

ANTIOXIDANT AND ANTI-INFLAMMATORY EFFECT OF *Morinda citrifolia*: A META-ANALYSIS AND SYSTEMATIC REVIEW

Ervina Vashti¹, Bernard Christoper Fernando Oen², Eric Ricardo Yonatan²,
Venna Bella Sabatina², Sherlyn Sean², Elisabeth Rukmini^{3*}

¹Department of Pharmacy, ²Medical Profession Study Program, School of Medicine & Health Sciences, Atma Jaya Catholic University of Indonesia, Jl. Pluit Raya 2, Jakarta, 14440

³Food Technology Department, Faculty of Engineering, Bina Nusantara University, Jakarta, Indonesia 11480

* Corresponding Author: elisabeth.rukmini@binus.ac.id

Submitted : May 6th, 2021

Revised : April 22nd, 2022

Accepted : June 3rd, 2022

Copyright © 2022 Universitas Pakuan



FITOFARMAKA: Jurnal Ilmiah Farmasi is licensed under a
Creative Commons Attribution-ShareAlike 4.0 International License

ABSTRACT

Morinda citrifolia (noni) is a tropical plant from the Rubiaceae family, which contains various active components that have several functions in medical fields that can act as an antioxidant and anti-inflammatory. To assess both effects, we conducted a systematic review and meta-analysis, with the PRISMA statement guidelines, to discuss the efficacy of *Morinda citrifolia* as an antioxidant and anti-inflammatory. The literature search was performed by searching through 12 databases: Sage Journals, ScienceDirect, Garuda, ProQuest, PubMed, Google Scholar, Web of Science, Taylor and Francis, Wiley Online Library, Cochrane Library, EBSCO, and SINTA from 2000 to 2020. From 4.605 identified record journals, we found six journals which were included in our study analysis. Our analysis showed that *Morinda citrifolia* has a moderate positive effect as antioxidant and anti-inflammatory agents, with an overall effect size of correlation 0.46 (CI 95% was 0.37-0.54). This study proves the potential of *Morinda citrifolia* as an alternative herbal medicine. Future research and studies are expected on *Morinda citrifolia* to investigate its further potential.

Keywords: *Morinda citrifolia*; noni, antioxidant; anti-inflammatory; systematic review; meta-analysis

INTRODUCTION

Morinda citrifolia or known as noni, is commonly used by the community for traditional medicinal purposes. *Morinda citrifolia* is a plant from the Rubiaceae family that grows in Polynesia and is included in tropical plants (Coutinho de Sousa et al., 2017). There are various parts of the plant that are used for medicinal purposes, such as roots, leaves, stems, or fruit. Noni has been commercialized

globally since 1996 and fruit juice is the predominant formulation to consume (Yilmazer et al., 2016).

Several potential benefits from noni have been researched, including antioxidant, anti-inflammatory, blood lipid normalization, immunomodulatory, and antiglycation (West et al., 2018). Noni has shown antioxidant activities by lowering free radicals concentration on plasma, thus reducing oxidative damage of

DNA (Wang et al., 2013). As an anti-inflammatory agent, there is some evidence that several bioactive compounds in noni modulate the cytokines, enzymes, transcription factors, and production of inflammatory mediators (Coutinho de Sousa et al., 2017). Although there are many studies that have shown noni benefits as an antioxidant (Ruhomally et al., 2016) and anti-inflammatory agent (Ali et al., 2016; Coutinho de Sousa et al., 2017), there has been no clear, deeper, and specific discussion of its total effect.

An in vivo study evaluated the beneficial effect of noni on the antioxidant effect of N-Methyl-N-Nitrosourea (NMU) which induces mammary carcinogenesis in mice. From the results of these studies, the effect of noni increases the concentration of antioxidant enzymes, such as superoxide dismutase (SOD) and catalase. In addition, the results also indicated that lipid peroxidation decreased from the NMU control group (Saminathan et al., 2014).

