Blood Spot by High Performance Liquid Chromatography - Photodiode Array</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1624020621)</td>
<td>Hening Puspa Seruni</td>
<td>Analysis of The Rate of Formation of 4-Hydroxycyclophosphamide in Volumetric Absorptive Microsampling of Breast Cancer Patiens after Administration of Cyclophosphamide using LC-MS/MS</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1626063637)</td>
<td>Kholis Amalia Nofianti</td>
<td>The Effect of Power on Synthesis of 4-(4-Methyl)Benzoiloksi-3-Metoxicynamate Acid Using Microwave Irradiation Method</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1626003585)</td>
<td>Roesyta's Fitria Noer</td>
<td>Development And Validation Of Method For Analysis Of Favipiravir And Remdesivir In Volumetric Absorptive Microsampling With Ultra High Performance Liquid Chromatography Tandem Mass Spectrophotometry</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>Presenter</td>
<td>Title</td>
<td>Type</td>
<td></td>
</tr>
<tr>
<td>----------------------------------</td>
<td>-------------------------------------------------------------------------------------------------</td>
<td>-----------------------</td>
<td></td>
</tr>
<tr>
<td>Siska Silvany Br. Sormin</td>
<td>Comparison of Three Types of Biosampling on Matrix Effect and Recovery on Analysis of Tamoxifen and Its Metabolites</td>
<td>Oral Presenter</td>
<td></td>
</tr>
<tr>
<td>Siti Ardyanti Rohadatul'aisy</td>
<td>Development and Validation of Quantification Method for Hydroxychloroquine in Volumetric Absorptive Microsampling (VAMS) Using High Performance Liquid Chromatography - Photodiode Array</td>
<td>Oral Presenter</td>
<td></td>
</tr>
<tr>
<td>Sri Wardatun</td>
<td>Analysis 3-Hydroxy Propyl Mercapturic Acid in Rat Urine on Cyclophosphamide Induced after Treatment Leucaena leucocephala (Lam.) de Wit Extract by Liquid Chromatography Tandem Mass Spectrometry</td>
<td>Oral Presenter</td>
<td></td>
</tr>
<tr>
<td>Steven</td>
<td>Development and Validation of Cyclophosphamide and 4-Hydroxycyclophosphamide Quantification Method in Volumetric Absorptive Microsampling by Liquid Chromatography - Tandem Mass Spectrometry</td>
<td>Oral Presenter</td>
<td></td>
</tr>
<tr>
<td>Winning Bekti Safitri</td>
<td>Analysis of N7-(2-carbamoyl-2-hydroxyethyl)guanine in Dried Blood Spot after Food Exposure by Ultra High Performance Liquid Chromatography - Tandem Mass Spectrometry</td>
<td>Oral Presenter</td>
<td></td>
</tr>
<tr>
<td>Al Lifia Rahmatul Ummah</td>
<td>Validation of a Simultaneous Analytical Method of Risperidone and 9-Hydroxyrisperidone in Dried Blood Spot Using Ultra High Performance Liquid Chromatography Tandem Mass Spectrometry</td>
<td>Poster Presenter</td>
<td></td>
</tr>
<tr>
<td>Okta Nursanti</td>
<td>Molecular Docking Compounds Contained in (Phyllanthus acidus L.) as Ligands to The Estrogen Receptor Alfa</td>
<td>Poster Presenter</td>
<td></td>
</tr>
<tr>
<td>Tesia Aisyah Rahmania</td>
<td>Synthesis And Antimicrobial Assay Of 3,5-Bis-(4'-Hydroxy-3',5'-Dichlorobenzyliden)-1-Methyl-4-Piperidone And 3,5-Bis-(4'-Hydroxy-</td>
<td>Poster Presenter</td>
<td></td>
</tr>
</tbody>
</table>
INFLUENCE OF Cyp2d6 POLYMORPHISM ON TAMOXIFEN METABOLISM

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Background: Tamoxifen is widely used as an adjuvant therapy in estrogen receptor positive (ER+) breast cancer. Tamoxifen will be metabolized by the CYP2D6 enzyme into more active metabolites such as endoxifen, 4-hydroxytamoxifen, and N-desmethyltamoxifen. Polymorphisms of the CYP2D6 genes are associated with an impaired response to tamoxifen.

Objective: to investigate the correlation of genetic polymorphisms in CYP2D6 with the steady state level of tamoxifen and its metabolites in Indonesian women with estrogen receptor-positive breast cancer.

Methods: 151 women who were prescribed tamoxifen for at least two months were recruited. Blood samples were drawn from a fingerprick using a volumetric absorptive microsampling method, while DNA samples were collected with a buccal swab. Genotyping was performed using the qPCR method while metabolite level measurement was performed using high performance liquid chromatography tandem mass spectrometry.

Result: The CYP2D6 phenotype found in patients was a normal metabolizer in 54%, an intermediate metabolizer in 40.67%, and a poor metabolizer in 1.3% of patients. No ultrarapid metabolizers were found. Endoxifen levels among the three metabolizers were significantly different (p-value = 0.00343). The highest number of IMs fall into the lowest quintile while the highest number of NMs fall into the highest quintile.

Conclusion: Our findings showed an association between CYP2D6 polymorphism and endoxifen levels. Patients with the IM and PM phenotype received less benefit from TAM adjuvant treatment, indicating the need for dose adjustment of this phenotype group.

Keywords: CYP2D6 polymorphism, tamoxifen, endoxifen, personalized therapy, pharmacogenomic
DEVELOPMENT AND VALIDATION METHOD FOR QUANTIFICATION OF FAVIPIRAVIR IN VOLUMETRIC ABSORPTIVE MICROSMALLING (VAMS) USING HIGH PERFORMANCE LIQUID CHROMATOGRAPHY–PHOTODIODE ARRAY

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ABSTRACT

Favipiravir is a prodrug made by modifying the pyrazine group from T-1105 compound which is given as a therapy of COVID-19. Favipiravir target concentration in blood for COVID-19 is 40–80 µg/mL, whereas according to in vitro studies, favipiravir can block hERG channels in the heart at a concentration of 157.1 µg/mL. The aim of this study was to develop and validate a quantification method of favipiravir in Volumetric A Absorptive Microsampling (VAMS) using remdesivir as internal standard. Analysis of favipiravir was performed using HPLC-DAD with C₁₈ column (Waters, Sunfire™ 5µm; 250 × 4.6 mm), injection volume was 50 µL, mobile phase consists of acetonitrile-0.2% formic acid-20 mM sodium dihydrogen phosphate pH 3.5 with gradient elution, flow rate of 0.8 mL/min, column temperature was 30 °C, run time 12 minutes, and wavelength was 300 nm. Sample preparation was carried out by the protein precipitation method using 500 µL of methanol. Samples were mixed on vortex for 30 seconds, sonicated for 15 minutes, and centrifuged at 10,000 rpm for 10 minutes. The LLOQ obtained is 500 ng/mL and the calibration curve ranges from 500 to 160,000 ng/mL with a correlation coefficient of 0.99825-0.99860. The method developed has successfully met the full validation requirements by Food and Drug Administration 2018.

Keywords: Favipiravir, Remdesivir, Volumetric Absorptive Microsampling (VAMS), High Performance Liquid Chromatography–Photodiode Array, COVID-19
ANALYSIS OF THE RATE OF FORMATION OF 4-HYDROXYCYCLOPHOSPHAMIDE IN DRIED BLOOD SPOT OF INDONESIAN BREAST CANCER PATIENTS AFTER ADMINISTRATION OF CYCLOPHOSPHAMIDE

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ABSTRACT

Cyclophosphamide (CP) is an alkylating agent for anticancer and effective in treating breast cancer, non-Hodgkin lymphoma, and others. CP must be converted to its active metabolite (4-hydroxycyclophosphamide/4-OHCP) to produce a therapeutic effect. CP is converted to 4-OHCP by several enzymes in the liver, cytochrome P450 2B6 (CYP2B) is one of them. CYP2B6 is one of the most polymorphic CYP genes that can affect transcriptional regulation, protein expression, and the level of 4-OHCP in the body. The level 4-OHCP can be a parameter of the effectiveness of therapy. Therefore, the purpose of this study is to determine the hydroxylation rate of 4-OHCP by comparing the level of 4-OHCP to CP. This study used a sample of 43 breast cancer patients Dried Blood Spot who contained CP in their regimen therapy which was taken in average time 2.23 ± 0.38 hours (tmax CP) after CP’s administration. Samples were extracted by protein precipitation method and analysed using Ultra Performance Liquid Chromatography-Tandem Mass Spectrometry (UPLC-MS/MS); Acquity UPLC BEH C₁₈ column (2.1 x 100 mm; 1.7μm); temperature was 50°C; 0.01% formic acid - methanol as mobile phase with gradient elution for 6 minutes; flow rate was 0.15mL/minute; and injected volume was 10 μL. Mass detection using a triple quadrupole with ESI (+) and multiple reaction monitoring detection with m/z values 260.65>140.03 for cyclophosphamide, 33.65>221.04 for 4-OHCP-SCZ, and 337.71>225.05 for 4-OHCP-d₄- SCZ. The result showed that from 43 patients, the CP levels ranged from 2106.16 – 34386.90ng/mL. and 24.85 – 995.071 ng/mL for 4-OHCP. Based on the 4-OHCP/CP ratio, 53% (23 subjects) were classified as rapid metabolizers, and 47% (20 subjects) were classified as poor metabolizers.

Keywords: cyclophosphamide, 4-hydroxycyclophosphamide, dried blood spot, UHPLC-MS/MS, breast cancer patients
VALIDATION OF RIFAMPICIN ANDISONIAZID QUANTIFICATION METHOD IN DRIED BLOOD SPOT BY HIGH PERFORMANCE LIQUID CHROMATOGRAPHY - PHOTODIODE ARRAY

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Background: Rifampicin and isoniazid are antituberculosis drugs which combined for use as a fixed dose combination (FDC). The use of these drugs can cause resistance in patients if the levels of rifampicin and isoniazid are below the therapeutic range. This can lead to therapy failure, so it is necessary to monitor drug therapy. Dried blood spot (DBS) sample method in therapeutic drug monitoring (TDM) is an option that can be used to analyze drug concentration in patient's blood. Objective: This research objective is to develop an optimum analytical method for rifampicin and isoniazid in DBS sample using High Performance Liquid Chromatography - Photodiode Array detector (HPLC-PDA) with validation based on 2018 Food and Drug Administration (FDA) guideline.

Materials and Methods: Analysis of rifampicin and isoniazid was performed using HPLC-PDA with C18 column (Waters, Sunfire™ 5μm; 250 x 4.6mm), injection volume of 20 μL, and column temperature of 40°C. The mobile phase contained buffer ammonium acetate - acetonitrile - methanol (40:30:30) with isocratic elution, flow rate of 0.5 mL/minute, and total analysis time of 18 minutes. Protein precipitation extraction method was used for sample preparation using 1 mL of acetonitrile – methanol as extraction solvent (1:4 v/v%). Conclusion: All validation results fulfilled the requirements of the 2018 FDA guideline. The Lower Limit of Quantitation (LLOQ) values obtained were 1.0 μg/mL for rifampicin with calibration curve range of 1.0 – 30 μg/mL and 0.4 μg/mL for isoniazid with calibration curve range of 0.4 – 10 g/mL.

Keywords: Rifampicin, Isoniazid, Dried Blood Spot, High Performance Liquid Chromatography - Photodiode Array
ABSTRACT

Hydroxychloroquine (HCQ) is a quinoline compound derived from chloroquine which is one of the drugs used in the treatment of Systemic Lupus Erythematosus (SLE). Hydroxychloroquine is stored in a cool place, not humid, and protected from direct light exposure, so the long-term stability of hydroxychloroquine was evaluated in vitro. However, in vitro stability evaluation does not reflect drug metabolism processes in the body because hydroxychloroquine is enzymatically metabolized into several metabolites, so an evaluation of the incurred sample stability is required. This study was conducted with the aim of obtaining a pharmacokinetic profile of hydroxychloroquine using Volumetric Absorptive Microsampling (VAMS) as a safe microsampling technique to use during the COVID-19 pandemic. Beside that also evaluating the stability of hydroxychloroquine in Volumetric Absorptive Microsampling (VAMS) containing the blood of healthy subjects taking 200 mg hydroxychloroquine sulfate film-coated tablets by evaluating the Incurred Sample Stability of hydroxychloroquine samples at 2 points of concentration around \( C_{\text{max}} \) and 1 point of elimination phase on days 7, 14 and 30. The chromatographic conditions used were column C\(_18\) (Waters, XBridge\(^\text{®}\); 250 × 4.6 mm; 5μm); mobile phase consist of acetonitrile-1% diethylamine (65:35); flow rate of 0.8 mL/min; column temperature 45°C; PDA detector analysis wavelength of 332 nm; injection volume 100 μL; chloroquine as internal standard; and analysis time of 12 minutes. The pharmacokinetic profile of hydroxychloroquine in the VAMS samples showed that the maximum concentration (\( C_{\text{max}} \)) of the six healthy subjects ranged from 322.61-505.32 ng/mL and an average of 425.33 ± 65.90 ng/mL; the peak time (\( t_{\text{max}} \)) obtained from the six healthy subjects was 4 hours; the average of \( t_{\frac{1}{2}} \) was 23.32 ± 9.65 hours; the average AUC\(_0\)\(-\text{72}\) was 5103.63 ± 1419.66 ng hour/mL; the average AUC\(_0\)\(-\infty\) was 5763.97 ± 2155.26 ng hour/mL; and the AUC ratio is above 80%. The incurred sample stability of hydroxychloroquine in the VAMS of six healthy subjects up to day 30 showed results that met the requirements of the 2011 EMEA Bioanalytical Guideline with the %diff value obtained no more than 20% from at least 67% of the samples reanalyzed.

Keywords: Systemic Lupus Erythematosus (SLE); Hydroxychloroquine; Volumetric Absorptive Microsampling (VAMS); HPLC; PDA; Incurred Sample Stability.
ANALYSIS OF THE RATE OF FORMATION OF 4-HYDROXYCYCLOPHOSPHAMIDE IN VOLUMETRIC ABSORPTIVE MICROSMPLING OF BREAST CANCER PATIENTS AFTER ADMINISTRATION OF CYCLOPHOSPHAMIDE USING LC-MS/MS

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ABSTRACT

Cyclophosphamide is an alkylating agent used as a first-line treatment for breast cancer. Cyclophosphamide is a prodrug that needs bioactivation into 4-hydroxycyclophosphamide (4-OHCP) by CYP2B6 to get its cytotoxic activity. Polymorphism of CYP2B6 will affect bioactivation, level of cyclophosphamide and 4-OHCP in the body, and will effect the effectiveness of the therapy. The study aims to analyze levels of cyclophosphamide and 4-OHCP in Volumetric Absorptive Microsampling (VAMS) and to study the type of 4-OHCP formation rate (hydroxylation) in breast cancer patients. The type of 4-OHCP formation rate is determined by comparing the level of 4-OHCP to the level of cyclophosphamide. VAMS samples of 43 breast cancer patients were prepared using the protein precipitation with methanol and analysis was carried out using ultra high-performance liquid chromatography - tandem mass spectrometry (LC-MS/MS). The mobile phase used was a mixture of 0.01% formic acid and methanol with gradient elution. In this method, cyclophosphamide is linear in the range of 5 - 60,000 ng/mL and 2.5 - 1000 ng/ml for 4-OHCP. The range of cyclophosphamide level obtained in 43 VAMS samples of breast cancer patients were 5,625 ng/mL to 29,922 ng/mL, while the 4-OHCP levels were obtained in the range of 2.94 ng/mL to 737.03 ng/mL. The type 4-OHCP formation rate of 25 patients (58%) were ultrarapid metabolizers (UM) and 18 patients (42%) were poor metabolizers (PM).

Keyword: 4-hydroxycyclophosphamide, breast cancer, cyclophosphamide, LC-MS/MS, rate of 4-hydroxylation cyclophosphamide, Volumetric Absorptive Microsampling (VAMS)
THE EFFECT OF POWER ON SYNTHESIS OF 4-(4-METHYL) BENZOILOKSI-3-METOXYCINNAMATE ACID USING MICROWAVE IRRADIATION METHOD

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Background: In silico, ferulic acid derivatives have been shown to have antiplatelet activity. The development of the synthesis method for these compounds will facilitate further activity tests. The 4-(4-methyl) benzoyloxy-3-methoxycinnamate acid was synthesized from the reaction of ferulic acid and p-methylbenzoyl chloride through the nucleophilic acyl substitution reaction. Objective: The purpose of this study was to determine the effect of power on the synthesis of these compounds through microwave irradiation. Method: This reaction was conducted under 40, 200 and 400 Watt using a microwave oven. Result: The results showed that the yield percentage at 40 Watt for 10x30 seconds was 65.2% ± 3.4, and increased to 80.9% ± 8.2 at 200 Watt for 10x30 seconds was. The largest yield percentage achieved at 200 Watt for 10x30 seconds. At 400 Watt for 2x30 seconds, the yield percentage decreased to 36.0% ± 9.7 due to damage. The 1H-NMR spectra of the three separation methods (column chromatography, multilevel extraction and recrystallization) showed the impurity of the synthesized compound due to a mixture of ferulic acid and p-methylbenzoic acid compounds. Conclusion: The proposed synthesis method can produce the desired compound, but it is still necessary to develop a method for separating the remaining starting materials.

