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Original Article

In vitro Immunomodulatory Effect of Lawsone Methyl Ether on Innate Immune Response of Human Phagocytes

Abdi Wira Septama[1]*, Pharkphoom Panichayupakaranant[2,*], Ibrahim Jantan[3]
[1]Faculty of Medicine, Universiti Sultan Zainal Abidin, Kuala Terengganu, 20400, Terengganu, MALAYSIA.
[2]Department of Pharmacognosy and Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Hat-Yai, Songkhla 90112, THAILAND.
[3]Faculty of Pharmacy, Universiti Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, 50300 Kuala Lumpur, MALAYSIA.

ABSTRACT

Objectives: Lawsone methyl ether (LME) is a naphtoquinone compound found in the leaf of *Impatiens balasamina* L. It has been semi synthesized by methylation of lawsone. This compound possessed several pharmacological properties including the use for the treatment of infectious diseases. This study was undertaken to determine of immunomodulatory effect of LME on immune response of human phagocytes. **Methods:** Trypan blue exclusion method was applied to determine cell viability. A modified 48-well Boyden chamber was used to assess chemotactic activity, luminol-based chemiluminescene assay was performed to evaluate the effect of compound on respiratory burst of human phagocytes, while Myeloperoxidase (MPO) activity was observed using colorimetric assay. **Result**s: LME at 6.25 and 100 μg/mL were non-toxic against the phagocytes after 25 h incubation. This compound showed strong inhibitory effect on the migration of polymorphonuclear cells (PMNs) towards chemoattractant with IC_{50} value of 7.63 μg/mL and was comparable to ibuprofen as a positive control. This compound also inhibited MPO enzyme system on PMNs with IC_{50} of 24.6 μg/mL. Preliminary screening on whole blood, LME strongly inhibited respiratory burst with IC_{50} value of 8.51 μg/mL. Furthermore, this compound also demonstrated a high inhibition effect on reactive oxygen species (ROS) production of PMNs and monocytes with IC_{50} of 9.43 and 6.49 μg/mL, respectively. **Conclusion:** These results suggest that LME was able to suppress human phagocyte at the different steps including chemotaxis and production of oxidative stress. This finding might emphasize that LME has potency as an anti-inflammatory agent by modulating innate response of human phagocytes.

Key words: Chemotaxis, Chemiluminescence, Immunomodulatory, Lawsone methyl ether, Myeloperoxidase.

Correspondence

Abdi Wira Septama, Faculty of Medicine, Universiti Sultan Zainal Abidin, Kuala Terengganu, 20400, Terengganu, MALAYSIA.

Phone: +60-10-9379287

Email: abdiwiraseptama@gmail.com

Pharkphoom Panichayupakaranant, Department of Pharmacognosy and Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Hat-Yai, Songkhla 90112, THAILAND

Phone: +66-74-428220

Email: pharkphoom.p@psu.ac.th

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INTRODUCTION

Inflammation is a complex mechanism involved the immune system to response any infections.[1] Innate immunity is the first line of host defense in which professional phagocytes, such as Polymorphonuclear leukocytes (PMNs), macrophage and monocytes play important role to eliminate pathogens.[2,3] In response of invading pathogens, innate immune cells will migrate to the site of infection by adhering to endothelial cells, followed by producing Reactive Oxygen Species (ROS) as a bactericidal agent.[4] Beside their advantageous for defensive mechanism, inflammation is also associated with various chronic diseases including arthritis rheumatoid.[5] Thus, it has been suggested that modulation immune cells by suppressing their over activity could be used a basis for the development of anti-inflammatory drugs.

Natural product has been widely used as alternative source for the treatment of inflammation disorder.[6] Plant-derived compounds, such as curcumin, colchicine and resveratrol exhibited potent anti-inflammatory activities.[7] *Impatiens balsamina* L. belongs to family Balsaminaceae, which has been used as a folk medicine for treatment several ailments, including abscesses and allergic reaction.[8] Lawsone methyl ether (LME) (Figure 1) is naphthoquinone isolated from *I. balsamina*.[9] This compound exhibited antifungal activity against *Candida albicans*.[10] Moreover, LME also possessed anti-allergic activity by suppressing degranulation RBL-2H3 cells. This compound has also reduced nitrite production in RAW 264.7 cells.[11] However, there is no data available regarding the immunomodulatory effects of LME on innate immune response. Therefore, this study was undertaken to investigate the effect of LME on phagocytosis activity such as chemotaxis, Reactive Oxygen Species (ROS) production as well as myeloperoxidase (MPO) activity.