A nine-days in vivo studies on mice with DSS-induced (dextran sulfate sodium) colitis showed significant anti-inflammatory activities. The analysis showed a significant reduction of nitric oxide (NO) and myeloperoxidase activities in mice treated with noni fruit juice. Inflammatory cytokines including TNF- α , INF- γ , and IL-17 also significantly reduced in mice treated with noni fruit juice (Fikri, 2015). However, there are also some studies that shown antioxidant activities of noni as weaker than approved pharmacological intervention. In a study, noni was tested for its antioxidant activity using the DPPH (1,1-diphenyl-2-picrylhydrazil) method using quercetin as a comparison. The results showed that noni had an IC₅₀ value < 50 μ g/mL which means it has strong antioxidant activity. Unfortunately, the

antioxidant effect of noni is still not better than quercetin (Rahmawati et al., 2015).

There is also a study that shows limited noni effect as anti-inflammatory compared with pharmacological intervention. Lipid transfer protein 1 extracted from noni seeds has shown significant results in reducing the edema volume induced by carrageenan compared with the control group. However, the result is still lacking behind dexamethasone, one of the popular anti-inflammatory drugs (Campos et al., 2017).

Questions regarding the effect of *Morinda citrifolia* as an antioxidant and anti-inflammatory agent would be deemed to be answered. Does *Morinda citrifolia* have a significant effect as an antioxidant and anti-inflammatory? A meta-analysis and systematic review of *Morinda citrifolia* as an antioxidant and anti-inflammatory agent would be critical.

Based on the reason mentioned above and concerning the biological and pharmacological activities of noni, this study aims to determine the effect size of positive or negative correlation of *Morinda citrifolia* as an antioxidant and anti-inflammatory agent. Also, we would like to find if the result is significant or insignificant.

METHODS

Search Strategy

The systematic review and meta-analysis was conducted with Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement guideline.

We did a comprehensive searching from databases, such as the Sage Journals, ScienceDirect, Garuda, Proquest, Pubmed, Google Scholar, Web of Science, Taylor and Francis, Wiley Online Library, Cochrane Library, EBSCO, and SINTA from 2000 to 2020. In this case, the inclusion criteria were articles featuring empirical studies that involve direct

observations and experiments of *Morinda citrifolia* on antioxidant and anti-inflammatory effects. Inclusion criteria also include articles with quantitative values such as the SD value and the mean or correlative coefficient (for meta-analysis studies). The keywords used include "Morinda citrifolia" OR "noni juice" OR "noni fruit" OR "noni extract" AND "antioxidant" OR "anti-inflammation" OR "immune system." Unpublished studies are taken from Atma Lib, Open Grey, and Academia.edu databases but do not have the relevant articles for this study. To remove duplicates, we used Zotero--a bibliographic management software. The PRISMA flowchart was presented in Figure 1.

Inclusion and Exclusion Criteria

The inclusion criteria were: 1) Literature in English or Indonesian language; 2) Literature published or written between 2000-2020; 3) Experimental studies; and 4) The writer(s) mentioned mean and SD in the literature. We excluded articles for the following reasons: 1) the articles were review studies; 2) They were in vitro studies; 3) Studies involving human subjects; and 4) Missing mean or SD in the literature.

Data Extraction and Analysis

A team of five students and one faculty member conducted this meta-analysis and systematic review. In the meta-analysis section, we collected and selected quantitative data such as the mean and SD values or articles with the correlation coefficient (r-value) between *Morinda citrifolia* and its antioxidants anti-inflammatory agents.

Data analysis software used to do quantitative meta-analysis is JASP

0.14.0.0. I² value indicates the heterogeneity across the studies. If the I² value is high, the study's data are heterogeneous. Thus, a random effect model will be used. The method used to do simple random effect analysis is restricted maximum likelihood (Restricted ML). The overall effect size as a point estimate needed a confidence interval (CI) of 95%. If p values less than 0.05, the studies were considered statistically significant. To describe individual and combined effect sizes with the standard error, we analyze the forest plot. Furthermore, the detection of publication bias will utilize a funnel plot. Additionally, a trim-and-fill analysis is conducted to detect the missing studies.

RESULTS AND DISCUSSION

Results

From the results of literature searching, we assessed 242 articles found for their eligibility. There were 236 articles excluded based on the inclusion and exclusion criteria. The exclusion because they were in vitro studies, had no mean and SD values, reviewed articles, failed to retrieve the articles, and used human subjects. Therefore, after the exclusion, we found six articles in qualitative and quantitative synthesis. Overall, the articles showed that *Morinda citrifolia* has antioxidant and anti-inflammatory effects.

