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REVIEW KARYA ILMIAH: JURNAL ILMIAH

Judul Artikel Ilmiah : **The Effect Of Alpha-Mangostin In Balancing The Ratio Of Cytokines Pro-And Anti-Inflammation-Gamma (Ifn-i3/II-10) And Severity of the Diseases In Mice Infected With Wycobacterium Tuberculosis Multidrug-Resistant**

Nama semua penulis : Dyah Kunthi Nugrahaeni, Suharyo Hadisaputro, **Ari Suwondo**, Edi Dharmana

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- Nama Jurnal : **Asian Journal Of Pharmaceutical and Clinical Research**
- Tahun terbit/Vol/No/halaman : 2016/Volume 8 /Nomor 9, Halaman 273-277
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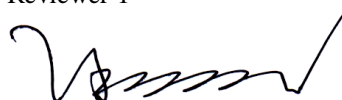
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c	Kecukupan dan kemutakhiran data/informasi dan metodologi (30 %)	12	11
d	Kelengkapan unsur dan kualitas jurnal (30%)	12	11
	Nilai Total	40	37,5
Nilai yang didapat pengusul: $37,5 \times 0,4 = 15 / 3 = 5$			

Catatan Penilaian artikel oleh Reviewer

a	Kelengkapan unsur isi artikel	Kelengkapan isi artikel sudah sesuai dengan pedoman Asian Journal Of Pharmaceutical and Clinical Research
b	Ruang lingkup & kedalaman pembahasan	Tulisan tentang, Alpha-Mangostin berpengaruh terhadap rasio Ifn-i3/II-10 dan mengurangi keparahan TB-MDR dengan menggunakan imunomodulator sudah sesuai dengan scope Asian Journal Of Pharmaceutical and Clinical Research.
c	Kecukupan dan kemutakhiran data/informasi dan metodologi	Metode penelitian cukup lengkap namun dari 32 artikel yang diacu, 5 diantaranya lebih dari 10 tahun terakhir
d	Kelengkapan unsur dan kualitas jurnal	Merupakan jurnal internasional bereputasi dan masih terindex di scopus

Semarang, 22 Maret 2020
 Reviewer 1



Dr. Ir. Mursid Rahardjo, M.Si
 NIP. 196608261997031002
 Unit kerja : Fakultas Kesehatan Masyarakat UNDIP
 Jabatan : Lektor Kepala

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c	Kecukupan dan kemutakhiran data/informasi dan metodologi (30 %)	12	11
d	Kelengkapan unsur dan kualitas jurnal (30%)	12	11
	Nilai Total	40	36,5
	Nilai yang didapat pengusul: $36,5 \times 0,4 = 14,6 / 3 = 4,866$		

Catatan Penilaian artikel oleh Reviewer

a	Kelengkapan unsur isi artikel	Kelengkapan isi baik dan sesuai dengan paduan dari Asian Journal Of Pharmaceutical and Clinical Research yaitu Introduction methods, Results, Discussion, conclusion, references.
b	Ruang lingkup & kedalaman pembahasan	pembahasan artikel cukup baik dengan kesimpulan bahwa Alpha-Mangostin berpengaruh terhadap rasio Cytokines Pro-And Anti-Inflammation-Gamma(Ifn-i3/II-10) dan mengurangi keparahan TB-MDR dengan menggunakan imunomodulator.
c	Kecukupan dan kemutakhiran data/informasi dan metodologi	Metode penelitian sesuai dengan tujuan penelitian dan artikel ini menggunakan referensi yang cukup yaitu 32 karya ilmiah meskipun 5 diantaranya kurang uptodate.
d	Kelengkapan unsur dan kualitas jurnal	Artikel terbit di jurnal masih terindex di scopus Q3 SJR 0,282, editor pada jurnal berasal lebih dari 4 negara.