MATERIALS AND METHODS

Chemicals and instruments

Lawsone Methyl Ether (LME) was prepared by methylation of lawsone in acid condition as previously described by Panichayupakaranant and Raenmongkol.[12] Serum opsonized zymosan A (*Saccharomyses cerevisiae* suspensions and serum), luminol (3-aminophthalhydrazide), Phosphate Buffer Saline (PBS), Hanks Balance Salt Solution (HBSS), ficoll, *n*-formyl-methionylleucyl-phenilalanine (fMLP), tryphan blue, phorbol 12-myristate 13-acetate (PMA), Dimethyl sulfoxide (DMSO), acetylsalicylic acid (purity 99%), ibuprofen (purity 99%) and indomethacin (purity 99%) were purchased from Sigma (St Louis, MO, USA). Haematoxylin and xylene were from BDH, UK. Lymphoprep® was from Stemcell technology, USA. Myeloperoxidase (MPO) activity colorimetric assay kit was purchased from Biovison, UK. Chemiluminscence was carried performed using a Luminoscan Ascent (Thermo Scientific, UK). A Boyden chamber 48-wells as well as a 3 μm and 5 μm polycarbonate membrane filter were

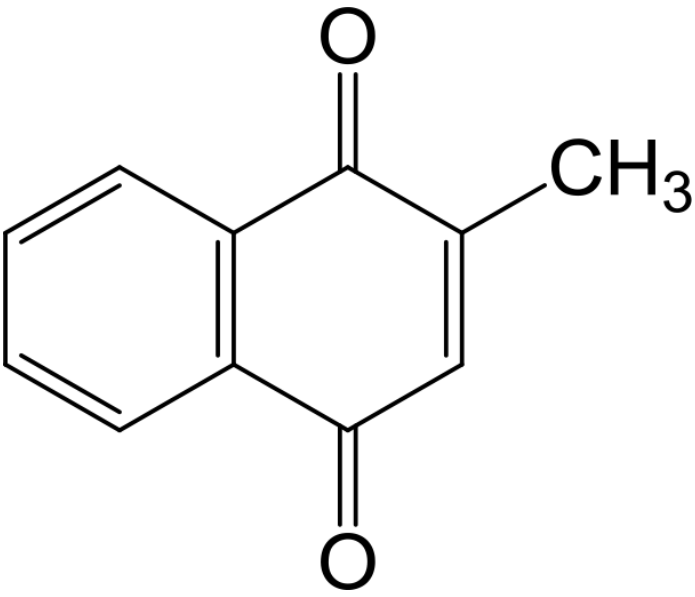

Figure 1: Chemical structure of lawsone methyl ether (LME).

from Neuro probe (Cabin Jhon, MD, USA). Microplate reader (Thermo Scientific, UK) was used. A CO_2 incubator (Shell Lab, USA) and light microscope (Leitz Watzler, Germany) were also used for chemotaxis assay.

Isolation of Human Polymorphonuclear Leukocytes (PMNs) and monocytes

The PMN isolation was performed according to method as described by Jantan *et al.*, with slight modification.[5] Briefly, the whole blood was obtained from healthy volunteers. The blood was then aliquot into falcon tubes and added with an equal volume of dextran and PBS, the mixture was left for sedimentation at room temperature for 45 min. The supernatant was centrifuged by Ficoll-gradient and then washed twice with distilled water to lysis red blood cells. A pellet of PMNs was collected from the bottom of the tubes. Meanwhile, the monocytes isolation was carried by using a modified method of Gmelig *et al.*[13] Briefly, the venous blood was diluted in an equal volume of physiological saline. Diluted blood was then carefully layered on Lymphoprep® and centrifuged at 400 × *g* for 45 min. After centrifugation, the mononuclear cells were retained at the medium interface and were carefully removed by using a pasteur pipette. The fraction was diluted with PBS and centrifuged at 250 × *g* for 10 min. These cells were then suspended in PBS and counted using heamocytometer and light microscope to obtain a final cell suspension of 1×10^6 cells/mL. The use of human blood was approved by the Human Ethical Committee, Faculty of Medicine, Universiti Kebangsaan Malaysia (approval number FF/2012/Ibrahim/23-May/432-May 2012-August 2013).

Cell viability

Viability test of isolated cells was performed using the standard tryphan blue exclusion method.[14] The cells (1×10^6) were incubated with 6.25 and 100 µg/mL of sample in triplicate at 37°C for 2 h. The blue dye uptake was indicated as cell death. The percentage viability was counted from the total cells.