Characteristics

Table 1 provided the data abstraction from the six articles. Each article produced some coded studies that enriched the effect size of antioxidant and anti-inflammatory of *Morinda citrifolia*. Total coded studies were 37 studies for the meta-analysis.

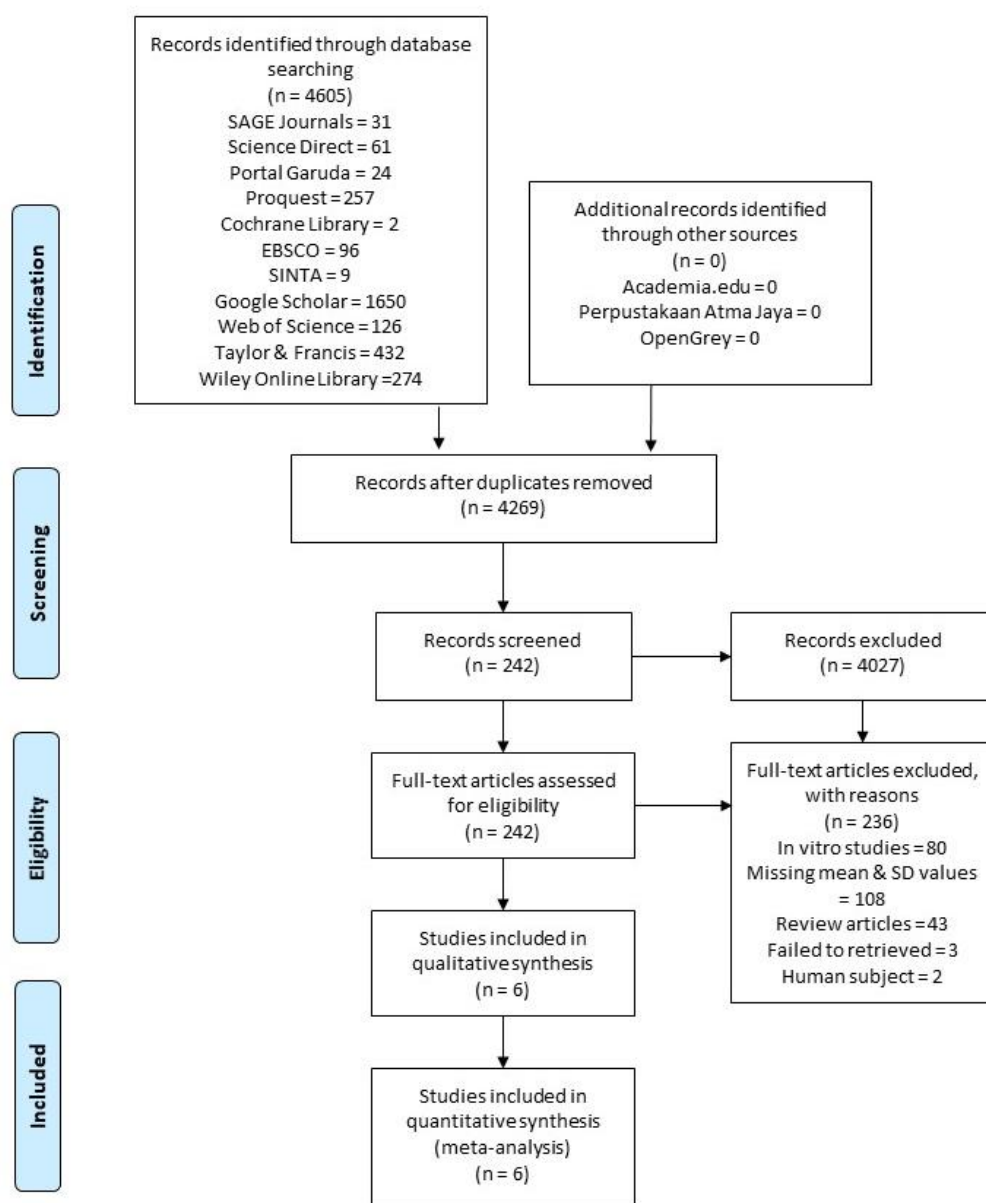


Figure 1. PRISMA

(www.prisma-statement.org/PRISMAStatement/FlowDiagram.aspx (prisma-statement.org) Flowchart of the meta-analysis and systematic review