Semarang, 19 Maret 2020

Reviewer 2



Dr. dr. Suhartono, M.Kes

NIP. 196204141991031002

Unit kerja : Fakultas Kesehatan Masyarakat UNDIP

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Asian Journal of Pharmaceutical and Clinical Research
Volume 9, December 2016, Pages 273-277

The effect of alpha-mangostin in balancing the ratio of cytokines pro-and anti-inflammation-gamma (IFN- γ /IL-10) and severity of the disease in mice infected with Mycobacterium tuberculosis multidrug-resistant (Article) (Open Access)

Nugrahaeni, D.K.^{a,b} , Hadisaputro, S.^a, **Suwondo, A.^a**, Dharmana, E.^a

^aDoktoral Program of Medical and Health Science, Faculty of Medicine, Diponegoro University, Semarang, Central Java, Indonesia

^bPublic Health Study Program, School of Health Sciences Jenderal Achmad Yani, West Java, Indonesia

Abstract

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Objective: The objective of this study was observed to measure the effect of alpha-mangostin in balancing the ratio of interferon-gamma (IFN- γ) and interleukin-10 (IL-10), and the severity of the disease in mice which infected with Mycobacterium tuberculosis multidrug-resistant (TB-MDR). **Method:** Infected BALB/c mice were consisted of five groups: Treated with anti-TB drugs+ α -mangostin, treated with anti-TB drugs, given α -mangostin during treatment, and control group. Cytokine levels of culture supernatant of spleen cells were measured by enzyme-linked immunosorbent assay. The number of bacterial colonies was derived from a primary cell culture of bronchoalveolar lavage. Statistical analysis was performed with Anova, Kruskal-Wallis test and correlation Pearson, and Spearman-rank test. **Result:** Median IFN- γ production was higher in mice, which given with α -mangostin during treatment is 1838.2 pg/ml and control is 1585.5 pg/ml compared treated with anti-TB drugs+ α -mangostin (1312 pg/ml) and anti-TB drugs (1429.3 pg/ml) ($p>0.05$). The highest result production of median IL-10 in the 3th group is (465.91 pg/ml) and the lowest in the control group is 195.29 pg/ml, $p>0.05$. Median IFN- γ /IL-10 ratio of the 3th group very low (3.94), it means the 3th group is experienced with severity of TB. Alpha-mangostin was decreased in severity of disease based on the number of TB-MDR bacterial colonies ($p\leq 0.05$). **Conclusion:** α -mangostin have an effect on the balancing IFN- γ /IL-10 ratio and reduce a severity of TB-MDR with using immunomodulator. © 2016 The Authors. Published by Innovare Academic Sciences Pvt Ltd.

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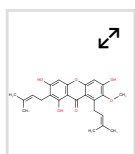
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Chemistry database information