Keywords: 4-(4-methyl) benzoyloxy-3-methoxycinnamate acid, microwave irradiation, ferulic acid derivatives, synthesis
DEVELOPMENT AND VALIDATION OF METHOD FOR ANALYSIS OF FAVIPIRA VIN AND REMDESIVIR IN VOLUMETRIC ABSORPTIVE MICROSMPLING WITH ULTRA HIGH PERFORMANCE LIQUID CHROMATOGRAPHY TANDEM MASS SPECTROPHOTOMETRY

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Favipiravir and remdesivir are drugs to treat COVID-19. Favipiravir acts as an antiviral by inhibiting the RNA-dependent RNA polymerase enzyme while remdesivir is metabolized to its metabolite GS-441524 or remdesivir triphosphate (RDV-TP) so that it becomes an ATP-like ligand that can terminate viral RNA synthesis. Previously, a method of analysis of favipiravir and remdesivir has been developed and validated but with a plasma matrix. This study aims to find an optimal and validated method for simultaneous analysis of favipiravir and remdesivir in Volumetric Absorptive Microsampling (VAMS). The use of VAMS can be an advantage because the volume of blood drawn is small and the blood collection process is only through finger prick technique. This can reduce the process of transmitting the virus because could be done by the patient. Sample preparation with VAMS was carried out by precipitation of protein using 500 µl of methanol. Analysis was carried out by ultra-high-performance liquid chromatography with mass spectrophotometry detector and positive electrospray ionization and multiple reaction monitoring with m/z 157.9 > 112.92 for favipiravir and 603.09 > 200.005 for remdesivir and at m/z 225.968 > 151.991 for acyclovir as the internal standard. The separation was carried out using an Acquity UPLC BEH C18 column (2.1 x 100 mm; 1.7 m), formic acid 0.2%-acetonitrile (50:50), flow rate 0.15 ml/min, and column temperature. 50°C. The analytical method has been validated in accordance with the requirements issued by the Food and Drug Administration (2018) and European Medicine Agency (2011). The LLOQ value obtained for favipiravir was 500 ng/ml with a concentration range of 500-160,000 ng/ml and the LLOQ for remdesivir was 2 ng/ml with a concentration range of 2-8,000 ng/ml.

Keyword: Favipiravir, Remdesivir, Acyclovir, LC-MS/MS, Volumetric Absorptive Microsampling, COVID-19
COMPARISON OF THREE TYPES OF BIO-SAMPLING ON MATRIX EFFECT AND RECOVERY ON ANALYSIS OF TAMOXIFEN AND ITS METABOLITES

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The analysis of tamoxifen and its metabolites is required in monitoring the drug in the blood to achieve efficient therapy. The purpose of this study was to optimize the extraction method in DBS to obtain results equivalent to VAMS. The Hematocrit effect was still a problem that causes recovery bias in dried blood spots. Samples with different hematocrit levels may have different matrix as well. Therefore, the matrix effect and recovery of different hematocrit levels need to evaluate on DBS Perkin Elmer 226, DBS Whatman 903, and VAMS. The extraction methods used were solvent extraction and sonication-assisted extraction. The separation was carried out on the UPLC Class BEH C18 column using 0.1% formic acid and 0.1% formic acid in acetonitrile for 5 minutes. The value of multiple reaction monitoring (MRM) was set to m/z 372.33 > 72.28 for tamoxifen, m/z 374.25 > 58.25 for endoxifen, m/z 388.22 > 72.28 for 4-hydroxytamoxifen, m/z 358.31 > 58.27 for N-desmethyltamoxifen, and m/z 260.26 > 116.12 for propranolol hydrochloride. The extraction method on DBS Perkin Elmer 226 and DBS Whatman 903 obtained recovery results of 83\%–97\%. The results of this study showed that there was no significant difference in the recovery and matrix effect between the three types of biosampling at different hematocrit levels. VAMS obtained slightly higher recovery results than DBS Perkin Elmer 226 and DBS Whatman 903. DBS Perkin Elmer causes higher ion suppression than DBS Whatman and VAMS.

Keywords: dried blood spot, matrix effect, recovery, tamoxifen, volumetric absorptive microsampling
DEVELOPMENT AND VALIDATION METHOD OF QUANTIFICATION HYDROXYCHLOROQUINE IN VOLUMETRIC ABSORPTIVE MICROSAMPLING USING HIGH PERFORMANCE LIQUID CHROMATOGRAPHY – PHOTODIODE ARRAY

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ABSTRACT

Hydroxychloroquine is an antimalarial drug that used for systemic lupus erythematosus, rheumatoid arthritis, and malaria treatment. However, hydroxychloroquine has several side effects such as ocular toxicity, neurotoxicity, gastrointestinal disorder, and severe toxicity like cardiotoxicity. Therefore, therapeutic drug monitoring of high dose or long-term use of hydroxychloroquine is needed. This study aims to obtain an optimum and validated analysis and preparation method for hydroxychloroquine in Volumetric Absorptive Microsampling (VAMS) using High Performance Liquid Chromatography – Photodiode Array Detector based on Food and Drug Administration guidelines (2018). Hydroxychloroquine quantification was performed using HPLC-PDA with Waters Sunfire™ C18 (5µm; 250 x 4.6mm) column with injection volume of 100 µL, and the temperature of column was controlled at 45 ºC. Mobile phases consist of acetonitrile 1% diethylamine (65:35, v/v) and delivered at a flow rate of 0.8 mL/min throughout the 12 minutes run. Sample in VAMS was extracted by liquid-liquid extraction with 1% ammonia and n-hexane-ethyl acetate (50:50 v/v), 500 µL each as a solvent. Blood in VAMS was dried for 2 hours, then added with internal standard solution and 1% ammonia solution. The samples were mixed on vortex for 15 seconds and sonicated for 5 minutes. n-hexane-ethyl acetate (50:50, v/v) was added to the samples, then mixed again on vortex for 15 seconds and centrifuged for 5 minutes at a speed of 10,000 rpm. The organic phase was separated and dried under nitrogen gas flow. The residue was reconstituted with 150 µL mobile phase and transferred to autosampler vial for analysis. This method has successfully qualified the Food and Drug Administration (2018) parameters, with 2 ng/mL of LLOQ, range of calibration curve 2-6500 ng/mL, and coefficient of correlation 0.99927-0.99969.

Keywords: Hydroxychloroquine, chloroquine, cardiotoxicity, Volumetric Absorptive Microsampling (VAMS), High Performance Liquid Chromatography – Photodiode Array Detector (HPLC-PDA)
ANALYSIS 3-HIDROXY PROPIL MERCAPTURIC ACID IN RAT URINE ON CYCLOPHOSPHAMIDE INDUCED AFTER TREATMENT Leucaena leucocephala (LAM.) DE WIT EXTRACT BY LIQUID CHROMATOGRAPHY TANDEM MASS SPECTROMETRY

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**Background:** The ethanol 70% of extract of *Leucaena leucocephala* (Lam.) de Wit seeds contain amount of sulphydryl active compounds. **Objective:** In this study, the ethanol 70% of extract of *Leucaena leucocephala* (Lam.) de Wit seeds was tested in the model of cyclophosphamide-induced hemorrhagic cystitis. **Materials and methods:** Male Sprague Dawley rats were treated with *Leucaena leucocephala* (Lam.) de Wit extract (300 mg/kg) or vehicle orally for 1 week and injected with cyclophosphamide (50 mg/kg) 1 h after the last treatment with extract. Urine was collected in 24 hours after administration of cyclophosphamide. The urine was analyzed using LC-MS/MS. Prior to analysis, the 3-hidroxy propil mercapturic acid in urine sample was carried out by dilution (1:5) containing labelled 3-hidroxy propil mercapturic acid as internal standard. The LC separation was performed on using Waters Acquity BEH C18 column (1.7 μm; 50 mm x 2.1 mm). The mobile phase consisted of 0.1% formic acid and acetonitrile, column temperature 30°C and flow rate of 0.2 ml/min. The 3-hidroxy propil mercapturic acid was detected at m/z 221.968>90.993, and labelled 3-hidroxypropil mercapturic acid at m/z 225.032>117. The method was linear in the range of 40–20000 ng/ml. **Result:** The result showed that *Leucaena leucocephala* (Lam.) de Wit ethanol 70% extract had significant effect to 3-hidroxypropil mercapturic acid level in urine rat. **Conclusion:** The *Leucaena leucocephala* (Lam.) de Wit ethanol 70% extract have potential ameliorating of cyclophosphamide side effect.

**Key words:** cyclophosphamide, 3-hidroxy propil mercapturic acid, *Leucaena leucocephala* (Lam.) de Wit, urine
DEVELOPMENT AND VALIDATION OF CYCLOPHOSPHAMIDE AND 4-HYDROXYCYCLOPHOSPHAMIDE QUANTIFICATION METHOD IN VOLUMETRIC ABSORPTIVE MICRO-SAMPLING BY LIQUID CHROMATOGRAPHY TANDEM MASS SPECTROMETRY

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ABSTRACT

Cyclophosphamide is an anticancer alkylating prodrug, metabolized by CYP450 into its active metabolite, named 4-hydroxycyclophosphamide (4-OHCP). Its therapeutic effectiveness is determined by the 4-OHCP concentration. Several analytical methods using plasma and Dried Blood Spot have been developed to analyze cyclophosphamide and 4-OHCP. However, there are lots of disadvantages. Therefore, this study was conducted to develop a validated cyclophosphamide and 4-OHCP analysis method with 4-hydroxycyclophosphamide-d₄ (4OHCP-d₄) as the internal standard in Volumetric Absorptive Microsampling (VAMS) using Ultra-High-Performance Liquid Chromatography-Tandem Mass Spectrometry. VAMS requires small volume of sample, is not affected by hematocrit, and more efficient sampling process. Sample preparation was started by derivatization with 5 µL semicarbazide hydrochloride to overcome the instability of 4-OHCP and 4-OHCP-d₄, which was absorbed by VAMS. Afterwards, 25 µL samples were absorbed into VAMS and extracted using the protein precipitation method with methanol. The analysis was performed using a triple quadrupole Mass Spectrometry with positive electrospray ionization mode. The optimum conditions were obtained using the Acquity® UPLC BEH C18 column (2.1 x 100 mm; 1.7 µm); flow rate 0.2 mL/min; mobile phase 0.01% formic acid and methanol; gradient elution mode for 6 minutes; multiple reaction monitoring detection with m/z values 260.65>140.03 for cyclophosphamide, 333.65>221.04 for 4-OHCP-SCZ, and 337.71>225.05 for 4-OHCP-d₄-SCZ. The method has met the validation requirements set by the FDA (2018). Cyclophosphamide LLOQ value was 5 ng/mL and the calibration curve range was 5 - 60,000 ng/mL. Furthermore, 4-OHCP LLOQ value was 2.5 ng/mL and the calibration curve range was 2.5 - 1,000 ng/mL.

Key Words : Cyclophosphamide, 4-hydroxycyclophosphamide, 4-hydroxycyclophosphamide-d₄, LC-MS/MS, Volumetric Absorptive Microsampling
DEVELOPMENT OF DERIVATIVE 1,4 BENZODIAZEPINE ANALYSIS METHODS IN BIOLOGICAL MATRIX USING HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC) AND LIQUID CHROMATOGRAPHY MASS SPECTROMETER (LCMS): SYSTEMATIC REVIEW

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ABSTRACT

Derivatives of 1,4 benzodiazepine are most frequently prescribed drugs as sedative, anxiolytic, and antiepileptic agents. Highly consumption of benzodiazepines can lead to addiction and abuse. This causes the drugs, and their metabolites are frequently present in both clinical and forensic toxicology cases. The systematic paper reviews aim to identify an efficient sample preparation procedure as well as analytical method able to determine benzodiazepines in various biological matrices. Based on PRISMA flow diagram, 24 articles that were systematically reviewed showed that the use of plasma and urine resulted in better accuracy and recovery than the other biological matrices. The development of SBSE extraction method using vinylpyrrolidone ethylene glycol dimethacrylate polymer provides efficient results with a recovery of 96% and the use of HPLC instruments is still selective and sensitive with LOD of 12 ng/ml and LOQ of 36 ng/ml.

Keyword: analysis method, matrix biology, alprazolam, diazepam, clonazepam, lorazepam, oxazepam.
ANALYSIS OF $N^7$-(2-Carbamoyl-2-hydroxyethyl)guanine in Dried Blood Spot After Food Exposure by Ultra High Performance Liquid Chromatography – Tandem Mass Spectrometry

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**ABSTRACT**

$N^7$-(2-carbamoyl-2-hydroxyethyl) guanine is a DNA adduct formed by glycidamide, which is the metabolite of acrylamide. Acrylamide can be found in foods containing reducing sugars and asparagine that are heated at high temperatures. Analysis of $N^7$-(2-carbamoyl-2-hydroxyethyl) guanine was performed in Dried Blood Spot (DBS) samples from 25 subjects of group test who consumed a lot of acrylamide-containing foods and 25 subjects of negative control group. This study aimed to determine whether there is a significant difference in the levels of $N^7$-(2-carbamoyl-2-hydroxyethyl) guanine between the two groups. DBS samples were extracted using the QIAamp DNA Mini Blood Kit and analyzed using Ultra High Performance Liquid Chromatography – Tandem Mass Spectrometry (UHPLC-MS/MS). Separation was performed using an Acquity UPLC BEH C18 column (2.1 mm x 100 mm; 1.7 mm), eluted a flow rate of 0.1 mL/minute under an isocratic of mobile phase of 0.1% formic acid and acetonitrile. The bioanalytical method of $N^7$-(2-carbamoyl-2-hydroxyethyl) guanine in DBS with allopurinol as the internal standard by using UHPLC-MS/MS has been validated. The calibration curve range of $N^7$-(2-carbamoyl-2-hydroxyethyl) guanine obtained was 10 – 300 ng/mL with a coefficient of correlation of 0.997. The results of the analysis on 25 test group subjects showed that the concentration of $N^7$-(2-carbamoyl-2-hydroxyethyl) guanine ranged from 1.87 to 23.71 ng/mL, while the 25 subjects in the negative group ranged from 1.18 to 8.47 ng/mL. The results of the Mann Whitney test showed that there was a significant difference in the levels of $N^7$-(2-carbamoyl-2-hydroxyethyl) guanine between the test group and the negative control group with p value less than 0.001.

**Keywords:** $N^7$-(2-carbamoyl-2-hydroxyethyl) guanine, acrylamide, dried blood spot, UHPLC-MS/MS
VALIDATION OF A SIMULTANEOUS ANALYTICAL METHOD OF RISPERIDONE AND 9-HYDROXYRISPERIDONE INDRIED BLOOD SPOT USING ULTRA HIGH PERFORMANCE LIQUID CHROMATOGRAPHY TANDEM MASS SPECTROMETRY

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Risperidone (RIS) is a secondary generation antipsychotic, used widely for psychiatric illness such as Schizophrenia. However, RIS and its major active metabolites, 9-Hydroxyrisperidone (9-OHRIS), showed variability levels based on the CYP2D6 polymorphisms, and it impacts on individual variability in the response of therapeutics and side-effect of medication. In the present study, we developed and the validated analytical method of RIS and 9-OHRIS simultaneously using UHPLC-MS/MS and Dried Blood Spots (DBS) to facilitate safety and response to treatment with therapeutic drug monitoring (TDM). The dried blood spots were extracted using methanol – acetonitrile as a protein precipitation, via ultrasound-assisted liquid extraction, and analyzed by LC-MS/MS. RIS, 9-OHRIS, and Clozapine (CLZ) were detected in the multiple reaction monitor (MRM), by monitoring of transition RIS 411,16 > 191,12; 9-OHRIS 427,16 > 207,11; and CLZ 327,10 > 270,10. This bioanalytical method was validated by FDA guidelines 2018. Linearity was shown over the range of 2.0 – 200 ng/mL for RIS and 9-OHRIS. The %CV and difference of within-run and between-run accuracy and precision were not more than 15% for quality control samples and not more than 20% for LLOQ. The DBS sample has shown good stability under storage in freezer (-20°C) for up to one month. The validated result performed well and was ready to be applied to the TDM of RIS and 9-OH-RIS blood levels.

Keyword: Risperidone, 9-Hydroxyrisperidone, Dried Blood Spot, analysis, validation, UPLC-MS/MS
MOLECULAR DOCKING COMPOUNDS CONTAINED IN *(Phyllanthus acidus* L.) AS LIGANDS TO THE ESTROGEN RECEPTOR ALFA

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**Background:** *Phyllanthus acidus* L empirically efficacious as anticancer. In this study conducted in silico test compounds contained in *Phyllanthus acidus* against estrogen receptor alpha (ER-α). **Objective:** The purpose of this study is to look among the compounds found in *Phyllanthus acidus* L. active as ligands to the estrogen receptor alpha. **Material and method:** The method used to test the compounds contained in *Phyllanthus acidus* L. is using in silico virtual screening protocol validated Anita et al. (2012). **Result:** The results of the virtual screening of compounds contained in *Phyllanthus acidus* that uses application-er.sh test, obtained the active compounds as ligands in the (ER-α) is phyllanthusol a, phyllanthusol b and hypogallic acid. Inactive compounds as ligands in the (ER-α), namely adenosine, 4-hydroxybenzoic acid, cafeic acid and kaempferol. Representative active compounds are phyllanthusol b and representative compounds are inactive 4-hydroxybenzoic acid, two compounds were visualized in 3D using PyMOL.