Table 1. Data Abstraction

Ref	Author, year	Treatment	Outcome	Coded Study (N)
[1]	Shalan, et al. (2016)	Oven-dried <i>Morinda citrifolia</i> leaves (60°C; 24 hours) were ground and extracted by boiling in distilled water for 3 hours (1:10, w/v). Then, the suspensions produced will be filtered and evaporated (60°C) to dryness (200 mg MCL/kg Group).	Noni successfully increases the number of GSH concentrations compared to negative control without exercise groups.	1a-1i (9)
[2]	Syarifah, et al (2019)	Inflammation agent 0,1 ml croton oil 4% was given and then smeared with 5% Noni extract peel off mask	Noni extract peel off mask successfully reduce the expression of COX-2 compared to the control group with significant difference (p<0,05).	2a-2b (2)
[3]	Fikri (2015)	Noni juice (0.81 ml/25g BW) was given orally for 3 days. Mice then wounded and the neutrophil counted every 12 hrs.	Noni successfully reduced neutrophil count 12-hour after being wounded.	3a-3c (3)
[4]	Ma, et al. (2013)	Investigate the role of DAA using Wistar rats and various concentration of DAA: 15, 30, or 60mg/kg body weight per day for 7 days. Serum MDA, SOD and GSH activities were measured and compared among groups.	DAA in noni fruit successfully reduced serum MDA concentration, DAA in noni fruit increased serum SOD activity, DAA intake in noni fruit were not influence GPx activity	4a-4f (6)
[5]	Kustarini, et al. (2012)	Noni ethanol extract in various concentration: 10, 20, 40, 80 mg/dl were evaluated in induced-diabetic rats.	Noni successfully increase neutrophil in diabetic rat	5a-5d (4)
[6]	Mahadeva-Rao, et al. (2017)	Control group was fed with HCD for 45 days. Experimental group was fed with HCD for 45 days + AEFM (300 mg/kg, orally) for the last 30 days.	Noni significantly increases renal antioxidant enzyme in hypercholesterolemic rats.	6a-6m (13)

Note: AEFM alcoholic extract of *Morinda citrifolia* fruit, CAT catalase, DAA deacetylasperuloside acid, FRSA free radical scavenging activities, GPx glutathione peroxidase, GSH glutathione, GST glutathione S-transferase, HCD hypercholesterolemic diet, LSD least significant difference, MDA malondialdehyde, SOD superoxide dismutase, SD *Sprague dawley*, WR Wistar

We used JASP v 0.14.0.0 to perform meta-analysis. The results showed an overall effect size of 0.46 (CI 95% was

0.37-0.54). The p-value of the effect size was $p < 0.001$, which indicated the results of the studies were statistically significant.

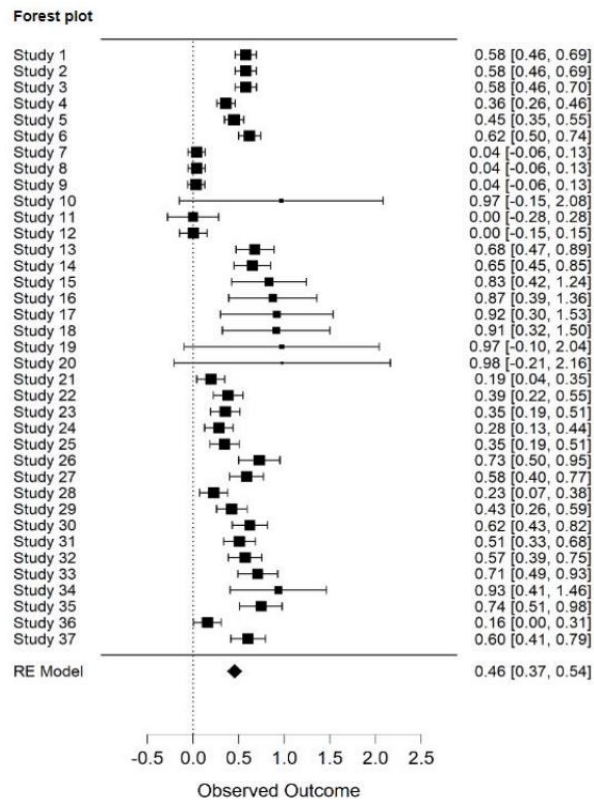


Figure 2. Forest Plot

The overall effect size showed a moderate effect (0.46, CI 95% ranged from 0.37 to 0.54). The forest plot (Figure 2) summarized this value. There were no negative or reversed effects of antioxidant and anti-inflammatory effects of *Morinda citrifolia*. The results indicated heterogeneity of studies with the I² value

of 89.261%. The tip of the overall effect diamond was not intersecting with the line of no effect. Therefore, the overall effect size was significant ($p < 0.001$). The effect size showed a moderate correlation of *Morinda citrifolia* as antioxidant and anti-inflammatory agents.