Chemotaxis assay

The testing was performed using a 48-well Boyden chamber with formyl-methionyl-leucyl-phenylalanine (fMLP) as a chemoattractant as previously described by Jantan *et al.*[5] Briefly, aliquot of 25 µL fMLP (10^{-8} M) was added at the lower part of chamber, 5 µL of serial dilutions of sample (6.25-100 µg/mL) were added to the upper part containing 45 µL PMNs/monocytes (1×10^6 cells/mL) suspended in $HBSS^{++}$. The final concentrations of samples in the mixture were adjusted to 10-0.625 µg/mL. The chemoattractant buffer (DMSO and HBSS, 1:1 ratio) as control, while ibuprofen was used as a positive control. The final concentration of DMSO in mixture was 0.5% in order to avoid interference the chemotactic study. The cells were then incubated in CO_2 incubator for 1 h at 37°C. The experiment was performed in triplicate. Migrated cells which adhered to the upper part of the membrane filter were fixed and stained by haematoxylin and xylene. The distance of cell migration was measured by a light microscope. The percentage inhibition (%) was calculated using the following formula:

$$\frac{\text{Distance travelled by control} - \text{Distance travelled by sample}}{\text{Distance travelled by control}} \times 100\%$$

Myeloperoxidase (MPO) activity assay

This assay was carried out using a myeloperoxidase activity colorimetric assay kit (Biovision). MPO assay was performed based on chemical reaction that involved the production of hyphochlorous acid (HClO) from stimulated PMNs, in which Cl^- will react with taurine to generate taurine chloramine, which then reacts with the 2-nitro-5-thiobenzoic acid (TNB) probe to eliminate color (412 nm). Briefly, the PMNs suspensions (1×10^6 cells/mL) were incubated with serial solution of sample for 10 min at 37°C. The cells were then activated with PMA (8×10^{-7} M) and incubated for 30 min at 37°C. Afterward, the cells were centrifuged at 450 × g for 10 min. The supernatants were collected to determine MPO activity. Supernatant obtained from PMA stimulated neutrophil where the sample replaced by PBS was considered as 100% of MPO release. Fifty µL supernatant of sample, positive control, and normal control were added into 96 wells plate, then 50 µL of reaction mix (40 µL MPO buffer assay + 10 µL MPO substarte) was added to each well containing the samples, indometachin and normal control. While, 50 µl of the sample background control (40 µL MPO buffer assay + 10 µL dH_2O) was added to background control (PBS). The mixture was then incubated at 25°C for 30 min. Two µL stop mix were added to all samples, positive control, normal control and background control and incubated for 10 min to stop reaction. Fifty µL TNB standard was added 50 µL to all wells. Then, the reading was taken using microplate reader at 412 nm.

Chemiluminescence assay

Luminol-amplified chemiluminescence assay was performed as described by Jantan *et al.*[5] Briefly, 25 µL diluted whole blood or 25 µL PMNs (1×10^6/mL) or 25 µL monocytes (1×10^6/mL) suspended in $HBSS^{++}$ were incubated with 25 µL serial solutions of samples (6.25-100 µg/mL). The cells were then stimulated with 25 µL opsonized zymosan followed by 25 µL of luminol (7×10^{-5} M) and $HBSS^{++}$ was added to adjust the final volume to 200 µL. The final concentrations of samples in the mixture were 12.5, 6.25, 3.13, 1.56 and 0.78 µg/mL. Control wells contained 0.6% DMSO, $HBSS^{++}$, luminol and cells but no samples. Acetylsalicylic acid was used as positive control. The test was performed in white 96-well microplates which were incubated at 37°C for 50 min in the thermostated chamber of luminometer. The results were monitored as chemiluminescence RLU (reading per luminometer unit) with peak and total integral values. The percentage inhibition (%) of each sample was calculated using the following formula:

$$\frac{\text{RLU control} - \text{RLU sample}}{\text{RLU control}} \times 100\%$$

Statistical analysis

All the data are represented as mean ± standard error median (SEM) from triplicate experiments. One way ANOVA was used for multiple comparisons followed by Tukey's test to identify any significant difference between groups. $P< 0.05$ was considered as a statistically significant. Graph PAD prism 6 analysis software was used to calculate IC_{50}.