**Keywords:** Molecular docking, *Phyllanthus acidus* L, ligands, estrogen receptor alpha.
SYNTHESIS AND ANTIMICROBIAL ASSAY OF 3,5-BIS-(4'-HYDROXY-3',5'-DICHLOROBENZYLIDEN)-1-METHYL-4- PIPERIDONE AND 3,5-BIS-(4'-HYDROXY-3',5'-DICHLOROBENZYLIDEN)-4- PIPERIDONE AS HEXAGAMAVUNONE-6 (HGV-6) ANALOGS

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ABSTRACT

Background: Infection is a disease caused by pathogenic microorganisms that can be transmitted directly or indirectly from one person to another. Hexagamavunone-6 (HGV-6) is a curcumin analogue compound which was synthesized by the Faculty of Pharmacy, Gadjah Mada University and known to have biological activity as an antimicrobial in Gram positive bacteria but requires a high concentration of compounds to inhibit the bacteria. Objective: This study aims to synthesize new analogous compounds of HGV-6 which were then tested for their activity as antimicrobial. Methods: The compound was synthesized using 3,5-dichloro-4-hydroxybenzaldehyde reacted with 1-methyl-4-piperidone and 4-piperidone by condensation reaction using HCl. All compounds were then characterized using spectroscopy (IR, 1H NMR, 13C NMR) and DI-MS. The compounds that were identified were tested for antimicrobial activity against S. aureus and E. coli using agar diffusion method. To assist in identifying molecular targets from the active side, the chemical docking method is used. Results: The synthesized compounds produced yields of 48% and 34% and then identified by structural elucidation data. The results of the antibacterial activity test showed that 3,5-Bis-(4'-hydroxy-3',5'-dichlorobenzyliden)-1-methyl-4-piperidone compound has activity until concentration 250 μg/mL. This is in accordance with the Insilico evaluation, showing that 3,5-Bis-(4'-hydroxy-3',5'-dichlorobenzyliden)-1-methyl-4-piperidone structure compound has activity to amino acid Phe, Gln and Asn. Conclusion: These findings demonstrate that the compounds can be synthesized using condensation reaction. The synthesized compound was evaluated for their antibacterial activity and indicated that have inhibitory activity in Gram positive and Gram-negative bacteria and have molecular target interaction with several amino acid in bacterial cell walls.

Keywords: Infectious disease, 3,5-Bis-(4'-hydroxy-3',5'-dichlorobenzyliden)-1-methyl-4-piperidone, 3,5-Bis-(4'-hydroxy-3',5'-dichlorobenzyliden)-4-piperidone, antimicrobial
ANALYTICAL METHOD DEVELOPMENT AND VALIDATION OF N7-(2-CARBAMOYL-2-HYDROXYETHYL) GUANINE IN DRIED BLOOD SPOT USING ULTRA HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY TANDEM MASS SPECTROMETRY

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ABSTRACT

Acrylamide is one of the substances categorized by the International Agency for Research on Cancer as a group 2A carcinogenic compound in humans. The Maillard reaction triggers the formation of acrylamide in foods heated at temperatures above 120°C. Acrylamide will be metabolized to glycidamide by the CYP2E1 and has greater potential to react with DNA to form DNA adducts. N7- (2-hydroxyethyl-2-carbamoyl) guanine (N7-GAG) is an adduct of acrylamide which is abundant in the body. N7-(2-hydroxyethyl-2-carbamoyl) guanine analysis can be one way to observe the relationship between lifestyle and potential carcinogenicity of N7-(2-hydroxyethyl-2-carbamoyl) guanine in human studies. This study aims to obtain a selective, sensitive, and validated analytical method using Ultra-High Performance Liquid Chromatography - Tandem Mass Spectrometry (UPLC-MS/MS). The N7-(2-hydroxyethyl-2-carbamoyl) guanine analysis was performed using a C18 Acquity® Bridged Ethylene Hybrid (BEH) column of 1.7 μm, 100 mm x 2.1 mm. The sample matrix used was Dried Blood Spot (DBS) with allopurinol as the internal standard, then DNA sample was extracted using the QIAamp DNA Mini Kit. The optimum analysis conditions were obtained in the mobile phase of the combination 0.1% formic acid - acetonitrile (95:5 v/v) with a flow rate of 0.1 mL / minute and eluted isocratically for 3 minutes. Quantification analysis was performed using triple quadrupole mass spectrometry with positive electrospray ionization (ESI) mode; detection at m/z 238.97 > 152.06 for N7-GAG and m/z 136.9 > 110 for allopurinol. The validated analytical method follows the 2018 Food and Drug Administration (FDA) guidelines with a linear concentration range of 10 - 300 ng/mL.

Keywords: Acrylamide, Glycidamide, Allopurinol, Dried Blood Spot, DNA Adduct, N7-(2-hydroxyethyl-2-carbamoyl) guanine, UPLC-MS/MS, Validation.
<table>
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<tr>
<th>Abstract ID</th>
<th>Name</th>
<th>Title</th>
<th>Category</th>
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<td>(A-1624075501)</td>
<td>Arif Rahmandani</td>
<td>Cost-Utility Analysis Of Treatment With Oseltamivir And Favipiravir On The Patient With Medium Degree Phase Of Covid-19 In Sentra Medika Hospital Cisalak Depok</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1626018272)</td>
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<td>The Effect Of Knowledge And Adherence To Clinical Outcome In Type 2 Diabetes Mellitus Patients In Several Health Centers In Bandar Lampung</td>
<td>Oral Presenter</td>
</tr>
<tr>
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<td>Harapan Parlindungan Ringoringo</td>
<td>The Role Of Ursodeoxycholic Acid And Phenobarbital In Children With Cholestasis: A Longitudinal Study</td>
<td>Oral Presenter</td>
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<tr>
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<td>Beyond Use Date Preparation Of Azithromycin Dry Syrup Against Staphylococcus aureus and Escherichia coli</td>
<td>Oral Presenter</td>
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<td>Cost Effectiveness Analysis Of Antipsychotics In Schizophrenia Patients</td>
<td>Oral Presenter</td>
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<tr>
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<td>Metrikana Novembrina</td>
<td>The Effectiveness Of Favipiravir As An Antiviral Therapy In The Treatment Of Covid-19 In The Several Hospital In Blora.</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-162658238)</td>
<td>Syahrul Tuba</td>
<td>Potential Of Pharmacological And Herbal Medicines For Treatment Covid-19 Patients: A Narrative Review</td>
<td>Oral Presenter</td>
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<td>Lansoprazole-Induced Thrombocytopenia In Elderly: A Case Report</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1626013694)</td>
<td>A.Thafida Khalisa</td>
<td>Taken A Lesson In Pandemic Covid-19: Are Supplements And Vitamin Needed?</td>
<td>Poster Presenter</td>
</tr>
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<td>(A-1626010779)</td>
<td>Atika Dalili Akhmad</td>
<td>Health Expenses In The Era Of National Health Insurance: A Household Survey In Bandar Lampung</td>
<td>Poster Presenter</td>
</tr>
<tr>
<td>ID</td>
<td>Presenter</td>
<td>Title</td>
<td>Category</td>
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</tr>
<tr>
<td>(A-1626055265)</td>
<td>Elbet Adib Verian</td>
<td>Albendazole for Treating Lymphatic Filariasis: a Review</td>
<td>Poster Presenter</td>
</tr>
<tr>
<td>(A-1624096399)</td>
<td>Essie Octiara</td>
<td>The Use of Lysozyme Toothpaste to Prevent Early Childhood Caries (ecc) in 24-Months Children (Based on S. mutans Colonization and Salivary Antibacterial)</td>
<td>Poster Presenter</td>
</tr>
<tr>
<td>(A-1626079685)</td>
<td>Fatkhu Rahman</td>
<td>Lactic Acidosis Associated With Metformin In Patients With Diabetic Kidney Disease: A Narrative Review</td>
<td>Poster Presenter</td>
</tr>
<tr>
<td>(A-1625314391)</td>
<td>Harapan Parlindungan Ringoringo</td>
<td>The Role of Methylprednisolone in Children with Immune Thrombocytopenic Purpura: a Case Report</td>
<td>Poster Presenter</td>
</tr>
<tr>
<td>(A-1622089090)</td>
<td>Ilham Arief</td>
<td>Correlation of clinical characteristics and drug use profiles with hematology parameters and length of stay covid-19 patients at yarsi hospital jakarta</td>
<td>Poster Presenter</td>
</tr>
<tr>
<td>(A-162601998)</td>
<td>Jesicca Dwiyanti</td>
<td>Level Of Public Knowledge Related To Covid-19 Supplementation</td>
<td>Poster Presenter</td>
</tr>
<tr>
<td>(A-1626104820)</td>
<td>Muhammad Fajar Ridho Darussalam</td>
<td>Astrazeneca Covid-19 Vaccine Efficacy A Narrative Review</td>
<td>Poster Presenter</td>
</tr>
<tr>
<td>(A-1626097810)</td>
<td>Nafrizal Fakhruzain</td>
<td>Character of Metformin in Combination with Antiretroviral Therapy for Non-Diabetic Patients</td>
<td>Poster Presenter</td>
</tr>
<tr>
<td>(A-1625839701)</td>
<td>Raka Rajendra</td>
<td>Comparison of the Effectiveness In Nasopharyngeal, Throat, Saliva, and Nasal Swab Sample Media of Detection SARS-Cov-2 using RT-PCR</td>
<td>Poster Presenter</td>
</tr>
<tr>
<td>(A-1626004630)</td>
<td>Savira Azhara Andavia</td>
<td>Level Of Community Knowledge And Behavior Regarding The Use Of Sunscreen Cosmetics</td>
<td>Poster Presenter</td>
</tr>
<tr>
<td>(A-1626008874)</td>
<td>Yudha Aditya Pradana</td>
<td>Penicillins Vs Macrolides In Diphtheria Treatment In Indonesia</td>
<td>Poster Presenter</td>
</tr>
</tbody>
</table>
COST-UTILITY ANALYSIS OF TREATMENT WITH OSELTAMIVIR AND FAVIPIRAVIR ON THE PATIENT WITH MEDIUM DEGREE PHASE OF COVID-19 IN SENTRA MEDIKA HOSPITAL CISALAK DEPOK

Arif Rahmandani

ABSTRACT

Coronavirus Disease 2019 (COVID-19) is a disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARSCoV-2). SARS-CoV-2 is a new type of corona virus that has never been previously identified in humans. The purpose of this study was to conduct a series of cost utility analyzes on patient with medium degree phase of COVID-19 in Sentra Medika Hospital Cisalak Depok on treatment Oseltamivir and Favipiravir. The research method used was cross sectional with prospective and observational non-experimental data collection. This research was conducted from December 2020 to February 2021. The parameters assessed include effectiveness by measuring the improvement in C Reactive Protein Value (CRP) and length of days of hospitalization. Quality of life measurements were carried out using the EQ-5D-5L instrument observing patients at the time of admission and who had been discharged from hospitalization. The subjects in this study were 108 patients who were hospitalized during December 2020 - February 2021. There were 50 patients using the Oseltamivir therapy regimen, while the Favipiravir therapy regimen was 58 patients. The mean ΔCRP value of patients using Oseltamivir, which was 18.52 mg / L, was almost the same as the mean ΔCRP of patients using Favipiravir, which was 19.36 mg / L. This illustrates the condition of patients after hospitalization between patients taking Oseltamivir and Favipiravir therapy who both experienced an improvement in CRP values. The mean total cost of patient care during hospitalization showed p value of 0.0025 <0.05, meaning that there was a significant difference between the total cost of patients using Oseltamivir antiviral which was IDR 32,794,002, ± 2,224,161 lower than the average total cost of patients who use Favipiravir antivirus for IDR 42,504,280, ± 2,578,802. The mean utility of Favipiravir (Δutility 0.438) gave higher results compared to patients using Oseltamivir antiviral (Δutility 0.489). The mean of Favipiravir antiviral QALY (ΔQALY 19.12) gave higher results compared to patients taking the antiviral Oseltamivir (ΔQALY 17.22). Oseltamivir's Cost Effectiveness Ratio (CER) value is IDR 1,770,734, lower than Favipiravir's Cost Effectiveness Ratio (CER) value of IDR 2,195,469. Oseltamivir's Cost Utility Ratio (CUR) is IDR 1,904,413, lower than Favipiravir's Cost Utility Ratio (CUR) of IDR 2,223,027, so that the value of the Incremental Cost Utility Ratio (ICUR) is Rp. 5,110,671, for an increase in 1 unit of Favipiravir QALY compared to Oseltamivir.

Keywords: COVID-19, Cost Utility Analysis, Oseltamivir, Favipiravir, EQ-5D-5L, Hospital, Inpatient
THE EFFECT OF KNOWLEDGE AND ADHERENCE TO CLINICAL OUTCOME IN TYPE 2 DIABETES MELLITUS PATIENTS IN SEVERAL HEALTH CENTERS IN BANDAR LAMPU NG

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Background: One of the barriers to good blood sugar control is the lack of knowledge or education about the goals of therapy in optimal blood sugar control and medication adherence. Objective: This study aimed to determine the effect of knowledge and adherence to the therapeutic achievement of type 2 diabetes mellitus patients in several health centers in Bandar Lampung. Methods: This study used a cross sectional design which was conducted in several health centers in Bandar Lampung in August-October 2020. This study applied DKQ-24 instrument to measure the level of knowledge and MARS-5 to measure the level of medication adherence. Outcome assessment of the clinic is based on the value of FPG, RPG. The data obtained were analyzed using Chi-Square analysis and logistic regression analysis. Results: The total respondents involved were 176 patients with the majority having unachieved clinical outcomes (69.3%), poor knowledge (70%), and relatively low levels of adherence (57.4%), based on the results of the chi square analysis. shows that there is no significant effect between the level of knowledge on the clinical outcome (p=0.651, OR=0.862). Significant results occurred in the relationship between adherence to clinical outcomes (p=0.048, OR=1.917, CI=1.002-3.665). Based on the logistic regression analysis, there were variables that influenced the influence of adherence to clinical outcomes, namely BMI (p=0.014), and Gender (p=0.016). Conclusion: These results indicate that adherence has an influence on clinical outcomes in Type 2 DM patients in several health center in Lampung which influenced by the variables of BMI and gender.

Keywords: Knowledge, Adherence, Clinical Outcome, DM Type 2
THE ROLE OF URSODEOXYCHOLIC ACID AND PHENOBARBITAL IN CHILDREN WITH CHOLESTASIS: A LONGITUDINAL STUDY

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ABSTRACT

Background: Cholestasis is a condition that starts in the first months of life and progresses with direct (conjugated) bilirubin increase and jaundice because of impaired bile production or excretion. Its incidence is known as 1 in 2,500 live births. Objective: This study aims that ursodeoxycholic acid (UDCA) and phenobarbital is effective in cholestasis management. Materials and method: A 28-days-old boy came with complaint of yellow eyes. At the age of 3 days, the patient looked yellow, had a fever and difficulty drinking, received phototherapy. After two weeks of treatment with neonatal sepsis, the patient was discharged in stable. The skin appears yellow, on a scale of 3, according to Kramer. Hb 10.7 g/dL, leukocytes 13,700/uL, platelets 305,000/uL, CRP (+) 48 mg/L. AST: 338 U/L, ALT: 125 U/L, total bilirubin: 11.71 mg/dL, direct bilirubin: 4.5 mg/dL, Gamma-GT 159 U/L, alkaline phosphatase 357 U/L. PT 11 sec, aPTT 42.1 sec. USG: The liver and gallbladder were normal. The diagnosis is cholestasis due to sepsis. Results: After 3 months of treatment with UDCA 15mg/kg/day, and phenobarbital 10mg/kg/day, jaundiced disappear and total bilirubin: 0.34 mg/dL, direct bilirubin: 0.11 mg/dL, AST: 53 U/L, ALT: 25 U/L. When the patient is 2 1/2 years old, total bilirubin: 0.08 mg/dL, direct bilirubin: 0.07 mg/dL, AST: 39 U/L, ALT: 10 U/L. Conclusion: Early diagnosis and timely treatment of UDCA and phenobarbital play a role in cholestasis improvement. On long-term observation, the child's growth and development are suitable according to his age and average laboratory results.

Keywords: Cholestasis, Ursodeoxycholic acid, Phenobarbital.
THE ROLE OF ATORVASTATIN IN MANAGEMENT OF ERUPTIVE XANTHOMA ON A BOY: A CASE REPORT

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ABSTRACT

**Background:** Eruptive xanthoma is a benign skin lesion caused by the accumulation of cholesterol and triglycerides in the skin's dermis. Xanthoma can be an early clinical manifestation of systemic diseases such as dyslipidemia, cardiovascular disease, diabetes mellitus. Clinical presentation varies from asymptomatic skin lesions to intense pruritus and tenderness. **Objective:** This study aims that oral atorvastatin is effective in treating a child with eruptive xanthoma. **Materials & Methods:** A three-year-old boy with an 8.4 kg body weight and 82.5 cm height came to the hospital with the chief complaint of small yellowish-white papules and nodes, discrete, 2-5 mm in size, painless on pressing, itchy, scattered, mainly in the lower extremity around the buttocks. On laboratory examination, Hb 11.5 g/dL, leukocyte 9,900/ul, platelet 413,000/uL, hematocrit 34%, blood sugar 66 mg/dL. Further evaluation revealed total cholesterol 814 mg/dL, LDL 970 mg/dL, HDL 341 mg/dl, triglycerides 621 mg/dL; there is no evidence of familial hypercholesterolemia. The diagnosis is eruptive xanthoma. **Results:** After starting treatment with atorvastatin 0.2 mg/kg body weight/day in one dose for six months, his cutaneous lesions gradually subsided and significantly decreased cholesterol, LDL, HDL, and triglyceride levels. **Conclusion:** Early therapy with atorvastatin will reduce the morbidity and mortality of eruptive xanthoma.