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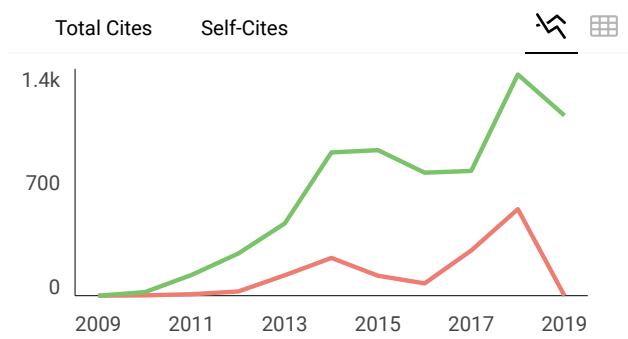
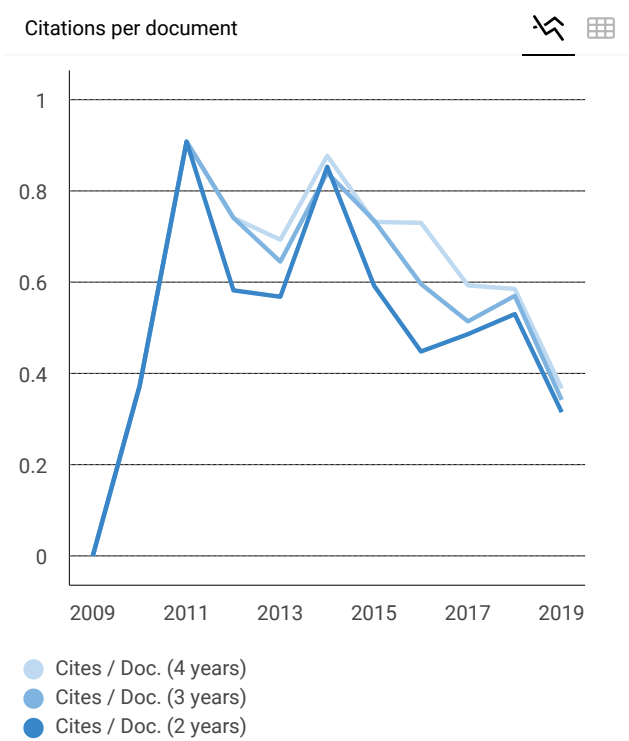
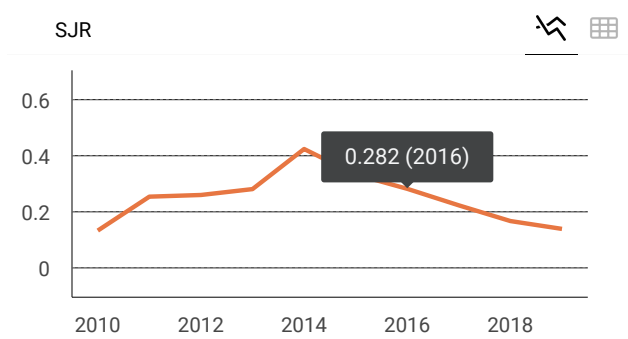
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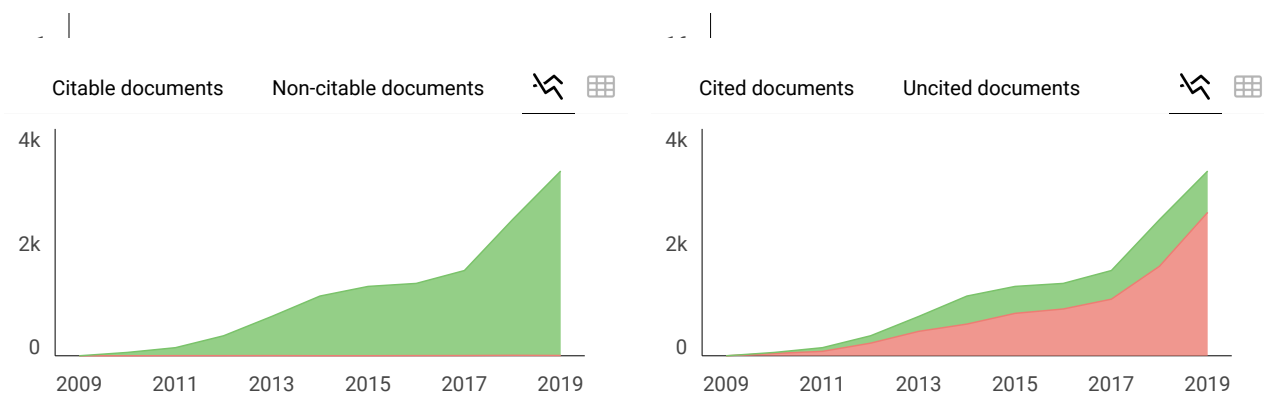
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DIPTI MOHAPATRA, TAPASWINI MISHRA, MANASI BEHERA, PRIYAMBADA PANDA

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DUCTAL CARCINOMA *IN SITU* AND INVASIVE BREAST CANCER-BASED DIFFERENTIAL GENE EXPRESSION STUDY FOR THERAPEUTIC DEVELOPMENT

HARSHITHA GOPISETTY RAMACHANDRA¹, INAMUL HASAN MADAR²,
SEETHALAKSHMI SAKTHIVEL¹, IFTIKHAR ASLAM TAYUBI³, SKM HABEEB^{1*}

¹Department of Bioinformatics, School of Bio-Engineering, SRM University, Chennai - 603 203, Tamil Nadu, India. ²Division of Chemical Engineering & Bio Engineering, Department of Bio Engineering, Hanyang University, Seoul, South Korea. ³Faculty of Computing and Information Technology, King Abdulaziz University, Rabigh-21911, Saudi Arabia. Email: habeeb_skm@yahoo.co.in

Received: 26 July 2016, Revised and Accepted: 27 August 2016

ABSTRACT

Objective: Breast cancer is the second most common cancer in women globally. Multiple inherited mutations in genes are predominantly associated with breast cancer. The gene expression profiling of breast tumors generated by DNA microarray analysis provides molecular phenotyping that determines and characterizes the classifications of these tumors.

Methods: In this work, we used gene expression profiling of breast cancer samples from Gene Expression Omnibus (GEO) database. The dataset GSE41194, retrieved from GEO, was used to investigate differential gene expression in ductal carcinoma *in situ* (DCIS) and invasive breast cancer (IBC). The dataset contains 26 DCIS and 24 IBC samples. The data were analyzed in R and Bioconductor. To normalize the data Robust Multiarray Average (RMA) method was applied, limma software was used to identify the differentially expressed genes (DEGs) in DCIS and IBC; an adjusted p value ≤ 0.05 was used to filter differentially expressed probe sets, and a fold change (FC) ≥ 2 to identify upregulated and ≤ -2 for downregulated genes. The DEGs retrieved were clustered and annotated using Database for Annotation, Visualization and Integrated Discovery (DAVID) Bioinformatics Resources with an EASE score ≤ 0.1 and count 2.