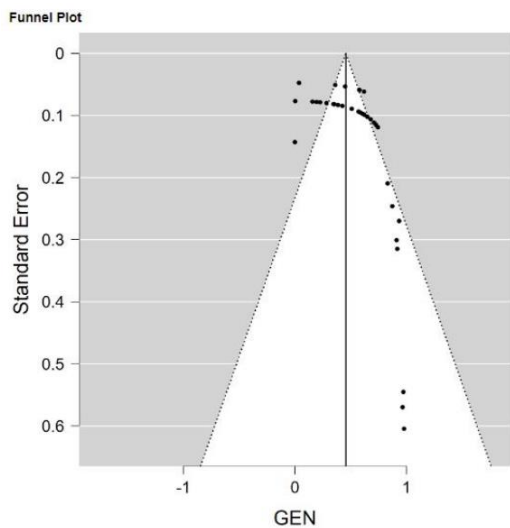


Figure 3. Funnel Plot

To further investigate any publication bias, we analyzed the funnel plot resulted from the JASP program. Unfortunately, the funnel plot (Figure 3) showed an asymmetrical funnel that deviates to the positive side, indicating a potential publication bias. A publication bias might occur due to language restrictions, which we only used Indonesian and English studies. Another reason was that some studies showed preliminary analysis.

We found a study with potential flaws in the results, which might affect the analysis's quality. The study by Syarifah, Sugihartini, and Nurani (2019) showed a questionable result, with a low mean value (22.63) but an unusually high SD value (2,218.73). We believed that the data might be widely scattered, resulting in an unusual number compared to other results or studies.

We run the JASP program to show the analysis of trim-and-fill. The result of the analysis with the trim-and-fill method showed that some missing studies were in needs to balance the plot represented in white dots. There were seven white dots suggested from the analysis as

publications that needed to eliminate the bias. We have searched from both published dan unpublished studies comprehensively from various search engines. Looking up unpublished articles were a big challenge in this study. This analysis showed that there might be a scarcity of experimental studies using *Morinda citrifolia* as the variables. The fact that only six published articles in this meta-analysis also revealed the lack of thorough experimental studies about *Morinda citrifolia*. The trim-and-fill analysis from the JASP showed that despite the analysis results if the missing studies were all filled up, the overall size effect will only be reduced slightly to 0.42. This reduction was not far different from the previous overall size effect (0.46). However, these missing studies still need to understand the other effect that might appear from noni utilization. We believe these missing studies indicated future potential studies about *Morinda citrifolia* effect, especially as antioxidant and anti-inflammatory. We expect the future study to provide complete results along with the table and graphs.