**Keywords:** case report, eruptive xanthoma, hypertriglyceridemia, atorvastatin.
BEYOND USE DATE PREPARATION OF AZITHROMYCIN DRY SYRUP AGAINST Staphylococcus aureus AND Escherichia coli

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ABSTRACT

Giving information about drug storage or time limits for usage must be maintained so that the stability and effectiveness of the drug are maintained. However, in reality, most people do not know about "Beyond Use Date." Beyond Use Date is the time limit for using the drug after the mixed or opened from its primary packaging. In addition, information Beyond Use Date is not always included in the container or secondary packaging of the drug. This research aims to know the effectiveness and effect of reconstitution time on the effectiveness of azithromycin dry syrup preparations. In this research, the effectiveness of azithromycin dry syrup was tested by the well's method about Staphylococcus aureus and Escherichia coli bacteria with various concentrations of 40, 20, 10, 5 mg and time intervals of 1, 7, 14, 21, 28, 58, and 88 days. The results of the effectiveness research were evidenced by the presence of a clear zone formed. Then statistical analysis was carried out, which showed the excellent effectiveness of azithromycin dry syrup preparations against Escherichia coli and Staphylococcus aureus bacteria on day one and day 7. Moreover, the reconstitution time affects the effectiveness of azithromycin dry syrup preparations marked by a decreasing value or clear zone starting from 14 to 88. Based on that, the use of azithromycin antibiotics should not be more than seven days.

Keywords: Azithromycin, Beyond Use Date, Effectiveness.
ABSTRACT

Background: Schizophrenia in the agitation phase is often accompanied by destructive or violent behavior. The patient must immediately be calm to avoid risk. Atypical monotherapy is preferred as first-line treatment. Objective: This study was to analyze effectiveness in schizophrenia patients using atypical mono therapy, atypical-atypical combination therapy or atypical-typical combination therapy that shown by decreasing the Positive and Negative Syndrome Scale Excited Component (PANSS EC) in agitation symptoms. Method: This study was non-experimental with retrospective data. Total sample showed 50 patients, consist of 11 atypical mono therapy, 12 atypical-atypical combination therapy, and 27 atypical-typical combination therapy. Average cost-effectiveness ratio (ACER) analysis showed that mono therapy treatment was RP.288.108/1 score PANSS EC with an average decrease of PANSS EC score of 9.72. There is no variant difference between the ACER data sets that compare because p = 0.011. Result of calculation of ICER A to C = (RP.2800.000 – RP.2593.820) / (9.72 - 8.59) = RP.182.829. Sensitivity analysis in the three of groups found that the most significant variables on cost-effectiveness analysis are administration and room. Results: This study showed that atypical mono-therapy risperidone is more effective in acute agitation schizophrenia than atypical-atypical combination therapy and typical-typical combination therapy. Conclusion: Atypical atypical mono therapy recommended as therapy in schizophrenic agitation acute.

Keywords: agitation acute, average cost effectiveness ratio (ACER), first generation antipsychotic (FGA), positive and negative syndrome scale excited component (PANSS EC), schizophrenia, second generation antipsychotic (SGA)
THE EFFECTIVENESS OF FAVIPIRAVIR AS AN ANTIVIRAL THERAPY IN THE TREATMENT OF COVID-19 IN THE SEVERAL HOSPITAL IN BLORA.

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ABSTRACT

The outbreak of Corona virus Disease 2019 (COVID-19) in December 2019 in China, has become a pandemic in March 2020. COVID-19 is a disease indicated by severe acute respiratory syndrome (SARS-CoV-2). The cases are increasing day by day, both globally and nationally, including in the district of Blora, Central Java. A clinical study in China on the effectiveness of favipiravir involving 320 Covid-19 patients stated that favipiravir was safe and efficacious in the treatment of Covid-19. In addition, other studies stated that favipiravir showed good outcomes in the treatment of COVID-19 related to disease progression and viral clearance. However, in Indonesia, the clinical studies on the effectiveness and the toxicity of the antiviral are so lacking that the further research will be needed.

This study aimed to analize the effectiveness of favipiravir as an antiviral therapy in the treatment of Covid-19 in several hospital in the district of Blora, Central Java, Indonesia. In this study as many as 266 samples of the patient's medical record which met the inclusion criteria were devided into group 1 which given favipiravir and group 2 which not given favipirafir. Data were then analized by using chi-square with continuity correction to evaluate the difference in proportion of those who were given the antiviral and those who were not, in relation to the outcome.

The result showed that as many as 92.5% of the patient given favipiravir showed an improved outcome and 7.5% of those were reported dead. As many as 80.5% of those not given favipiravir showed an improved outcome and 19.5% of those were reported dead. Based on the chi square with continuity correction, it revealed that there was significant difference in the proportion among the groups in relation to the outcome (p<0,05).

Keywords : antiviral, covid-19, favipiravir.
POTENTIAL OF PHARMACOLOGICAL AND HERBAL MEDICINES FOR TREATMENT COVID-19 PATIENTS: A NARRATIVE REVIEW

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Background: The pandemic coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) presents an unprecedented challenge to identify effective drugs in the prevention and treatment process. At present, there is no proven therapy for this disease, although therapeutic approaches continue to be carried out using traditional medicines (herbal) and pharmacological therapy. Information about SARS-CoV-2 virology has rapidly developed and scientists try to provide several potential drugs. Remdesivir has strong in vitro activity against SARS-CoV-2.

Objective: This review aims to examine among candidate drugs for treatment COVID-19 patients based on literature studies.


Result: Several potential drugs are currently underway in a clinical trial. Chloroquine, hydroxychloroquine, and oseltamivir have not been proven to have efficacy, and the benefits of corticosteroids are still diverse.

Conclusion: Current clinical evidence does not support the termination of angiotensin-converting enzyme 2 (ACE2) inhibitors or angiotensin receptor blockers, coagulation therapy in patients with COVID-19 concomitant with comorbidities.

Keywords: COVID-19, pharmacology, herbals, clinical trial
LANSOPRAZOLE-INDUCED THROMBOCYTOPENIA IN ELDERLY: A CASE REPORT

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ABSTRACT

Introduction: SRMD (stress related mucosal disease) or stress ulcers are often encountered in critical patients. Proton Pump inhibitor (PPI) are one class of drugs used commonly both for treatment and prophylactic therapy for stress ulcers in ICU. Case: We reported a case of critical patients admitted in ICU with diagnosis of CVA infarction and Sepsis. Thrombocytopenia was noted after a few days taking lansoprazole. There was more than 50% decrease in platelet count in present case after initiation of lansoprazole. In present case, previous exposure to omeprazole did not cause thrombocytopenia. The platelets recovered over the next few days after stopping lansoprazole.

Discussion: In the present case series, other exposures to parenteral lansoprazole, in a dose of 30mg once daily reproduced the same adverse drug reaction (ADR). Despite lansoprazole induced thrombocytopenia one case had been tolerating omeprazole. This finding highlight there is no cross reactivity among PPI. In comparison with previous reports our case report confirm that thrombocytopenia was neither related to dose nor route of administration.

Conclusion: Lansoprazole may cause thrombocytopenia, regardless of the route of administration and the dose. Lansoprazole induced thrombocytopenia may not resulted cross reactivity among PPI.
**TAKEN A LESSON IN PANDEMIC COVID-19: ARE SUPPLEMENTS AND VITAMIN NEEDED?**

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**ABSTRACT**

**Background:** The world is under attack from a virus that has become a pandemic, called by COVID-19. Where public health measures that can reduce the risk of infection and death in addition to quarantine are urgently needed. The demand for vitamin supplements, in the era of a pandemic, is remain growing, as well as public awareness to maintain health and evade Covid-19. This study aims to determine people's behaviour in the use of vitamins during the COVID-19 pandemic, as well as our suggestions for community pharmacist practice. **Methods:** In our study design was descriptive analysis that included in a survey by questionary. This type of research method is answering clinical questions that are used in good ways of taking supplements and vitamins in the era of the Covid-19 pandemic. **Results:** We are used statistically analysis (SPSS) for validity, reliability and correlation data by Cronbach’s Alpha with using 300 sample subject study. We assume that supplements become a necessity that could have ability to overcome, prevent, or cure diseases. However, it is not a complete substitute for food and still needs to consume a wide variety of healthy foods to meet daily needs. In fact, some supplements contain active ingredients that have biological effects in the body that if used excessively or inappropriately dose can be harmful if not used appropriately and ascertain whether it is really necessary to take or need supplements. **Conclusions:** All forms of vitamins and supplements cannot prevent and are not a reference in dealing with Covid-19. Many recommendations for taking supplements or vitamins in the right dosage according to the recommendations of doctors do not use them excessively for enhancing immunity. Then, to validate this research further research is needed. **Keywords:** Covid-19, Vitamin, Supplements, Toxicity
HEALTH EXPENSES IN THE ERA OF NATIONAL HEALTH INSURANCE: A HOUSEHOLD SURVEY IN BANDAR LAMPUNG

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ABSTRACT

The low financing policy in the health system causes a high incidence of out-of-pocket in health services, this becomes a financial burden for the community. National health insurance, namely Jaminan Kesehatan Nasional (JKN) has been implemented in Indonesia since 2014 which aims to provide equal distribution of health services and financial protection to reduce health expenses, but the impact of this goal is not widely known. This study aims to determine whether JKN has an impact on the level of out-of-pocket expenses and willingness to pay for additional fee of health costs at health facilities. This research was conducted at clinics, primary health care, and community pharmacies at Bandar Lampung city from August to October 2020. The method used is descriptive analytic with cross sectional survey design. Data were collected using survey form. Descriptive analysis was performed to determine the incidence of out-of-pocket and willingness to pay nominal. Statistical analyses were used to determine the factors that influence the incidence of out-of-pocket and willingness to pay. Study result show that the incidence of out-of-pocket was 31.62% (80 form 253 respondents). Bivariate analysis result that health facilities (p = 0.004) and membership status (p = 0.040) influenced the incidence of out-of-pocket. Multivariate analysis with logistic regression analysis in patient’s demographic factors show that clinics clinics (p = 0.018), participation status on JKN : independent participants (p = 0.039) and Penerima Biaya Iuran (PBI) (p = 0.039) had a significant effect on the incidence of out-of-pocket. Willingness to pay analysis results the average nominal of willingness to pay (n = 50) is IDR 202,000. Chi-square analysis of demographic factors that influenced willingness to pay was only the type of participation (p = 0.021).

Key words: National Health Insurance, Out-of-Pocket, Willingness to Pay, Health Facilities
ALBENDAZOLE FOR TREATING LYMPHATIC FILARIASIS: A REVIEW

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Background: Lymphatic filariasis (FL) is a disease caused by parasite worms that have three species such as Wuchereria bancrofti, Brugia malayi and Brugia timori. Those species of worm is carried by female mosquitoes from several clans such as Culex, Anopheles, Mansonia and Aedes. Lymphatic filariasis affects an estimated 120 million people worldwide, mostly in the tropics and subtropics. Filariasis is now the most parasite-infested disease, with over 80 countries classified as "endemic" status.


Result: In tackling lymphatic filariasis infection, there are 3 drug regimens, namely albendazole, a combination of 2 drugs, namely albendazole with ivermectin, or diethylcarbamazine citrate with albendazole, or a combination of the three. The results of the study reported the three-drug regimen of ivermectin plus diethylcarbamazine plus albendazole was more effective in clearing microfilaria W. bancrofti from the blood than the two-drug regimen diethylcarbamazine plus albendazole. Conclusion: Albendazole will have an influence on the therapy of lymphatic filariasis. It is obvious when taken with other medicines, especially ivermectin and diethylcarbamazine, in patients. In therapy the use of albendazole alone did not reveal a distinct impact. Hence, more investigation of the impact of albendazole alone is necessary.

Keyword: Albendazole, lymphatic filariasis
THE USE OF LYSOZYME TOOTHPASTE TO PREVENT EARLY CHILDHOOD CARIES (ECC) IN 24-MONTHS CHILDREN (BASED ON S. mutans COLONIZATION AND SALIVARY ANTIBACTERIAL)

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ABSTRACT

Background: Routine tooth brushing is an action that is quite effective to prevent ECC. Lysozyme added to toothpaste can serve as an antimicrobial that can lyse bacterial cell walls. Objective: To analyze the effect of using non-fluoride lysozyme toothpaste for five weeks against ECC prevention, which was evaluated from deft and defs records, S. mutans colonies, sIgA, and lysozyme activity in 2 years old children. Material and Methods: This investigation is a clinical trial with 68 children aged 14-35 months as samples, including 29 children without caries and 39 with ECC. Dental examination and saliva were taken before and after using toothpaste. Saliva was reviewed to discover the amount of S. mutans, sIgA, and lysozyme activity. S. mutans cultured using TYS20B media, sIgA evaluated by ELISA technique, and lysozyme activity by spectrophotometry. Data interpretation is determined using paired and unpaired t-test with p-value <0.05. Results: The amount of S.mutans colonies in saliva following the use of lysozyme toothpaste in the ECC group lessened significantly (p=0.001). There was a higher decrease in sIgA in ECC than the control group after using lysozyme toothpaste (p=0.001). The highest increased in lysozyme activity was found in ECC children after using lysozyme toothpaste (p=0.001). Lysozyme toothpaste can reduce the increase in defs index by 50% in ECC children compared to the control group. Conclusion: Lysozyme toothpaste can be used to prevent ECC, marked by the reduction in defs index, the amount of S. mutans colonies, and its effect in the sIgA mechanism of action and lysozyme activity.

Keywords: ECC, lysozyme toothpaste, S.mutans, sIgA, lysozyme activity
LACTIC ACIDOSIS ASSOCIATED WITH METFORMIN IN PATIENTS WITH DIABETIC KIDNEY DISEASE: A NARRATIVE REVIEW

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Background: Diabetes Mellitus is a metabolite disorder with parameters of high blood sugar levels. In the management of diabetes can be used the drug metformin is the gold of choice to achieve a therapeutic effect and rarely causes side effects of the drug, but it still has debate view. However, if used in excessive doses for patients with kidney disease, it will be contraindicated with side effects such as lactic acidosis. Objective: This study aims to evaluate the side effect of Metformin for Diabetic Kidney Diseases patients.

Method: This study used the Narrative Review Method that was obtained from 2011 to 2021, in the English language from PubMed, Google Scholar, and Cochrane Library.

Results: Metformin is at the forefront of the treatment of type 2 diabetes mellitus (DM2). Metformin is likely to have lactic acidosis-related adverse effects in CKD patients, such as increased arterial lactate. Lactic acidosis is defined as an increase in arterial lactate with an indicator of more than five mmol/L and an arterial blood pH of less than 7.35. Metformin-induced lactate levels are considered to be below the parameters. DKD risk factors can be conceptually classified as several susceptibility factors, initiation factors, and developmental factors. The two most prominent risk factors are hyperglycemia and hypertension. Conclusion: Metformin can increase lactate levels in CKD patients but is still below the parameters of lactic acidosis. This study may have some weaknesses and requires further prospective research to validate the results.

Keyword: Diabetic, Chronic Kidney Disease, Metformin, Acidosis Lactate.
THE ROLE OF METHYLPREDNISOLONE IN CHILDREN WITH IMMUNE THROMBOCYTOPENIC PURPURA: A CASE REPORT

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ABSTRACT

Introduction: ITP is a bleeding disease that is often found by doctors, with an incidence of about 1 in 10,000 children, rarely found in infants <1 year old. Bleeding often occurs when the platelet is <20,000/uL. Objective: The purpose of this study is to show that methylprednisolone is effective in severe thrombocytopenia therapy. Materials & Method: A girl of 2 months and nine days, weighing 5.6 kg, came to the hospital with complaints of ptekie on the forehead, cheeks, extremities. The patient is not feverish, pale, weak, cannot drink. No history of trauma. Purpura on the elbows and knees. Laboratory: Hb 8.1 g/dL, leukocytes 12,290/uL, platelets 1000/uL, hematocrit 22.2%, Diff Count: basophils 0%, eosinophils 3%, stems 1%, segments 17%, lymphocytes 70%, monocytes 9%. RBC 2.8 million/uL, MCV 82.9fL, MCH 28.9pg, MCHC 34.9%, RDW_CV 16.7%. Peripheral blood features hypochromic, microcytic, lymphocytosis, platelets not found. The diagnosis is ITP with anemia due to bleeding. Result: The patient was treated at HCU, given 2U platelet transfusion, 75 mL PRC transfusion, 1-2 mg/kg body weight of methylprednisolone every 12 hours for seven days. The patient went home in good condition. Conclusion: Methylprednisolone in the acute phase can increase the platelet count. Platelet suspension transfusion is only done if thrombocytopenia is accompanied by bleeding that is difficult to resolve.