Results: The analysis obtained 72 DEGs with a $p \leq 0.05$. The $FC \geq 2$ identified 38 upregulated probesets and $FC \leq -2$ identified 34 downregulated probe sets. The up and downregulated genes obtained in various comparisons were characterized based on gene ontology (GO) and pathway analyses in DAVID, which retrieved six genes that had principal pathways targeting breast cancer.

Conclusion: Identification of these genes and pathways enhances the knowledge and progression of DCIS to IBC; paving a novel way for developing new therapies for treating patients with breast cancer.

Keywords: Molecular phenotyping, Gene Expression, Ductal carcinoma *in situ*, Invasive breast cancer.

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INTRODUCTION

Breast cancer is the most commonly diagnosed malignancy among females. While decrease in both, breast cancer incidence and mortality, have been apparent in recent years, the societal and economic impact of this malignancy continues to be enormous [1]. The cases of incidence were 1.8 million in 2013 and 464 thousand deaths approximately [2]. Nearly, 30% of all cancers in women occur in breast both in the developed and the developing world [3]. The genetic abnormalities such as variations in high-penetrance genes play a major role in about 90% of breast cancer cases. Several risk factors for breast cancer have been identified. Some mutations particularly in *BRCA1*, *BRCA2*, *p53*, *PTEN*, *ATM*, *NBS1*, and *LKB1* result in a very high risk for breast cancer [4].

Breast cancers are of two different types, invasive and non-invasive. Invasive cancers spread to other tissues in the breast from the milk ducts, whereas the non-invasive cancers do not invade other tissues in the breast. The non-invasive breast tumors are referred to as "*in situ*." These are classified as ductal carcinoma *in situ* (DCIS) or intraductal carcinoma and lobular carcinoma *in situ* [4].

DCIS is characterized by malignant epithelial cells confined to the ductal system of the breast, without evidence of invasion through the basement membrane into the surrounding stroma [5]. Once thought to be a rare breast lesion, DCIS now constitutes 20% of all newly diagnosed breast cancer cases (<http://seer.cancer.gov>, Accessed October 2013; <http://www.cancer.org>, Accessed June 1, 2012). Invasive breast cancer (IBC) starts in a milk duct of the breast, breaks through

the wall of the duct and grows into the fatty tissue of the breast. At this point, it may be able to spread (metastasize) to other parts of the body through the lymphatic system and bloodstream [5]. Invasive breast carcinoma constitutes 70-85% of the incidence; the remaining 15-30% are *in situ* carcinomas, 80% of which are DCIS (<http://www.cancer.org>, Accessed June 1, 2012).

The factors that stimulate the breast cancer risk include gender, age, family history and additionally alcohol intake, dietary fat, obesity in postmenopausal age, and hormonal stimulations. These factors are said to have increased the progression of breast cancer along with the individual factors almost half a century. The dramatic increase in breast cancer research and its prevention has shown positivist approach in the current years [6].

With the advent of microarray technology, the procedure to measure gene expression on a genome-wide scale has transformed cancer biology by providing the tools to measure differences in diseases [7]. This technology utilizes differential gene expression patterns in cancer cells and normal cells or those of other subtypes of cancer to identify the genes that are over-expressed and under-expressed [8]. However, the analysis produces a large amount of data, which is challenging to interpret. With the employment of modern computational and statistical analysis packages and bioinformatics tools, the data analysis has been greatly flexible in the recent years. The microarray technology has been applied to a range of applications, including discovering novel disease subtypes, developing new diagnostic tools, and identifying underlying mechanisms of disease or drug response [9].

LACTOBACILLUS-FERMENTED PLANT JUICE AS A POTENTIAL INGREDIENT IN COSMETICS: FORMULATION AND ASSESSMENT OF NATURAL MOUTHWASH

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ABSTRACT

Objective: Oral care cosmetics are essential for all populations and are systematically used to treat oral problems. The chemicals free natural cosmetics are the choice of many people. Thus, this study was aimed to formulate and to assess the natural mouthwash (MW) solution from *Lactobacillus*-fermented Thai medicinal plants juice.