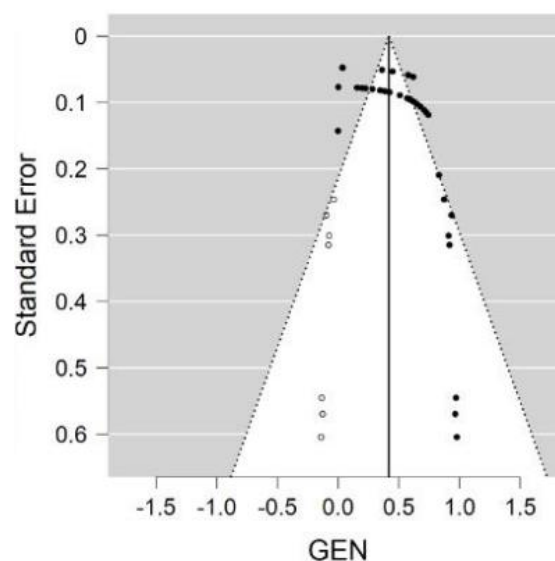


Figure 4. Trim-and-Fill Analysis

Discussion

Based on the result, we analysed the effect of Noni as an antioxidant and anti-inflammatory, and it showed a moderate effect, with an overall correlation effect size of 0.46 (CI 95% was 0.37-0.54). From the six articles being included, we found that the study conducted by Fikri (2015) showed the most significant effect of *Morinda citrifolia* as anti-inflammatory compared to other studies. Meanwhile, the study conducted by Rao and Sundaram (2017) shows the most significant effect of *Morinda citrifolia* as an antioxidant. The differences between studies including (1) the use of mice and rat as the experimental subject, (2) parts of *Morinda citrifolia* plant chosen for the studies, such as leaves and fruits, (3) Noni preparation such as extract and juice, (4) the duration of the experiment, (5) the analyzed organs, (6) the tests used to analyze the anti-inflammatory and antioxidant effect of *Morinda citrifolia*, and (7) the dose used for treatment. The test for the anti-inflammatory effect used reduces COX-2 (Syarifah et al., 2019) and reduces neutrophil count (Fikri, 2015; Kustarini & Dewi, 2012). The test used for antioxidants is the reduction of MDA (Ma et al., 2013; Shalan et al., 2016) and increase amount of SOD and GPx (Ma et al., 2013). The study by Rao (2017) draws the interest of authors by using the various test to find the antioxidant effect of noni. The test used in this study showed an increment in antioxidant enzymes (SOD, CAT, GPx, GR, and GST), increase in antioxidant non-enzymes (GSH, Vitamin C, and Vitamin E), reduction in LPO (TBARS, hydroperoxide), and reduction in serum renal markers (urea, creatinine, uric acid).

The analysis results from Fikri (2015) on scratch-wounded mice showed that Noni significantly reduced the neutrophil count on inflammation. Both mice in the control and experimental

groups were scratch-wounded and had their neutrophils counted on 12, 24, 36, 48, 60, and 72-h after being wounded. Before being wounded, mice from the experimental groups were fed with Noni juice (0.81 ml/25g BW, orally) for three days. LSD test was used to analyze the difference between the neutrophil count from control and experimental groups. The results showed that the neutrophil count was significantly reduced in experimental groups compared to the control group. Noni's potential anti-inflammatory and anti-microbial activities lessen the neutrophil reactions on the wound lesion. Less neutrophil on wound lesions was associated with faster recovery and reduction of the bothersome inflammatory effect (Fikri, 2015).

The study conducted by Rao and Sundaram (2017) shows the AEFM effect on renal antioxidant enzymes (SOD, CAT, GPx, GR, and GST) and non-enzymes (GSH, Vitamin C, and Vitamin E). All the enzyme activities were lowered ($p < 0.01$) on the HCP-only diet group than the normal diet group. After being fed with AEFM (300 mg/kg, orally) for the last 30 days, all the enzyme activities were considerably increased ($p < 0.01$) compared to the HCD-only group. Not only increased, but the enzyme activities were also significantly reverted ($p < 0.01$) near to the normal state compared to the normal diet group. An increase in antioxidant enzyme activities could prevent cholesterol-induced renal damage in hypercholesterolemic rats. Furthermore, there was a significant reduction in LPO (TBARS, hydroperoxide) and serum renal markers (urea, creatinine, uric acid). This shows the protective effect of noni against free radicals on renal, thus preserving renal function compared to the control group.

The results from Syarifah et al. (2019) showed groups that had given the intervention with an inflammatory agent

with three different amounts of Noni extract in the peel-off mask given to each group of mice significantly reduced the expression of COX-2 with the p-value <0.05 . The group with 5% of Noni extract showed COX-2 expressions 22.63 ± 2218.73 , the group with 10% showed 18.99 ± 5.04 , and the group with 15% showed 20.31 ± 4.35 . All of them showed lower COX-2 expressions compared to the control group (30.52 ± 7.23). The results showed that Noni extract has an anti-inflammatory effect by reducing COX-2 expression.

Ma et al. (2013) showed that the administration of DAA doses of 15, 30, and 60 mg/kg on serum MDA levels had a decreased effect compared to the control group, which was not given the DAA dose. It can also be seen that the increased dose of DAA results in decreased MDA levels. It was stated that the percentage decrease that occurred in the mean serum MDA level for the moderate and high doses was 19.7% and 22.6%, respectively. Furthermore, if we look at the levels of SOD (superoxide dismutase), it tends to increase with the provision of DAA doses. The low DAA doses indicated that the SOD level tended to be 10% greater than the control group value but showed a p-value of 0.098. For SOD levels at moderate and high DAA doses, both showed significantly greater values than the control group with p-values of <0.05 and <0.01 , respectively. Furthermore, looking at the results of GPx (glutathione peroxidase) activity data tends to give insignificant results, or it can be said that the DAA doses, both low, moderate, and high doses, do not affect GPx activity.