Keywords: ITP, child, methylprednisolone.
THE ROLE OF ORAL CEFIXIME IN 3 MONTHS OLD INFANT WITH TYPHOID FEVER: A CASE REPORT

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ABSTRACT

Background: Typhoid fever is a bacterial infection caused by Salmonella typhi. The transmission is fecal-oral. Typhoid fever rarely occurs under one year of age. Objective: The purpose of this study is to show that oral cefixime is effective in infant typhoid fever therapy. Materials & methods: A 3-month-old boy, weighing 6.1 kg, came to the hospital with fever complaints about six days fluctuating, not coughing. The patient is conscious, weak, cannot drink, with a temperature 39.5oC. Eye and ENT, no abnormalities. Heart, Lungs, and abdomen within normal limits. Laboratory results: Hb 10.9 g/dL, leukocytes 21,300/uL, platelets 357,000/uL, hematocrit 33%, Diff count: basophils 0%, eosinophils 0%, stems 4%, segments 41%, lymphocytes 44%, monocytes 11%. RBC 3.87 million/uL, MCV 85fL, MCH 28.0pg, MCHC 33%, ESR 1 hour 66 mm, 2 hour 84 mm. Non-Reactive Covid-19 IgM & IgG Rapid Test. Peripheral blood picture: normochromic, normocytic, leukocytosis, normal platelets. Widal: S. typhi titer O 1/320, Tubex Test +4. The diagnosis is typhoid fever. Result: Patients were given oral Cefixime 10 mg/kg body weight/day in divided doses for seven days. The patient went home in stable. Conclusion: Fever ≥6 days in infants should consider the possibility of typhoid fever. Oral cefixime can be a treatment option for typhoid fever in infants. The importance of personal hygiene education for parents and caregivers.

Keywords: Typhoid fever, Infant, Cefixime.
CORRELATION OF CLINICAL CHARACTERISTICS AND DRUG USE PROFILES WITH HEMATOLOGY PARAMETERS AND LENGTH OF STAY COVID-19 PATIENTS AT YARSI HOSPITAL JAKARTA

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ABSTRACT

In this current time, we still face the 2019 coronavirus disease (COVID-19) pandemic and there is no specific and effective treatment to fight the SARS-CoV-2 virus currently. This research was to analyse correlation data between clinical characteristics and drug use profiles on hematology parameters and length of stay for COVID-19 patients at Yarsi Hospital Jakarta.

The research was conducted in analytical-observational with cohort design and retrospective study from medical records data from March to October 2020 period. Statistical analysis was performed using Spearman Rank test and Wilcoxon signed test. Found 221 cases that met with inclusion criteria with highest symptom is cough (61.09%) and fever (47.96%). Clinical characteristics based on their severity have a significant correlation with patient length of stay (p =0.187) and have significant correlation to eosinophils, neutrophils, lymphocytes, sedimentation rate, and neutrophil-lymphocyte ratio (NLR)(p<0.05). The correlation between the drug use group did not have a significant correlation with the length of stay (P=0.361) because most patients with mild symptoms and productive age might still had good immunity. Comparing before and after drug use on haematology parameters showed that the results had significant differences in the haematology parameters of eosinophils (p<0.05). Clinical characteristic based on severity have significant correlation with immunity cell and length of stay. Drug use have given difference before and after use for hematology parameters.

Keyword: COVID-19, clinical characteristics, drug use, haematology, length of stay
LEVEL OF PUBLIC KNOWLEDGE RELATED TO COVID-19 SUPPLEMENTATION

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Background: COVID-19 is a disease associated with a novel type of coronavirus, SARS-CoV-2. Efforts to find the best treatment to deal with this pandemic are still ongoing. In addition to drugs, several studies are underway to determine the potential for COVID-19 supplementation. The appropriate use of supplements may help prevent and support the treatment of COVID-19. Objective: Based on the potential, it is important to obtain an overview of public knowledge regarding COVID-19 supplementation. This overview can help to assess educational needs. Methods: A questionnaire that has been already validated was distributed by an online form and analysed using descriptive methods. The study used a population-based survey of 412 individuals in the age range of 17-50 years from different background. Results: Data shows that the domicile of the respondents is diverse with 44.7% are from Bandung, 10.2% are from Pangandaran and 45.1% are from outside Bandung/Pangandaran. The results show that public knowledge regarding COVID-19 supplementation is still lacking. Comparison shows that percentage of the right answers are bigger in pharmacy students than public. Fortunately, many respondents aware that supplements can be used to prevent and support COVID-19 treatment. As an additional question, the public's curiosity regarding information about COVID-19 supplementation was asked and the result shown by 93% of respondents wants to know more about it. Based on the analysis, 70.4% of respondents said that pharmacists could provide education related to COVID-19 supplementation. Conclusion: Public knowledge regarding supplements is still lacking and can be improved.

Keyword: COVID-19, supplement, zinc, method, atomic absorption spectrometry
ASTRAZENECA COVID-19 VACCINE EFFICACY: A NARRATIVE REVIEW

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Objective: The ChAdOx1 nCoV-19 (AZD1222) vaccine was developed at the University of Oxford and consists of a replication-deficient chimpanzee, the adenoviral ChAdOx1 vector, which contains the SARS-CoV-2 structural surface glycoprotein antigen gene (surge protein: nCoV-19). The Oxford-AstraZeneca vaccine is based on the virus’ genetic instructions for building spike proteins. Aims: This study aims to evaluate the effectiveness of the AstraZeneca vaccine developed at the University of Oxford.

Method: The study used Narrative review method that obtained from Google Scholars, Crossref, PubMed and Scopus range from 2020 to 2021, in English language.

Result: Serious adverse events in some of the research subjects were thought to be absent or infrequently treatment-related deaths that occurred in ChAdOx1 nCoV-19 recipients. Higher than 40°C in participants still closed for group allocation. The observed difference in dose-based efficacy is inconsistent with results from previous immunogenicity trials of this vaccine, which were similar for participants receiving two low doses and two standard doses; there are no immunogenicity data for the mixed dose regimen.

Conclusion: This vaccine is thought to be better than the mRNA vaccine from Pfizer and Moderna. This study still requires more rigorous research to validate the results.

Keywords: Vaccine, AstraZeneca, Virus, COVID-19.
EFFECTIVITY OF DEXAMETHASONE THREATENING SEVERE COVID-19 PATIENTS; DOES STILL RELIABLE USED FOR COVID-19?

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Background: Covid-19 has been declared as a pandemic by WHO (World Health Organization) since March 2020. However, there is confusion of the therapy that should be used for covid-19. This virus enters the human body by binding to ACE-II receptors in the human body then causing an inflammatory response and a decrease in the body’s immune response. Objective: to figure out the effectivity of Dexamethasone to treat severe COVID-19 patients who are using actively ventilator respiratory. Material and Methods: This study used Narrative review journals from several leading platforms such as PubMed, NEJM, NCBI and others as well as from government websites such as WHO, selected between 2019 and 2021 in English language. Results: Dexamethasone is a corticosteroid class of drugs that can act as anti-inflammatory and immunosuppressive. The drug inhibits the expression of genes that induce inflammatory proteins. In a case of severity covid-19, Dexamethasone was used in patients who had decreased oxygen saturation, after being treated using this drug, intravenously the patient showed a positive result, namely an increase in oxygen saturation levels. Conclusion: Dexamethasone therapy was effective and may have acceptable in severe Covid-19 patients that actively ventilator respiratory. Then, more rigorous investigation of the impact of Dexamethasone is needed.

Keywords: SARS-CoV-2, Corticosteroids, Dexamethasone, Covid-19
CHARACTER OF METFORMIN IN COMBINATION WITH ANTIRETROVIRAL THERAPY FOR NON-DIABETIC PATIENTS

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ABSTRACT

HIV infection is considered a pandemic. The HIV-1 pandemic is a complex problem for all countries and regions in the world, and is undoubtedly the current public health crisis. ART as a therapy used so far has not shown a significant increase in cure rates. Therefore, this study is useful for combining existing ART therapy with an active drug ingredient that has a relationship in the benefit of repairing T cells.

Antiretroviral Therapy (ART) as Anti-HIV drugs decrease the number of serious infections that people with Human Immunodeficiency Virus (HIV). However, participants taking Antiretroviral Therapy do not achieve suffice in T-cells, such as ratio of CD4 (Cluster of Differentiation 4) recovery and decrease cluster of CD8 (Cluster of Differentiation 8) cells. Patients with low CD4/CD8 ratio remain at risk for developing AIDS and non-AIDS related complications. Therefore, the new anti-HIV drugs are needed to increase effectiveness of HIV treatment.

Metformin is the most widely used medication to handle type 2 diabetes, is well tolerated with minimal side effects. It has been related to anti-aging and weight reducing properties in non-diabetic persons. Because of its ability to repair immune functions, metformin could be a promising addition to Antiretroviral Therapy in HIV patients. Metformin is a well-tolerated antihyperglycemic which has been shown to return T-cells function. T-cells damaged by the HIV disease will recover with the antihyperglycemic properties of metformin. Therefore, the immune system will return to normal. It is also reported to transformation the composition of microbes in the gut which may repair inflammation.

Keywords: Antiretroviral Therapy, Human Immunodeficiency Virus, metformin, antihyperglycemic
COMPARISON OF THE EFFECTIVENESS IN NASOPHARYNGEAL, THROAT, SALIVA, AND NASAL SWAB SAMPLE MEDIA OF DETECTION SARS-COV-2 USING RT-PCR

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ABSTRACT

Objective: SARS-CoV-2 is a coronavirus microorganism found in humans. Covid-19 disease is caused by a viral infection known as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Covid 19 has caused confusion among the public because of the different places where the samples were taken. Sampling was taken from the Nasopharynx, Throat, Saliva, and nasal Swab.

Aims: To evaluate effectivity results among Nasopharyngeal, Throat, Saliva, and Nasal Swab Sample Media for Detection SARS-Cov-2 virus using RT-PCR.

Method: This study used Mini review journals from several leading search engine such as PubMed, Elsevier, jamanetwork, BMJ, Cochrane, Wiley, medRXiv, Lancet and others as well as from government websites such as WHO selected between 2020 and 2021 in English language.

Result: Each sampling place has its own advantages and disadvantages. Any place that is used as the gold standard is the nasopharyngeal.

Conclusion: Each approach has its own benefits and drawbacks. This paper attempts to compare the efficacy of four sample media to find the best method for detecting the SARS-CoV-2 virus. It is hoped that repeating this paper can make us aware of every method that we can use in detecting the SARS-CoV-2 virus and can reduce the spread of this virus which is increasingly widespread.

Keywords: SARS-CoV-2, RT-PCR, Covid 19
LEVEL OF COMMUNITY KNOWLEDGE AND BEHAVIOR REGARDING THE USE OF SUNSCREEN COSMETICS

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Background: Indonesian used sunscreen as means of protection from ultraviolet rays which categorized as highly until very extremely hazardous for skin health. Product information and its safety are crucial for consumers to acknowledge in order to obtain optimal benefits. Objective: The aims of this study was to evaluate the knowledge and people behavior of sunscreen. Moreover, the study was to determine educational needs related to the use of sunscreen based on the level of knowledge and behavior. Materials and Methods: The study using a population-based survey of 405 individuals in West Java with the age of 17-50 years followed by descriptive frequencies analysis. Results: Based on gender characteristics both women (61,20%) and men (57,90%) were at moderate level of knowledge, while level of behavior were categorized less correct. Based on the age range, 17-28 years (65,0%) categorized at moderate level, 29-39 years (41,4%) categorized at low level, and age 40-50 years (41,7%) categorized at good level of knowledge, while behavior level of all three-age range are less correct. Based on educational background, pharmacy (64,7%) and non-pharmacy (58,0%) are at moderate level of knowledge, behavior level of both categorized as less correct. Based on domicile, there are three group such as Kota Bandung (62,30%), Kabupaten Pangandaran (60,87%), and other (59,06%) categorized at moderate level of knowledge, while the level of behavior is less correct. The result of educational needs such as knowledge of SPF and UVA PF on sunscreen and the second one is habit of reapplying sunscreen. Conclusion: Knowledge level of group majority categorized as moderate and behavior level categorized as less correct.

Keywords: Sunscreen, Knowledge, Behavior, Survey, Educational needs
PENICILLINS VS MACROLIDES IN DIPHTHERIA TREATMENT IN INDONESIA

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Based on cumulative data during 2017, 907 cases were detected with 44 of them dying in Indonesia caused by an infectious disease, namely Diphtheria. Diphtheria is an infection caused by the bacteria Corynebacterium diphtheriae that attacks the nose and throat. These infections can be treated with antibiotics to stop the bacterial toxins and prevent transmission in the community. The antibiotics of choice recommended for cases and close contacts with diphtheria are penicillins and macrolides, especially erythromycin. This study aims to evaluate penicillin and macrolide drugs that have high efficacy and safety. This study uses the mini review method obtained from Google Scholars, Medline, and PubMed in the range of 2000 to 2020, in English and Indonesian. The results obtained were the level of susceptibility of C. diphtheriae to macrolides was higher than penicillin. The side effects caused by the penicillin group are more than the macrolide group. Side effects to watch out for with penicillins such as urticaria and anaphylactic reactions can be fatal. Other side effects that can be caused by penicillin are rash and itching. While the side effects of macrolides are rash, itching, difficulty breathing, dark urine, unusual tiredness, seizures, fast, pounding or irregular heartbeat, but this can still be tricked by adjusting the dose. Therefore, macrolides can be the first choice in diphtheria therapy with antibiotics. It is hoped that the results obtained can help the selection of antibiotics as one of the main diphtheria treatments in Indonesia.

**Keywords:** Penicillin, Macrolides, Diphtheria, Corynebacterium diphtheriae, Indonesia
MILITARY PHARMACY
<table>
<thead>
<tr>
<th>Abstract ID</th>
<th>Name</th>
<th>Title</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A-1626496351)</td>
<td>Ahmad Rofee Ramadhan</td>
<td>Management Dual Endemics Of Malaria And Covid 19 When A Tropical Cyclone Occurs In East Nusa Tenggara: A Narrative Review</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1625800218)</td>
<td>Aliyah Nur Ariza</td>
<td>Military Pharmacy Education In Indonesia</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1626090341)</td>
<td>Arya Wijaya Harahap</td>
<td>In Silico Study: Molecular Docking Targeting Kras Receptor in Lung Cancer</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1626057961)</td>
<td>Gilang Bhakti Nusantara</td>
<td>The Role Of Military Pharmacy In Medical Intelligence For State Defense With Sedative Agents</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1626108673)</td>
<td>Riyas Muhammad Agung Kotta</td>
<td>Pharmacy As The Foundation Of The Nation: Indonesia's Preparedness In Facing Bioterrorism</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1626009002)</td>
<td>Sionvhory Shvidarvy Sroyer</td>
<td>Optimization Therapy Using Combination Of Antiretroviral Therapy And Red Fruit Extract To Reduce Morbidity Of Hiv/Aids</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1626435808)</td>
<td>Arief Budi Witarto</td>
<td>Emerging Genetic Technologies to Prepare for The Next Pandemic</td>
<td>Poster Presenter</td>
</tr>
<tr>
<td>(A-1626101605)</td>
<td>Musadat Furqon Baihaki</td>
<td>Candidates Targeted Therapy Of EGFR For Lung Cancer: In Silico Study</td>
<td>Poster Presenter</td>
</tr>
<tr>
<td>(A-1626490395)</td>
<td>Nizam Iqbal Rayhan</td>
<td>Nutraceutical to Support National Defense System</td>
<td>Poster Presenter</td>
</tr>
<tr>
<td>(A-1626660972)</td>
<td>Yolanda Safitri</td>
<td>Potential of Ethanol Eextract of Ocimum americanum L. as Hepatoprotector in Antituberculosis Drugs-Induced Hepatotoxicity</td>
<td>Poster Presenter</td>
</tr>
</tbody>
</table>
MANAGEMENT DUAL INFECTIOUS DISEASES OF MALARIA AND COVID 19 WHEN A TROPICAL CYCLONE OCCURS IN EAST NUSA TENGGARA: A NARRATIVE REVIEW

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Background: Currently, tropical cyclone Seroja disaster in East Nusa Tenggara is a media talk, in every news claim that many buildings have been destroyed and humans massacred. In East Nusa Tenggara, Malaria is a common infectious disease in the area with a bad environment, sanitation and hygiene supporting the spread of this disease. After the tropical cyclone Seroja disaster, the endemic was worse than before. Beside as endemic Malaria, East Nusa Tenggara also get impact of spread of COVID-19 is pandemic global infectious from new emerging diseases. Objective: The purpose of this studies is searching for the relevance between dual infectious are Malaria and COVID-19 with tropical cyclone Seroja disaster and how to prevent it. Method: In this study, the Narrative Review Method was used which was obtained from 2004 to 2021, in English from PubMed and WHO. Result: COVID-19 and Malaria are both infectious diseases had spreaded in East Nusa Tenggara in 2020. The spreading way of COVID-19 is different with Malaria disease, where COVID-19 is spread through saliva or droplets from people infected with the SARS Corona virus (SARS CoV), which causes infection with symptoms such as fever, dry cough, fatigue, respiratory disease, anosmia, and orbital diseases. While in Malaria disease it is spread through anopheles’ mosquitoes that carry plasmodium malaria with symptoms fever and flu-type illnesses, such as chills, muscle aches, headaches, and fatigue. Also, that can occur is vomiting, nausea, and diarrhea. When tropical cyclone Seroja disaster occured, the surrounding environment is disturbed, especially in water sanitation, therefore medical and health services are thought to have decreased significantly. There were 98 people with new virus cases and the first Covid-19 death case after the cyclone Seroja disaster hit, the local public health centre less anticipating the impact that occurs after the cyclone Seroja disaster happen. There was a new case of COVID-19 by 232 people during cyclone Seroja disaster in East Nusa Tenggara. There are no reports of specific rates of Malaria disease occurred in East Nusa Tenggara during cyclone Seroja disaster. Medical service and limited capacity healthcare make the COVID-19 and Malaria diseases more sever because some crowded place such as shelter, and public hospital being overused. Steps of preventive action are needed to anticipate impact of cyclone Seroja disaster by increasing mitigation, prevention, increasing detection and identification, handling victims and handling refugees and rehabilitation. Conclusion: Tropical cyclone Seroja disaster that occurred in East Nusa Tenggara which caused an increasing number of infectious diseases such as COVID-19 and Malaria diseases. Both are infectious diseases and have worsened after this tropical cyclone.
Medical service and limited capacity healthcare make these two diseases grow and infectious people. And for its prevention and mitigation, detection, and identification, and respond the cyclone and rehabilitation are needed. But in the end, the government was able to overcome this by enchance capacity such as activating the public health center in the area potential disaster areas and their anticipation.