Methods: The selected (betel, green tea, clove, black galingale, mangosteen, and noni) plant juices were subjected to *Lactobacillus plantarum* mediated fermentation. The fermented plant juices (FPJ) were formulated into MW solution with different concentrations of peppermint oil. MW formulations were assessed for physical appearance, stability, and anti-microbial activities.

Results: About 2% of peppermint oil in FPJ was found as organoleptically optimum. The pH and refractive indexes of the MWs were not affected during storage and stability assessments. All the FPJ-MWs formulations showed antimicrobial activity against Group A *Staphylococcus*, and other oral pathogens - *Escherichia coli*, *Streptococcus aureus*, and *Pseudomonas aeruginosa*. Moreover, black galingale, mangosteen, and noni based MW formulas also exhibited anti-candida activity. The MW made from fermented black galingale (*Kaempferia parviflora*) juice was the most potent antimicrobial formulation with excellent physical stability.

Conclusion: The study concluded that fermented plant-herbal juices can be used as natural MW recipe with 2% of peppermint oil to improve the flavor and aroma. The formulations were stable, free of microbial contamination, and also exhibited antimicrobial activity. Further extended stability study and clinical trials are necessary to develop a commercial FPJ-based natural MW recipe.

Keywords: Fermentation, Formulation, *Lactobacillus*, Mouthwash.

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INTRODUCTION

Oral care cosmetics are essential for all populations and are systematically used to treat oral malodor, prevent tooth decay, and for general sanitation purposes. There are many oral care preparations among that toothpaste and mouthwashes (MWs) are most popular. The healthcare market for health care reaches about \$ 4.1 billion and the significant share (73.4%) from toothpaste and toothbrushes marketing worldwide [1]. Several kinds of natural toothpaste formula and the products are available, whereas very few natural MW formulas are existing.

In general, MW is made out of any active compounds, surfactants, flavor, preservatives, and water [2]. The botanical extracts (*Camellia* spp., *Piper betel*), essential oils, antibacterials (chlorhexidine, triclosan and cetylpyridinium chloride, fluoride, salts of zinc), and phytochemicals are used as active principles in MW [3]. Some of the MW preparations contain alcohol to its freshness, but many companies claim that their products are alcohol-free and safe for alcohol-sensitive customers. The medicated MW products, which contain chlorhexidine and its salt, are commonly used and prescribed by several dentists. Even though chlorhexidine is considerably safe and efficient, it causes some adverse effects like discoloration of the teeth, desquamation of oral mucosa, taste alteration, burning sensation at oral mucosa and it even affects fibroblast and keratinocyte cell proliferation, which leads to impairment in wound healing [4]. The opposing effects of chemically formulated MW urge the researchers to work on natural products.

In Thailand, several native plants have been traditionally used as mouth sanitizer and oral medicine. Based on the usage and popularity among

Thai people, we have selected six plants for the study such as betel (*P. betel* L.), green tea (*Camellia sinensis* [L.] Kuntze), clove (*Syzygium aromaticum* [L.] Merrill and Perry), black galingale (*Kaempferia parviflora* Wallich. ex Baker.), mangosteen (*Garcinia mangostana* L.), and noni (*Morinda citrifolia* L.).

Betel (*P. betel* L.) is commonly used as chewing mouth freshener and used in Thai cooking (e.g. Miang-Khum Bai Chaplu). The ethanolic extract of betel leaf has antioxidant, analgesic, antibacterial, and anti-inflammatory activity [5,6].

Green tea is obtained from the leaf of *C. sinensis* (L.) Kuntze. It is one of the most popular healthy herbal beverages in the world. Catechins are the most abundant active ingredient present in green tea, possessing many biological activities including antimicrobial activity [7,8].

Clove (*S. aromaticum* [L.] Merrill and Perry) is one of the traditional herbs used by Thai people for dental pain. Clove oil is also used in dentistry procedures as a disinfectant. It was reported that methanolic extract and flavones of clove are active against periodontal pathogens and also have anti-inflammatory, antioxidant properties [9-11].

Black galingale (*K. parviflora* Wallich. ex Baker.) is used as a tonic to treat gastrointestinal problems, leucorrhea, and oral diseases in Thai folk medicine. Black galingale extracts exhibit anti-inflammatory effects [12].

Mangosteen (*G. mangostana* L.) is a famous tropical plant and called "queen of fruit." It is known for antimicrobial, antioxidant, antibacterial, anti-HIV, cytotoxic, anti-inflammatory, and anti-histamine activities [13].