The effect of Noni ethanol extract against the neutrophil count by Kustarini and Dewi (2012) shows the increase of neutrophil count with the p-value = 0.547. The control group had the neutrophil count of 2.85 ± 1.39 , and it increases in group 2, which receives the 20 mg/dl/day of noni

extract, with the neutrophil count of 3.31 ± 0.88 . The highest increase is in group 3, which receives 40 mg/dl/day of noni extract and has a neutrophil count of 4.56 ± 2.89 . While group 4, which receives 80 mg/dl/day of noni extract, had a decrease in neutrophil count than group 3, with the neutrophil count of 4.16 ± 2.81 . The increase of neutrophil count in diabetic disease is good as diabetes can cause a decrease in neutrophil activity.

The result of the study performed by Shalan et al. (2016); regarding the use of *Morinda citrifolia* as an antioxidant by measuring GSH level on blood plasma, skeletal muscle, and liver showed contradictory results between the 200 mg MCL/kg group and 400 mg MCL/kg group. GSH is a non-enzymatic antioxidant which plays a role in preventing cytotoxicity due to ROS. The results show that the 200 mg MCL/kg group had a blood plasma GSH concentration of $8.9 \pm 0.9 \mu\text{M}$, which were two times higher than the control group with exercise ($3.9 \pm 0.3 \mu\text{M}$). However, the 400 mg MCL/kg group showed lower blood plasma GSH concentrations of $3.9 \pm 0.3 \mu\text{M}$. This may be due to the optimal dose for MCL use, which is at a dose of around 200 mg/kg, while 400 mg/kg is accounted as excessive. The results of the GSH level on skeletal muscle and liver tissue were insignificant (2016).

CONCLUSIONS

This study proved that there is a positive correlation between *Morinda citrifolia* as an antioxidant and anti-inflammatory agent. We conducted a meta-analysis from six articles that comprised thirty-seven coded studies. The correlation showed a moderate effect, with an overall effect size of 0.46 (CI 95% was 0.37-0.54). Further analysis of trim-and-fill analysis (Figure 4) showed potential publication bias. This study may further enrich by additional coded studies that

have a negative correlation. Future studies on *Morinda citrifolia* would enhance the effect and function of this important plant.

ACKNOWLEDGEMENT

The authors acknowledge the Dean of the School of Medicine & Health Sciences for providing a free training fee on meta-analysis and systematic review.