**Keyword:** Covid-19, Dual infectious, Malaria, Tropical Cyclone.
MILITARY PHARMACY EDUCATION IN INDONESIA

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ABSTRACT

Background: Indonesia has large territorial boundaries as this country is being susceptible to any threats in national defense. Therefore, The Minister of National Defense establishes a new strategy to emphasize medical, pharmaceutical, engineering, and basic sciences in military personnel by setting up a curriculum integrating science curriculum with military education. These newly established study programs are conducted in The Republic Indonesia Defense University for full scholarship undergraduate degrees, in particular Military Pharmacy. Objective: As this new strategy aims to reinforce national defense and national security, this recent study program is appealing to be explored further on the distinction to other pharmacy education in other universities. This article brings this topic up to be discussed. Materials and Methods: This article is a narrative comprehensive review of urgency, distinction, and future projection of Military Pharmacy Education in Indonesia. Conclusion: Military Pharmacy integrating curriculum in undergraduate study program proposed to accelerate highly qualified pharmacist soldiers who are not only experts in pharmaceutical science or clinical pharmacy, but also skilled in the military field.

Keywords: Military Pharmacy, Education, Curriculum, Indonesia
IN SILICO STUDY: MOLECULAR DOCKING TARGETING KRAS RECEPTOR IN LUNG CANCER

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ABSTRACT

Background: Indonesia is a mega-biodiversity country with a high number of herbal plants, Murraya koenigii and Nigella sativa. Their extract reported having activities as anti-cancer, including lung cancer. It is one type of cancer which has a high mortality rate. One of the important receptors for lung cancer is Kirsten rat sarcoma virus (KRAS) which grows in lung adenocarcinoma, a subtype of Non-small Cell Lung cancer (NSCLS). Recent treatment such as sotorasib could cause side effects and serious adverse effects, thus an alternative treatment is needed. The currently developed method for screening new compounds targeted KRAS receptors is molecular docking. Objective: This study aims to find candidates for several ligands that have interactions with the KRAS receptor in lung cancer to have better activity than sotorasib. Materials and Methods: We carried out an in-silico study by docking candidate ligands with the KRAS receptor using the MOE 2015 V.10 application. Result and Discussion: 5 out of 10 candidate compounds have interactions through hydrogen bonding with the KRAS receptor. Dithymoquinone is the compound with the lowest Gibbs free energy, which is -12.3107 joules/kg.mol, and has the strongest bond. Conclusion: Dithymoquione derived from the Nigella sativa (Black cumin) corresponds to sotorasib for ligand-interaction when docked with the KRAS G12C receptor. This finding could be a potential new drug for lung cancer. However, further studies, such as in vitro, in vivo, and clinical trials need to be conducted to confirm the activities, safety, and efficacy of the new drug.

Keywords: lung cancer, KRAS receptor, molecular docking, in silico
THE ROLE OF MILITARY PHARMACY IN MEDICAL INTELLIGENCE FOR STATE DEFENSE WITH SEDATIVE AGENTS

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ABSTRACT

Background: National defense is closely related to the role of an intelligence officer who is strong and capable of safeguarding the country’s sovereignty. Intelligence covers many fields, one of which is medical intelligence. Objective: To analyze of sedative agent in intelligent medical purposing of military aspect. This paper tends to determine the role of Military Pharmacy in medical intelligence to support national defense using natural substances that contain as a sedative agent. Method: we are used mini review method for this study obtained from Crossref, google scholar, PubMed, and Scopus range 2010 to 2021 in English language. Result: Mitragynine binds to three types of receptors with different affinities, with the highest affinity for K-and-opioid receptors which are useful as sedative agents in medical intelligence to support national defense. Conclusion: Kratom is a plant endemic to Southeast Asia, this plant has a sedative effect at high doses. Kratom leaves contain thirty-seven alkaloid compounds. Both alkaloid compounds are Mitragynine and 7-hydroxy mitragynine, both of which are included in the indole alkaloid compound which is the main compound of kratom. Plants that are used when facing the battlefield in maintaining national defense are very complex owned by the Indonesian state, one of which is the kratom plant. This study needs to validate with more rigorous study in the future.

Keyword: National defense, medical intelligence, Kratom, Mitragynine, Sedative agent
PHARMACY AS THE FOUNDATION OF THE NATION: INDONESIA’S PREPAREDNESS IN FACING BIOTERRORISM

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ABSTRACT

The development of the times and the increasingly rapid use of science and technology have resulted in increasingly complex dynamics and forms of threats that will be faced by each country. Developed countries have started to change their way of attacking other countries’ defenses by using a bioterrorism strategy. The use of military forces which are increasingly spending a lot of budgets is no longer considered the right option to use because the world economy is not doing well in recent times, causing them to start developing attacks using bioterrorism. The bioterrorism here is CBRNE. Threats in the CBRNE sector are in the form of impacts caused by CBRNE disasters which can damage facilities, facilities or materials containing these elements. including among others the misuse of weapons that can cause health problems such as epidemics of infectious diseases or death to humans, animals, plants and damage to the environment so that they can threaten national defense. To increase knowledge and understanding of the hazards and impacts caused by exposure to materials containing these CBRNE elements, it is necessary to have good national defense in dealing with them.

Keywords: Anthrax, Bioterrorism, CBRNE, Pharmacy
OPTIMIZATION THERAPY USING COMBINATION OF ANTIRETROVIRAL THERAPY AND RED FRUIT EXTRACT TO REDUCE MORBIDITY OF HIV/AIDS

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ABSTRACT

There are many successful therapies using natural products as a co-therapy, including those studied in the field of HIV/AIDS. Until now, only one HIV-AIDS treatment is commonly used, namely, antiretroviral therapy (ARV). The key goals of ARV therapy are to improve overall immune function with increases in CD4+ cell count, prolong survival, reduce HIV-associated morbidity, improve the overall quality of life, and reduce the risk of transmission of HIV. Several ARV drugs such as Azidothymidine, Nevirapine, Raltegravir, and Saquinavir. ARV therapy should be used for a lifetime that had negative adverse effects to the patient. Therefore, to reduce the side effects and to optimize the therapy combining the ARV drugs with natural product seems to give promising results one of the natural products that can be used is a red fruit extract. The red fruit extract has several secondary metabolite compounds such as carotene, β-carotene, tocopherol dan also contains several other substances such as oleic acid, linoleic, acid, linolenic acid, and decanoate. Objective: This study sum the review of the effect of red fruit extracts on patients with HIV on antiretroviral therapy. Materials and Methods: The method used is a narrative review of research journals from the publish or perish application and methods in a journal that is by this study. Result: Treatment using antiretroviral + red fruit can increase the number of CD4+ cells instead of using only antiretroviral therapy. Conclusion: Based on the results, it was concluded that the red fruit extract has an excellent immunomodulatory effect and can help patients with HIV with antiretroviral therapy.

Keywords: Pandanus conoideus, antiretroviral therapy, HIV/AIDS, immunomodulatory,
"The Best Defense is a Good Offense". This old saying is very relevant to prepare for the next Pandemic. This paper proposes how emerging genetic technologies may prevent Pandemic to come. From recent avian flu Pandemic to current global Pandemic of COVID-19, viruses from animals jump to human are the main cause of Pandemic. So, the first strategy is establishment of Virus Genetic Bank. Wild animals such as bats, pangolins, palm civets known to harbor viruses with > 90% genetic identities to SARS-CoV-2 and SARS-CoV are all present in Indonesia. Periodic sampling can be done by soldiers from KODIM throughout Indonesia archipelago with little training, then send them to Central Laboratory for identification and deposit. Next, samples are screened for targeted viruses using specific primers with a real-time PCR. For further identification, partial DNA sequence can be read with Sanger method. All results are analyzed by comparing with databases. When candidates appear, next step is confirming virus’s ability to infect human cells in vitro using cell lines such as Vero cells inside a BSL3 laboratory. Larger quantity of viruses from cell culture can be used for whole genome sequencing using Next Generation Sequencing/NGS. With a deposit of many virus variations in the Bank, it makes possible to simulate virus mutation in test tube since major Pandemic always originated from mutated viruses. Directed evolution is the best choice here, started by DNA shuffling where DNA from different viruses are cut small then ligated again randomly to obtain variation such as new receptor binding domain as in the case of SARS-CoV-2. Resulted sequenced can be first checked for receptor binding by expressing it using cell-free protein translation system. Binding affinity can be checked easily using Surface Plasmon Resonance/SPR technique. Increase binding affinity can be obtained by error-prone PCR and selection using phage display method. “The Good Offense” here is that possible cause of next Pandemic can be identified first in the Lab, and then it is rather easy to prepare for candidate drugs and vaccines. Because Pandemic is like a Blitzkrieg, fast response is the key. Without learning from past failure, we will repeat to defeat against this bio threat. Faculty of Military Medicine has started small by creating a Synthetic Biology Club to prepare young military cadets with skills and vision on emerging genetic technologies.
CANDIDATES TARGETED THERAPY OF EGFR FOR LUNG CANCER: IN SILICO STUDY

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ABSTRACT

Background: Lung cancer is the highest death rate among other cancers. Available targeted therapy for its treatment is tyrosine kinase inhibitors for Epidermal Growth Factor Receptor (EGFR). It is one of the receptors on the lung surface. Gefitinib is one of the EGFR TKI used for lung cancer. However, 60% of patients developed resistance at 9 to 11 months after treatment. Currently, molecular docking is provided in silico models for discovering novel drugs targeted the EGFR. Objective: This study aims to develop a candidate agent as an alternative to gefitinib from natural ingredients for lung cancer targeted therapy using in silico study. Materials and Methods: We conducted research using Molecular Operating Environment (MOE) 2015 V.10 software and the EGFR used were obtained from RCSB. Result and Discussion: There are 8 ligands that interact with EGFR through the hydrogen, aromatic, and carbonyl bond with amino acids. The other 2 ligands interact with the receptor by the ligand exposure. Procyanidin A2 is the compound that has lower S value energy (\(-15.1153\) Joule/Kg.mol), which produces the strongest binding to the EGFR. Conclusion: Procyanidin A2 from the telang flower (Clitroia ternatea) had comparable interaction with gefitinib for targeting EGFR. This compound can be used as a candidate for lung cancer therapy. However, further study such as in vitro and in vivo in the laboratory are needed to confirm its activity.

Keywords: EGFR, lung cancer, in silico, molecular docking, procyanidin A2
NUTRACEUTICAL TO SUPPORT NATIONAL DEFENSE SYSTEM

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Background: Nutraceutical are food products that have medicinal properties. Besides being able to cure disease, nutraceutical products can improve health and prevent chronic disease. Objective: Nutraceutical products can be used as an alternative to medicine. However, of course if it is consumed in excess, it will have negative effects. In Indonesia, nutraceutical products exist in various types, such as herbal drinks. Result: Nutraceutical products can be used as an effort to improve the health status of the Indonesian people by providing alternatives to the community so that they do not get adverse effects from drugs. Conclusion: The high degree of public health will boost the national defense.

Keyword: Nutraceutical, disease prevention, promote health, Indonesian society, defense system
POTENTIAL OF ETHANOL EXTRACT OF OCIMUM AMERICANUM.L AS HEPATOPROTECTOR IN ANTITUBERCULOSIS DRUGS-INDUCED HEPATOTOXICITY

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Background: Drug induced liver injury is a potentially effect of antituberculosis regimens containing isoniazid and rifampicin that cause hepatotoxicity due to bioactivation of the metabolites and oxidative stress. Ocimum americanum (OA) contains antioxidant molecules and provides protection against free radicals caused by oxidative damage.

Objective: This study attempts to investigate the hepatoprotective activity of Ocimum americanum L. ethanol extract against fixed-dose combination (FDC) antituberculosis-induced hepatotoxicity mice.

Materials and Methods: The level serum of alanine transaminase (ALT) and aspartate transaminase (AST) were investigated. Treatment group 1 (FDC +OA 2.8 mg/20gr BW) and treatment group 2 (FDC +OA 5.6 mg/20gr BW) were compared to positive control group and normal control group for 14 days.

Results: There were statistically significant of mean differences in serum AST level between each group of study subjects (p-value 0.00). This finding also found in serum ALT level (p-value 0.00). Next step in post-hoc multiple comparison test, there was no significant difference in FDCs group toward treatment groups in AST and ALT serum levels. By this analysis, treatment groups did not seem to decrease of AST and ALT level statistically. But, on mean difference, each treatment group was able to reduce the AST and ALT level compared to FDCs group and the decrease in serum AST and ALT levels were affected by the number of administered dosages of Ocimum americanum ethanol extract.

Conclusion: These results suggest the potential hepatoprotection role of Ocimum americanum L. ethanol extract as hepatoprotection in antituberculosis drugs-induced hepatotoxicity

Keywords: Ocimum americanum, hepatoprotector, antituberculosis drug
### PHARMACOLOGY & BIOMEDICAL SCIENCE

<table>
<thead>
<tr>
<th>Abstract ID</th>
<th>Name</th>
<th>Title</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A-1628009542)</td>
<td>Febriana Aquaresta</td>
<td>Comparison Between GenoType MTBDRsl VER 2.0 Assay and Phenotypic Method on Rifampicin Resistant Mycobacterium tuberculosis</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1625799960)</td>
<td>Mikael Ham Sembiring</td>
<td>Bottleneck Current Therapy for Malaria: a Narrative Review</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1626004630)</td>
<td>Muhamad Azhar</td>
<td>Pax3 And Pax7 Induces Skeletal Muscle Stem Cells In Injury Healing: A Narrative Review</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1626013761)</td>
<td>Muhammad Raihan Zulfikar</td>
<td>CRISPR/Cas9 Genome Editing: Future Treatment of Duane Retraction Syndrome</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1626081009)</td>
<td>Ni Made Dwi Sandhiutami</td>
<td>Nephroprotective Effect Of Ethanol Extract Abelmoschus Manihot L. Leaves In Gentamicin-Induced Mice</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1626090458)</td>
<td>Sella O. Sefa</td>
<td>Monoclonal Antibody Therapy in Humans Against The SARS CoV-2 Virus</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1625048799)</td>
<td>Siti Farah Rahmawati</td>
<td>Corticosteroid effects on airway neuroplasticity in experimental models of asthma</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1623160672)</td>
<td>Widhi Kusuma Wardhana</td>
<td>From Zero To Hero: A Review On Potential Of Kirinyuh For Improving The Histological Features Of Fatty Liver In Dyslipidemic Rats</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1625983310)</td>
<td>Yandi Permana</td>
<td>Grasp Of Antimalarial Drug Resistance In Indonesia Population: Focused On Genetic Polymorphism</td>
<td>Oral Presenter</td>
</tr>
<tr>
<td>(A-1626099348)</td>
<td>Aliqbal Nohea</td>
<td>Reducing animal testing with AI</td>
<td>Poster Presenter</td>
</tr>
<tr>
<td>ID</td>
<td>Name</td>
<td>Title</td>
<td>Role</td>
</tr>
<tr>
<td>----------</td>
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<td>-----------------------------------------------------------------------------------------</td>
<td>-------------</td>
</tr>
<tr>
<td>(A-1626110163)</td>
<td>Bantari Wisnu Kusuma Wardhani</td>
<td>Genome editing as an alternative to develop anti-cancer resistance model</td>
<td>Poster</td>
</tr>
<tr>
<td>(A-1626090393)</td>
<td>Dewa ayu agung puspita dewi</td>
<td>Effect of Acalypha Indica L. Root Ethanol Extract on Lipid Profile and Troponin-T of Rat Hearts Treated with High Fructose Cholesterol Diet</td>
<td>Poster</td>
</tr>
<tr>
<td>(A-1626106058)</td>
<td>Soni Siswanto</td>
<td>Environmental pollutants-induced pulmonary fibrosis: causal and mechanism</td>
<td>Poster</td>
</tr>
<tr>
<td>(A-1626057614)</td>
<td>Kurnia Sandy</td>
<td>The Effect Of Populations That Have Mutations In The SARS COV-2 Virus variant Alpha in the United Kingdom and Variant Beta in South Africa On the Efficacy Of The Viral Vector Platform Vaccine</td>
<td>Poster</td>
</tr>
</tbody>
</table>
Gene Mutations in *Mycobacterium tuberculosis* Based on Pyrosequencing Assay and Its Role on Antituberculosis-Drug Resistance: A Literature Review

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**Background:** *Mycobacterium tuberculosis* as the cause of tuberculosis disease is known to have some various genotype variations which can cause antibiotic resistance or cause the bacteria more susceptible to resistance than any other variation. **Objective:** to determine the mutation in the genes of *Mycobacterium tuberculosis* detected by pyrosequencing assay that could cause rifampicin and isoniazid resistance. **Methods:** A literature review is carried out on the included articles obtained from PubMed and Google Scholar database search results. The literature search used the PRISMA flowchart principle. Articles from the search result are checked for duplication and selected through predetermined inclusion and exclusion criteria, in which the journal's reputation is checked according to the Scopus index or SINTA and a critical review of each article is carried out. Selected articles will be analyzed using the narrative review method. **Results:** The search results using the PubMed and Google Scholar database are 725 articles. After going through duplication checks, selection according to inclusion and exclusion criteria, as well as checking journal reputation and critical studies, five articles will be analyzed to answer the research objective. In rifampicin resistance, many gene mutations occurred in rpoB Ser531Leu, while in isoniazid resistance mutations occurred in katG Ser315Thr and inhA 15 C-T. **Conclusion:** There are some mutations in *Mycobacterium tuberculosis* associated with antituberculosis-drug resistance that can be detected by pyrosequencing assay.

**Keywords:** *Mycobacterium tuberculosis*; drug resistance; pyrosequencing; gene mutation
COMPARISON BETWEEN GENOTYPE MTBDR<sub>sl</sub> VER 2.0 ASSAY AND PHENOTYPIC METHOD ON RIFAMPICIN RESISTANT <i>Mycobacterium tuberculosis</i>

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ABSTRACT

Background: Multi-drug resistance tuberculosis remains a crisis and threat to world health. Line Probe Assay is a molecular technique for rapid diagnosis of second line drugs MDR-TB. However, there is less sufficient information on the clinical viability of this test and lack of evidence in the diagnosis of MDR-TB use of this Line Probe Assay technique in Indonesia. The aim of this study is to determine performance of line probe assay GenoType MTBDR<sub>sl</sub>/VER 2.0 assay on rifampicin-resistance <i>Mycobacterium tuberculosis</i> isolates compared to phenotypic Lowenstein Jensen Drug Susceptibility Test as a gold standard.

Method: A cross sectional study with analytic observational approach conducted from January–June 2020. There were 157 <i>Mycobacterium tuberculosis</i> isolates used in this study. A total of 26 rifampicin resistance <i>Mycobacterium tuberculosis</i> isolates were collected and tested with rapid molecular multiplex PCR GenoType MTBDR<sub>sl</sub>/VER 2.0 assay and phenotypic Drug Susceptibility Test after being examine with Xpert MTB/RIF. Statistical analysis was performed to determine sensitivity, specificity, PPV, NPV and accuracy of second line tuberculosis drugs.

Results: Our study found three fluoroquinolone resistant <i>Mycobacterium tuberculosis</i> isolates (11.5%) and one amikacin resistant <i>Mycobacterium tuberculosis</i> isolate (3.8%). The performance of GenoType MTBDR<sub>sl</sub>/VER 2.0 assay is shown 100% (95% CI 84.6–100%) sensitivity, 100% (95% CI 39.8–100%) specificity, 100% (95% CI %) PPV, 100% (95% CI %) NPV and 100% (95% CI 86.8–100%) accuracy

Conclusion: GenoType MTBDR<sub>sl</sub>/VER 2.0 assay showed a high performance compared to phenotypic method to determine resistance of fluoroquinolone and Second Line Injectable Drugs.

Keywords: Line Probe Assay, GenoType MTBDR<sub>sl</sub> ver 2.0, Drug Susceptibility Test, MDR-TB, Second Line Injectable Drugs
BOTTLENECK CURRENT THERAPY FOR MALARIA: A NARRATIVE REVIEW

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ABSTRACT

Malaria is an endemic disease that causes death in many places around the world, including Indonesia. This disease is caused by Plasmodium family parasites transmitted by Anopheles sp. mosquito vector. Currently, the pharmacological therapies for malaria are artemisinin, tetracyclines, 4-aminoquinolines, and lincosamide. However, drug resistance is an inevitable occurred. Furthermore, malaria therapy faces interaction between plasmodiums that induce disease complexity or vice versa, reducing the severity of infection. Moreover, challenges in prevention and treatment for malaria are co-infection, concomitant condition, inadequate vaccine, as well as community behaviour pattern in drug use and self-diagnostic. Hence, this narrative review article elucidates all related obstacles in current malaria therapy. We also purpose the strategy and future research to overcome those obstacles, particularly exploring Indonesia originated natural medicine, applied nano-biotechnology, and genetic engineering.

Keywords: bottleneck malaria therapy, anti-malaria resistance, concomitant condition, co-infection, community behavior pattern
PAX3 AND PAX7 INDUCES SKELETAL MUSCLE STEM CELLS IN INJURY HEALING: A NARRATIVE REVIEW

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Background: Skeletal muscle accidents are one of the most common occurrences in society, especially among athletes and the military population. From the various urgency, this accident needs to be cured more quickly. However, the current treatment still has some shortcomings and is less effective. In this case, Pax3 and Pax7 proteins could be potential to be an alternative treatment for skeletal muscle injuries. Objective: to compare the current treatment of skeletal muscle injuries and the potential treatment of Pax3 and Pax7 proteins for skeletal muscle injuries. Material and Methods: We made a Narrative Review by collecting several scientific journals from several leading platforms such as PubMed, Cell Stem Cell, NCBI and others. Results: Skeletal muscle is one of the most common accidents. The causes are quite a lot, it can be in the form of workplace and non-workplace causes. The highest risk occurs in the athlete and military environment. Treatment of current skeletal muscle injuries are RICE, NSAIDs, and mechanical stimulates. However, it is considered less effective especially in NSAIDs because it inhibits myogenic cell division. Recent treatments for satellite cells or skeletal muscle stem cells that are influenced by regulation by factors Pax3 and Pax7 which accelerate cell proliferation. This can accelerate the healing of wound victims, especially wounds to the skeletal muscles. Conclusion: After compared, Pax3/7 have potential to be one of skeletal muscle injuries treatment.

Keywords: Pax3 and Pax7, skeletal muscle, stem cells, cell proliferation, injuries
CRISPR/Cas9 GENOME EDITING: FUTURE TREATMENT OF DUANE RETRACTION SYNDROME
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ABSTRACT
Duane Retraction Syndrome (DRS) is characterized by limited eye movement. One of its causes is a mutation in the CHN1, MAFB, or SALL4 gene. Nowadays, the treatment for DRS is glasses, occlusion, and surgery. However, this treatment has not been able to cure the disease's hereditary issue. Another strategy that can be considered is CRISPR/Cas9, a tool for performing gene editing with a wide range of applications, including treating genetic diseases. Hence, this article elucidates the possibility of using CRISPR/Cas9 for the treatment of DRS. We investigated several studies in the electronic scientific database platform through Pubmed, Google Scholar, and Scopus in July 2021, consisting of randomized, non-randomized, or case reports in clinical trials. We also made sgRNA as a first step in using CRISPR/Cas9 as a treatment for DRS in silico using the CCTop website. By computing sgRNA, conducting tests, and analyzing the results, CRISPR/Cas9 may repair genetic mutations. There are no reports on the use of CRISPR/Cas9 in DRS at the moment. Hence, this would be very useful as a starting point for using CRISPR/Cas9 as a DRS treatment. However, it needs to be further proven through in vivo, in vitro, and clinical trials.

Keywords: CRISPR/Cas9, Duane Retraction Syndrome, Gene Editing, Genetic Diseases
NEPHROPROTECTIVE EFFECT OF ETHANOL EXTRACT *Abelmoschus manihot* L. LEAVES IN GENTAMICIN-INDUCED MICE

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Gentamicin is the prototype of the aminoglycoside group. The most common side effect of gentamicin is nephrotoxicity. Several mechanisms of nephrotoxicity caused by the use of gentamicin can occur due to the formation of oxidative stress. *Abelmoschus manihot* L. leaves contain flavonoid compounds that have antioxidant activity. The purpose of this research to obtain the nephroprotective effect of *Abelmoschus manihot* L. leaves to reducing nephrotoxicity in gentamicin-induced mice. This research was conducted experimentally, using mice which were divided into 7 groups. Normal group, negative group, solvent group, test group (given ethanol extract of *Abelmoschus manihot* L. leaves at doses of 50, 100, 200, 400 mg/kgBW) which was administered orally for 7 days and on the 8th day gentamicin 112 mg/kgBW was induced intraperitoneally. Furthermore, on the 11th day the the mice were given anesthesia to take blood serum for examination of creatinine and urea and their kidneys were taken for histological examination. The results showed that creatinine levels and BUN induced by gentamicin increased not according to the normal value, while the results of the study given ethanol extract *Abelmoschus manihot* L. leaves and gentamicin-induced decreased according to the normal value. Histological results of the kidney tissue of mice that were given gentamicin were damaged, while the tissue of mice that were given ethanol extract *Abelmoschus manihot* L. leaves and gentamicin-induced showed improvement. From the research results can concluded that ethanol extract *Abelmoschus manihot* L. leaves showed a nephroprotective effect in mice induced by gentamicin.

**Keywords:** *Abelmoschus manihot* L., gentamicin, nephroprotection, kidney histopathology
MONOCLONAL ANTIBODY THERAPY IN HUMANS AGAINST THE SARS CoV-2 VIRUS

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ABSTRACT

Background: COVID-19 is an acute respiratory disease caused by SARS-CoV-2 virus. This infectious disease spreads very quickly and causes susceptibility to infection from mild to severe, even leading to death. Currently, the global world is faced with an epidemic that threatens world health. The spread of the newly emerging COVID-19 has reached a pandemic level that has a significant public and global impact, resulting in more than 4.8 million new cases, more than 25 million infected cases and more than 0.85 million deaths worldwide. Objective: Handling this global health emergency due to SARS-CoV-2 requires effective therapy. Therapy with monoclonal antibodies is more specific, pure, and has a lower risk of bloodborne pathogen contamination than intravenous immunoglobulin therapy and serum therapy, working specifically targeting human antibodies. This antibody therapy has specific similarities to vaccines in targeting SARS-CoV-2. Material and methods: This article is a narrative review based on the publication of several journals from various sources (such as: PubMed, NCBI, JAMA, etc.) to confirm. Conclusion: Monoclonal antibody therapy is currently still being developed by experts to fight COVID-19. Theoretically, the development of monoclonal antibody therapy (mAbs) is considered effective and safe so that it can be used by any patient. Currently, many researchers are combining, engineering the development of mAbs for therapeutic achievements in the discovery of antigens for the future.

Keywords: COVID-19; SARS-CoV2; antibody therapy; treatment; monoclonal antibodies
CORTICOSTEROID EFFECTS ON AIRWAY NEUROPLASTICITY IN EXPERIMENTAL MODELS OF ASTHMA

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Background: Airway neuroplasticity occurs in asthma and contributes to airway hyperresponsiveness (AHR). Corticosteroids, an established asthma therapy, are known to reduce airway inflammation and improve lung function. However, their effect on airway neuroplasticity has not been described yet.

Aim: To investigate the effects of corticosteroids on airway neuroplasticity.

Methods: BALB/cByJ (Jax-strain) mice were sensitized and challenged to ovalbumin (OVA) for 4 weeks to develop murine chronic asthma model. Budesonide was administered before every OVA challenge. 24 hours after the last challenge, lungs were collected for immunohistochemistry. To elucidate the direct effect of corticosteroids on airway cholinergic neurons, we exposed human embryonic stem cell (hESC)-derived airway cholinergic neurons to dexamethasone for 5 days.

Results:

Figure 1. Corticosteroids inhibit airway neuroplasticity in a murine chronic asthma model and prevent hESC-derived airway cholinergic neuronal differentiation. a)
Budesonide treatment hindered eosinophil infiltration into the airway basal membrane in a murine chronic asthma model, suggesting inhibition of airway inflammation. 

**b)** Budesonide downregulated class III β-tubulin protein expression (neuronal marker) in the murine airway (One way ANOVA with Newman-Keuls posthoc analysis, p<0.05).

**c)** The eosinophil count correlated with β-III-tubulin expression irrespective of treatment arm (Pearson correlation, two-tailed, p<0.0001). (◊) Sal group, (Δ) OVA group, (●) OVA/BUD group.

**d)** Dexamethasone exposure on hESC-derived airway cholinergic neurons reduced choline acetyltransferase (ChAT) and β-III-tubulin double-positive staining, indicating reduced differentiation into cholinergic neurons (* Paired t-test, two-tailed, p<0.05)

**Conclusions:** Corticosteroids inhibit airway neuroplasticity in a murine chronic asthma model and prevent ESC-derived airway cholinergic neuronal differentiation. Therefore, both indirect (anti-inflammatory effects) and direct inhibition of neuronal marker expression may contribute to the effects.

**Keywords:** Asthma, airway neuroplasticity, corticosteroids, murine chronic asthma, human embryonic stem cell (hESC)-derived airway cholinergic neurons.
ABSTRACT

Background: Animals have been used in research and teaching for a long time. However, clear ethical guidelines and pertinent legislation were instated only in the past few decades, even in developed countries with Judeo-Christian ethical roots. Using animals for cosmetics and medical tests has contributed towards a debate based on conflicting interests. Despite the efforts in justifying the value of animals in conducting analyses, this study seeks to elaborate whether or not it is rational to use animals as test subjects in medical and cosmetics fields. With advances in technology, AI can also be used to reduce the use of animal testing and can even replace it. Objective: With the help of AI, it is hoped that the use of animals as test materials will decrease, because many people already disagree with the use of animals as test materials, therefore a team has developed a computer method of chemical testing that can save 2 million animals and more than $1 billion per year. With the support of many people the team has succeeded in developing new algorithms and databases to analyze chemicals and determine their toxicity. This program is called Read-Cross Structure Activity Relationship (RASAR). Material and methods: This article is a narrative review based on the publication of several journals from various sources to confirm. Conclusion: In reducing the use of animals for testing AI has worked well because it has been programmed to analyze the chemicals to be tested and can also speed up the process.

Keywords: animal research, medical testing, AI, drug toxicity
FROM ZERO TO HERO:
A REVIEW ON POTENTIAL OF KIRINYUH FOR IMPROVING THE
HISTOLOGICAL FEATURES OF FATTY LIVER IN DYSLIPIDEMIC RATS

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ABSTRACT

Background: The prevalence of dyslipidemia sufferers in Indonesia continues to increase especially in Padang and Jakarta. Dyslipidemia can be a risk factor for Non-Alcoholic Fatty Liver Disease (NAFLD). One of the drugs that used for reducing dyslipidemia is statin, but statin contains some side effect. So, herbal plants are used to minimalizing that side effect. One of underrated herbal plant that used to reduce dyslipidemia is Kirinyuh (Chromolaena odorata L.). Currently, research has shown that kirinyuh extract can reduce dyslipidemia. However, research on the potential of kirinyuh on the histopathology of NAFLD still needs to be done. The writing of this Systematic Literature Review is expected to identify how the potential of kirinyuh extract improves the histopathology of fatty liver in dyslipidemic albino rats (Rattus norvegicus).

Method: Systematic Review by conducting a literature search using Google Scholar and PubMed. Literature that discusses Chromolaena odorata, albino rats, dyslipidemia, and NAFLD. Result: There are 3 studies concluded that Chromolaena odorata can reduce levels of dyslipidemia in rats and 4 studies concluded that the content of flavonoid can improve the image of NAFLD in albino rats. Conclusion: Chromolaena odorata has the potential to improve the histopathological picture of NAFLD in albino rats with dyslipidemia.
Malaria is an endemic tropical parasitic infectious disease in Indonesia, the easternmost. In addition to HIV/AIDS and tuberculosis, the prevention and elimination of malaria are becoming part of the Sustainable Development Goals (SDGs) as a global commitment that must be achieved by the end of 2030. Currently, the elimination of malaria programs has made great progress despite the generation of antimalarial-resistant plasmodium strains. It remains an unresolved problem in eradicating malaria besides genetic polymorphism which was appointed as one of the reasons behind. This polymorphism leads to inadequate activity of antimalarial drugs to undertake plasmodium infection by several molecular mechanisms. For example, dihydroartemisinin (DHA), piperaquine, and primaquine are the first line therapy for malaria in Indonesia. However, the resistance is unavoidable. Therefore, this review summarized genetic polymorphism in DNA resistance in Indonesia population, as well as its mechanism and drug candidates. We highlight strategies to overcome these obstacles in malaria therapy.