BIBLIOGRAPHY

- Ali, M., Kenganora, M., & Manjula, S. N. (2016). Health benefits of *Morinda citrifolia* (Noni): A review. *Pharmacognosy Journal*, 8(4), 321-334.
<http://dx.doi.org/10.5530/pj.2016.4.4>
- Campos, D. C., Costa, A. S., Luz, P. B., Soares, P. M., Alencar, N. M., & Oliveira, H. D. (2017). *Morinda citrifolia* Lipid Transfer Protein 1 Exhibits Anti-Inflammatory Activity by Modulation of Pro- and Anti-inflammatory Cytokines. *International Journal of Biological Macromolecules*, 103, 1121-1129.
<http://dx.doi.org/10.1016/j.ijbiomac.2017.05.148>
- Coutinho de Sousa, B., Reis Machado, J., da Silva, M. V., da Costa, T. A., Lazo-Chica, J. E., Degasper, T. do P., Rodrigues Junior, V., Sales-Campos, H., Uber Bucek, E., & Freire Oliveira, C. J. (2017). *Morinda citrifolia* (Noni) Fruit Juice Reduces Inflammatory Cytokines Expression and Contributes to the Maintenance of Intestinal Mucosal Integrity in DSS Experimental Colitis. *Mediators of Inflammation; Hindawi*.
<https://doi.org/10.1155/2017/6567432>
- Fikri, K. (2015). Potensi Buah Mengkudu (*Morinda citrifolia* L.) Sebagai Anti Radang pada Luka Gores Mencit Jantan (*Morinda citrifolia* L. Fruit Potency as Anti Inflammatory in Male Mice Scratch). *Saintifika*, 17(1).
- Kustarini, I., & Dewi, S. S. (2012). Efek Ekstrak Etanol *Morinda Citrifolia* L (Mengkudu) Terhadap Kadar Gula Darah, Jumlah Neutrofil, dan Fibronektin Glomerulus Tikus Diabetes Mellitus. *Media Medika Indonesiana*, 46(3), 178-183.
- Ma, D.L., Chen, M., Su, C. X., & West, B. J. (2013). In Vivo Antioxidant Activity of Deacetylasperulosidic Acid in Noni. *Journal of Analytical Methods in Chemistry; Hindawi*.
<https://doi.org/10.1155/2013/804504>
- Rahmawati, R., Muflihunna, A., & Sarif, L. M. (2015). Analisis Aktivitas Antioksidan Produk Sirup Buah Mengkudu (*Morinda citrifolia* L.) dengan Metode DPPH. *Jurnal Fitofarmaka Indonesia*, 2(2), 97-101.
<http://dx.doi.org/10.33096/jffi.v2i2.177>
- Rao, U. M., & Sundaram, C. S. (2017). Antihypercholesterolemic, Antioxidant and Renal Protective Effects of Mengkudu (Rubiaceae) Fruit in Nephropathy-induced Albino Rats. *Chinese Journal of Integrative Medicine*, 1-8.
<https://doi.org/10.1007/s11655-017-2785-1>
- Ruhomally, Z., Somanah, J., Baborun, T., & Neergheen-Bhujun, V. S. (2016). *Morinda citrifolia* L. Fruit Extracts Modulates H₂O₂-induced Oxidative Stress in Human Liposarcoma SW872 Cells. *Journal of Traditional and Complementary Medicine*, 6(3), 299-304.
<https://doi.org/10.1016/j.jtcme.2015.09.003>
- Saminathan, M., Rai, R. B., Dhama, K., Jangir, B. L., Suresh, S., Ranganath, G. J., Sophia, I., Karuppanasamy, K., Barathiraja, S., & Gopalakrishnan, A. (2014). Effect of

- Morinda citrifolia* (Noni) Fruit Juice on Antioxidant, Hematological and Biochemical Parameters in N-Methyl-N-Nitrosourea (NMU) Induced Mammary Carcinogenesis in Sprague-Dawley Rats. *International Journal of Pharmacology*, 10(2), 109–119. <https://dx.doi.org/10.3923/ijp.2014.109.119>
- Shalan, N. A. A. M., Mustapha, N. M., & Mohamed, S. (2016). *Morinda citrifolia* Leaf Enhanced Performance by Improving Angiogenesis, Mitochondrial Biogenesis, Antioxidant, Anti-inflammatory & Stress Responses. *Food Chemistry*, 212, 443–452. <https://doi.org/10.1016/j.foodchem.2016.05.179>
- Syarifah, M., Sugihartini, N., & Nurani, L. H. (2019). Formulasi dan Uji Anti Inflamasi Masker Peel Off Ekstrak Etanol Buah Mengkudu (*Morinda citrifolia* L.). *Jurnal Ilmu Kefarmasian Indonesia*, 17(2), 175–182.
- <http://dx.doi.org/10.35814/jifi.v17i2.564>
- Wang, M.-Y., Peng, L., Jensen, C. J., Deng, S., & West, B. J. (2013). Noni Juice Reduces Lipid Peroxidation–derived DNA Adducts in Heavy Smokers. *Food Science & Nutrition*, 1(2), 141–149. <https://doi.org/10.1002/fsn3.21>
- West, B. J., Deng, S., Isami, F., Uwaya, A., & Jensen, C. J. (2018). The Potential Health Benefits of Noni Juice: A Review of Human Intervention Studies. *Foods*, 7(4), 58. <https://doi.org/10.3390/foods7040058>
- Yilmazer, N., Coskun, C., Gurel-Gurevin, E., Yaylim, I., Eraltan, E. H., & Ikitimur-Armutak, E. I. (2016). Antioxidant and Anti-inflammatory Activities of a Commercial Noni Juice Revealed by Carrageenan-induced Paw Edema. *Polish Journal of Veterinary Sciences*, 19(3), 589–595. <http://dx.doi.org/10.1515/pjvs-2016-0074>