**Keywords:** Antimalarial-resistance, Dihydroartemisinin, Eastern Indonesia, Polymorphism.
GENOME EDITING AS AN ALTERNATIVE TO DEVELOP ANTI-CANCER RESISTANCE MODEL

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Chemotherapeutic drug resistance cancer remains clinically important problems. Development of specific drug resistance models are critical in the study of chemotherapy resistance cancer. One of the approaches is using the drug resistance cell lines. Developing drug resistance cell lines from available cell lines is a challenging process that commonly takes 3 - 18 months. This process includes several key steps, such as optimizing dose of anti-cancer drugs, treatment interval, and duration of treatment to induce resistance. Another problem is reversibility of cancer cell lines, even after 18 months of treatment. Therefore, this article brings an alternate strategy to generate anti-cancer cells resistance using genome editing techniques. One powerful technique is CRISPR-Cas9 systems. This genome editing mediates DNA modification by replacement in the presence of exogenous donor DNA template in knock-in and resection in the absence of exogenous DNA template in knock-out. This technique results in specific chemotherapeutic cell lines for studying anti-cancer resistance.

Keywords: genome editing, anti-cancer drug resistance, CRISPR-Cas9 systems, knocked in, knocked out.
EFFECT OF *Acalypha indica* L. ROOT ETHANOL EXTRACT ON LIPID PROFILE AND TROPONIN-T OF RAT HEARTS TREATED WITH HIGH FRUCTOSE CHOLESTEROL DIET

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**ABSTRACT**

**Background:** Sugar-sweetened and high fructose beverages are the risk factor for hyperlipidemia and cardiovascular disease. Hyperlipidemia is a predisposing factor for the development of the cardiovascular disease. Pharmacological therapy for hyperlipidemia has various side effects along increasing dosage. To increase the effectiveness of the therapy, natural compound can be used as adjuvant therapy. *Acalypha indica* L. (AI) is one type of plant that has antihyperlipidemic properties so that it can reduce lipid profiles. Thus, the risk of cardiovascular disease can be prevented.

**Methods:** Thirty Sprague-Dawley rats were induced with 825 mg of High Fructose-Cholesterol Diet (HFCD) twice a day, and feed by 10% cholesterol. The induction lasted for 12 weeks. Rats were randomly divided into 4 groups: negative control (NC), Gemfibrozil 31 mg/kgBW/day (GEM), AI 400 mg/KgBW/day, and AI+GEM groups. After the induction completely done, all treatments were performed for 8 weeks. Troponin levels and lipid profiles were investigated.

**Results:** HFCD induction increase triglycerides, Low Density Lipoprotein (LDL), total cholesterol, and troponins. After 8 weeks of therapy, there was a significant reduction in triglycerides, LDL, total cholesterol, and troponins. The rats that were given AI+GEM tend to have better effectiveness of therapy among the others.

**Conclusion:** The therapy of GEM, AI, and GEM+AI in HFCD-induced reduce the risk of heart damage. However, the administration of AI as an adjuvant therapy combination with GEM reduces the incidence of heart damage than the other therapy groups.

**Keywords:** *Acalypha indica*, Hypertriglyceridemia, Troponin-T
ENVIRONMENTAL POLLUTANTS-INDUCED PULMONARY FIBROSIS: CAUSAL AND MECHANISM

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ABSTRACT

Idiopathic pulmonary fibrosis (IPF) is a specific form of chronic progressive interstitial lung disease with very limited therapeutic options. Older adults have been primarily reported to have IPF that is characterized by worsened lung function. Some environmental pollutants were reported that induced IPF in humans, in particular asbestos, silica, mercury, cadmium, and benzo(a)pyrene. To date, some studies have focused on various pollutants which are induced. However, the molecular mechanism of various pollutants to induce IPF remained unexplored. Hence, this narrative review articles describe its molecular mechanism in generating IPF comprehensively. It is useful to portray the IPF pathogenesis, as well as on its drug discovery and development. Collectively, this article also revealed animal models and measured outcome to mimicking human pathogenesis of IPF.

Keywords: idiopathic pulmonary fibrosis, animal models, lung disease, drug discovery and development.
THE EFFECT OF POPULATIONS THAT HAVE MUTATIONS IN THE SARS COV-2 VIRUS VARIANT ALPHA IN THE UNITED KINGDOM AND VARIANT BETA IN SOUTH AFRICA ON THE EFFICACY OF THE VIRAL VECTOR PLATFORM VACCINE

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ABSTRACT

Background: The Covid-19 pandemic has spread since 2019 due to the SARS COV-2 virus is still ongoing today. The SARS COV-2 virus has mutations mainly in the Spike Protein and Receptor Binding Protein (RBD) sections, including variant alpha which first appeared in the UK and beta which appeared in South Africa. Various efforts have been made to overcome the Covid-19 pandemic, one of them is preventive efforts in the form of vaccines. Method: Narrative review based on clinical and non-clinical trial publications to strengthen the explanation of mechanisms taken from data sources: PubMed, Cochrane, Lancet, Nejm, etc. The material used is 23 journals Publication. Discussion: The vaccine produced by AstraZeneca is given in two doses with the first dose is half the standard dose and the second dose in the standard dose with a duration of 12 weeks to achieve the best efficacy. This vaccine has decreased efficacy due to the mutation of the SARS COV-2 virus due to viral resistance to antibody neutralization. In case alpha showed a minimal impact on the efficacy of the AstraZeneca vaccine while in case beta showed a significant effect of decreasing the efficacy of the AstraZeneca vaccine on the neutralizing capacity of the virus using a pseudotype or infectious virus neutralization test. Conclusion: ChAdOx1 vaccine nCoV-19 decreased efficacy significantly in SARS CoV-2 variant beta while at Varian alpha did not show any significant effect on the efficacy of the vaccine.

Keywords: Covid-19, Vaccine, Viral Vector, AstraZeneca
<table>
<thead>
<tr>
<th>Abstract ID</th>
<th>Name</th>
<th>Title</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A-162394414)</td>
<td>Dhadhang Wahyu Kurniawan</td>
<td>Formulation Of Cinnamon Bark Essential Oil Gel As Mosquito Repellent</td>
<td>Oral</td>
</tr>
<tr>
<td>(A-1626076124)</td>
<td>Endang Wahyu Fitriani</td>
<td>Design Of Tea Tree Oil Loaded Nanostructured Lipid Carrier: Preparation And In-Vitro Antifungal Activity</td>
<td>Oral</td>
</tr>
<tr>
<td>(A-1622127123)</td>
<td>Uce Lestari</td>
<td>Development Of Facial Wash Gel From Activated Charcoal Palm Shell Using Habatussaudah Scrub As Natural Detoxification</td>
<td>Oral</td>
</tr>
<tr>
<td>(A-1626058569)</td>
<td>Nor Liliyana</td>
<td>The Effect Of Different Gelling Agents On The Sun Protection Factor From Emulgel Formula Of Binjai (Mangifera Caesia Jack. Ex. Wall) Leaves Methanol Extract</td>
<td>Poster</td>
</tr>
<tr>
<td>(A-1626106757)</td>
<td>Rahmah Elfiyani</td>
<td>Comparison of Allicin Decomposition Kinetics Between Garlic Extract and Phytosomes of Garlic Extract</td>
<td>Poster</td>
</tr>
<tr>
<td>(A-1626090987)</td>
<td>Siti Maimunah</td>
<td>Formulation And Antioxidant Properties From Emulgel Of Binjai (Mangifera Caesia Jack. Ex. Wall) Leaves Methanol Extract</td>
<td>Poster</td>
</tr>
</tbody>
</table>
FORMULATION OF CINNAMON BARK ESSENTIAL OIL GEL AS REPELLENT

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ABSTRACT

Background: The content of most repellent in the market nowadays is N,N-diethyl-meta-toluamide (DEET) which has many adverse effects such as hypersensitivity symptoms, irritation, urticaria, and for long period could instigate cancer. Hence, we must explore a new alternative repellent that gives a better performance than DEET. Natural products could be a solver to this problem, and the herb is known as a good repellent is Cinnamomum burmanii. Objective: The purpose of this research is to make a cinnamon bark essential oil gel preparation, determines the physical characteristic and physical stability during storage, and examines the activity of repellent from the best gel preparation. Materials and Methods: The formulations of gel were made with variations in the concentration of Carbopol 940 (0.5%, 1.5%, and 2%) contain 1% of cinnamon bark essential oil. The gel evaluated about physical characteristic and physical stability. The activity of repellent is determined by an Aedes aegypti mosquitoes for 6 hours with 2 hands respondents. The parameters of organoleptic, homogeneity, and pH are analyzed descriptive, while the viscosity, spread power, and adhesion are analyzed using one-way ANOVA at the level confidence 95%, continued by using HSD Tukey/Dunnet T3 test. The effectivity of repellent protection is counted by the percentage of protection power. Results: The studies showed that all of gel preparations qualified the organoleptic, homogeneity, and pH parameters. Viscosity and adhesion decreased during storage, whilst spread power has increased. Conclusion: Based on the results, the best gel is the formula I which has repellent activity effective for 6 hours like DEET.

Keywords: Cinnamon (C. burmanii) bark, essential oil, gel formulation, repellent, DEET
DESIGN OF TEA TREE OIL LOADED NANOSTRUCTURED LIPID CARRIER: PREPARATION AND IN-VITRO ANTIFUNGAL ACTIVITY

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ABSTRACT

Background: Tea tree oil (TTO) is a promising essential oil that has great potency as antifungal. TTO has several limitations for pharmacological applications, including volatile and extensive range of partition coefficient. To overcome the limitations, TTO can be loaded in the Nanostructured Lipid Carrier (NLC). The combination of solid and liquid lipid in the NLC and the manufacturing conditions will affect the characteristics of the NLC formed. Objective: This study aims to design and evaluate TTO loaded NLC with appropriate particle size to improve therapeutic efficacy as an antifungal agent. Methods: TTO loaded NLC formula contains TTO, solid lipids, liquid lipids, Poloxamer 188, Span 80 and distillated water. The TTO loaded NLC were prepared by high shear homogenization method and characterized with particular attention to average particles size and polydispersity, zeta potential, pH, and viscosity. Stability testing was performed for 1 month period under room temperature (27±2°C). An in-vitro antifungal activity was also tested on TTO using the disk diffusion method. Results: Optimized formulation ware found that NLC’s with stearic acid, glyceryl monostearate and cetyl alcohol as solid lipid and Migyol 128 and olive oil as liquid lipid showed a smaller average particle size and polydispersity. The stirring speed does not affect the particle size. The in-vitro antifungal activity test results showed that TTO has antifungal activity as good as ketokonazole cream. Conclusion: TTO loaded NLC was successfully formulated using several types of solid and liquid lipids, has great stability for 1 month storage and great potency as an antifungal.

Keywords: Tea tree oil, Nanostructured lipid carrier, particle size, In-vitro antifungal activity
ABSTRACT

The human body is very susceptible to toxins from food preservatives and air pollution. Toxins will accumulate to attack body tissue cells, resulting in allergies, premature aging and a decreased immune system. Therefore, natural detoxification is needed for prevention. Natural detoxification can be obtained by using habatussaudah which has the ability to increase the natural elimination of toxins from our bodies. To improve the ability of facial wash gel from activated charcoal palm shell in terms of absorption of toxins, it was further developed with the addition of habatussaudah as a scrub. This study aims to determine the formula for facial wash gel activated charcoal palm shell with habatussaudah as a scrub has physical properties according to standard parameters and to determine the safety and effectiveness as a natural detoxification. Facial wash gel is made into 3 formulas with concentrations of activated charcoal palm shell and habatussaudah 2:1 (FII), 4:2 (FIII) and 6:3 (FIII). The stages of the procedure in this study include making activated charcoal palm shell charcoal and habatussaudah powder, making facial wash gel, evaluating physical properties (organoleptic, homogeneity, spreadability, viscosity, foaming ability, cycling test), irritation test, hedonic test and facial skin moisture test. and the effectiveness of natural detoxification using a digital microscope that is compared before and after use. Facial wash gel biore as a positive control. The results showed that FII had good physical properties and was safe at the time of use and was most favored by the panelists compared to other formulas. Testing the effectiveness of facial detoxification showed that FII was able to remove toxins and impurities after use and had a higher water content than the positive control. From the results of these studies, it can be concluded that the FII facial wash gel with a concentration of 4:2 has the best physical properties, is safe to use and is effective as a natural detoxification.

Key words: facial wash gel, Habatussaudah, natural detoxification
THE EFFECT OF DIFFERENT GELLING AGENTS ON THE SUN PROTECTION FACTOR FROM EMULGEL FORMULA OF BINJAI (Mangifera caesia Jack. Ex. Wall) LEAVES METHANOL EXTRACT

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ABSTRACT

Background: Quercetin is a flavonoid compounds with very strong antioxidant and photoprotection properties. Binjai (Mangifera caesia Jack. Ex. Wall) is one of the Mangifera species with a better antioxidant source and significantly high flavonoid contents so that has potential as a sunscreen. Objective: This study aims to identify quercetin and determines the sun protection factor (SPF) of Binjai leaves methanol extract and the effect of the different gelling agents on the SPF of the sunscreen emulgel formula. Materials and Methods: Binjai leaves were extracted with methanol using the Soxhlet apparatus. Gas Chromatography-Mass Spectrometry (GC-MS) was used for the remaining methanol solvent. The quercetin identification was examined by DPPH (2,2-diphenyl-1-picrylhydrazyl) spray-on Thin Layer Chromatography (TLC). The emulgel was made in 3 optimum formulas with different gelling agents (Carbopol, Na-CMC, and tragacanth). Determination of the SPF was done by measuring the absorbance using UV-Vis Spectrophotometer. Result: The extract was identified as not containing methanol solvent residual. Identification with TLC showed one yellow spot from the extract that was parallel with quercetin on a purple background after sprayed by the DPPH. The extract with a concentration of 2500 ppm obtained an SPF of 23.01 compared with quercetin in 50 ppm which has an SPF of 16.93. The emulgel of the extract with the highest SPF of 21.38 was obtained from Carbopol formula. Conclusion: The results of the study show that the Binjai leaves methanol extract has ultra protection as a sunscreen with an emulgel that did not affect the activity is Carbopol formula.

Keywords: Binjai Leaves, emulgel, gelling agent, Sun Protection Factor (SPF).
COMPARISON OF ALICIN DECOMPOSITION KINETICS BETWEEN GARLIC EXTRACT AND PHYTOSOMES OF GARLIC EXTRACT

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ABSTRACT

Background: Garlic extract contains allicin which had many pharmacological activities, one of it as an antidiabetic. Allicin was unstable compound, so it was easy to decompose. To increase its stability, the allicin contained in the garlic extract was loaded to the phytosome delivery system. Objective: The aimed of this study was to compare the decomposition kinetics of allicin from garlic extract and phytosome at 25°C. Materials and Methods: Garlic extract was made by maceration method using methanol solvent. Garlic extract was loaded into phytosome by the thin layer hydration method. The extracts and phytosomes were stored for 8 weeks at 25°C. Furthermore, allicin contains were determined every 2 weeks using a UV-Vis spectrophotometer. Results: The decomposition order of allicin in the extract or phytosome was zero order. While the yield of allicin decomposition rate in garlic extract was 0.2728 %/week and the decomposition rate of allicin in the phytosome garlic extract was 0.0185 %/week. Conclusion: The decomposition mechanism of allicin in extracts and phytosomes follows the zero order, and the rate of decomposition of allicin in phytosomes is slower than allicin in garlic extract.

Keywords: decomposition kinetics, allicin, garlic extract, phytosome, order and rate of decomposition
ABSTRACT

Background: Binjai (*Mangifera caesia* Jack. Ex. Wall) is one of the endemic wild species in Kalimantan and a better antioxidant source than other *Mangifera* species. The high natural antioxidant potential of Binjai can be developed into a topical preparation that is useful for the treatment and prevention of oxidation-mediated diseases. **Objective:** This study aims to find out the optimum emulgel formula and influence of gelling agents on antioxidant activity of Binjai leaves methanol extract against radical DPPH (2,2-diphenyl-1-picrylhydrazyl). **Materials and Methods:** Binjai leaves were extracted with methanol using the Soxhlet apparatus. The formulation of emulgels using 3 gelling agents (Carbopol, Na-CMC, and tragacanth) with various optimum concentrations. All formulas were carried out by physical stability tests at freeze-thaw condition. Measurement of antioxidant activity was examined by DPPH scavenging method. **Result:** The Binjai leaves methanol extract has very strong antioxidant activity with IC₅₀ = 6.467 ppm. The nine formulas showed that emulgels have stability properties before and after freeze-thaw condition, but according to the hedonic test showed the most favorite formulas are emulgels with gelling agents Carbopol 0.75%, Na-CMC 1%, and tragacanth 2%. Antioxidant activity of the three optimum formulas obtained IC₅₀ value from the most powerful to the less which are emulgels with gelling agents Carbopol 0.75% (21.2895 ppm), tragacanth 2% (23.4529 ppm), and Na-CMC 1% (65.1603 ppm). **Conclusion:** The results of the study show that the formulation affected the activity of Binjai leaves methanol extract which that emulgel with a gelling agent carbopol formula provides the most powerful antioxidant activity.

**Keywords:** Binjai Leaves, emulgel, gelling agent, antioxidant.
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