RESULTS

Chemotaxis

The ability of LME in inhibiting of chemotaxis was determined using Boyden chamber. The entire test showed a dose-dependent manner. The IC_{50} values were presented in Table 1. LME revealed strong activity with IC_{50} value of 7.63 μg/mL, which is slightly comparable to ibuprofen (1.52 μg/mL).

Myeloperoxidase (MPO) activity

Colorimetric assay was used to determine MPO activity. The result obtained (Table 2) showed that LME could inhibit the release of MPO enzyme with IC_{50} value of 23.44 μg/mL. The activity of this compound was comparable to indomethacin with IC_{50} value of 24.6 μg/mL.

Chemiluminescence

Preliminary screening of LME on whole blood cells demonstrated that this compound strongly inhibited ROS production with IC_{50} value of 8.51 µg/mL, while acetylsalicylic acid also exhibited inhibition activity with IC_{50} value of 2.50 µg/mL (Table 3). LME was further investigated for its activity on isolated PMNs and monocytes. This compound revealed strong inhibitory effect on PMNs and monocytes with IC_{50} values of 9.43 µg/mL and 6.49 µg/mL, respectively.

DISCUSSION

The cytotoxic effect of LME on isolated PMNs and monocytes at 6.25 and 100 μg/mL were conducted using tryphan blue exclusion method. The viability test results demonstrated that both concentrations are non-toxic on isolated cells, in which the cells are still viable (more than 90%) after 2 h incubation.

Chemotaxis refers to the movement of cells toward chemical gradient. In response of invasive bacterial, phagocyte cells will be attracted through the production of chemoattractants such as *n*-formylated peptides, the fifth component of complement ($C5_a$), leukotrient B_4 and interleukin-8 (IL-8). Chemoattractants are then recognized by specific receptors on phagocytes surface that activate intracellular cascading pathway, which

Table 1: Percentage inhibition and IC_{50} values (μg/mL) of chemotaxis activity of LME and ibuprofen on PMNs (Mean ± SEM, *n*=3).

Sample	Concentration (μg/mL)	Percentage inhibition (%)	IC_{50} (μg/mL)
LME	10	60	
	5	49	
	2.50	26	7.63 ± 1.6
	1.25	20	
	0.63	10	
Ibuprofen	10	75	
	5	65	
	2.50	55	1.52 ± 1.2
	1.25	48	
	0.63	38	

Table 2: Percentage inhibition and IC_{50} values (μg/mL) of MPO inhibitory activity of LME and indomethacin on PMNs (Mean ± SEM, *n*=3).

Sample	Concentration (μg/mL)	Percentage inhibition (%)	IC_{50} (μg/mL)
LME	25	52	
	12.50	33	
	6.25	12	24.6 ± 1.2
	3.13	9	
	1.56	8	
Indomethacin	25	51	
	12.50	40	
	6.25	30	1.52 ± 1.2
	3.13	13	
	1.56	7	

Table 3: Percentage inhibition and IC_{50} values (μg/mL) of ROS inhibitory activity of LME and aspirin on WBC, PMNs and monocytes (Mean ± SEM, *n*=3).

Sample	Concentration (μg/mL)	WBC		PMN		Monocytes	
		Percentage inhibition (%)	IC_{50} (μg/mL)	Percentage inhibition (%)	IC_{50} (μg/mL)	Percentage inhibition (%)	IC_{50} (μg/mL)
LME	12.5	54		61		56	
	6.25	48		49		48	
	3.13	30	8.51 ± 1.2	23	9.43 ± 0.8	42	6.49 ± 1.7
	1.56	20		17		30	
	0.78	8		12		18	
Acetylsalicylic acid	12.5	72		92		91	
	6.25	61		80		82	
	3.13	56	2.50 ± 1.0	62	1.11 ± 0.9	70	0.82 ± 1.2
	1.56	42		42		48	
	0.78	18		23		32	

WBC (whole blood cells), PMNs (polymorphonuclear cells).

cause migration of phagocytes to the infection site.[15] Thus, accumulation of immune cell will lead to inflammation. The inhibition effect of LME on chemotaxis activity of PMNs was carried out using a modified 48-well Boyden chamber. Chemoattractant buffer which contains HBSS and DMSO in equal volume was used a negative control, while ibuprofen which is the most active NSAID in inhibiting the migration of PMNs toward fMLP was selected as positive control.[16] LME showed strong inhibition effect in chemotaxis. This result is in agreement with previous study by Oku and Ishiguro. It has been reported that naphthoquinones isolated from *I. balsamina*, including LME has strong anti-inflammatory activity.[17]

Furthermore, upon stimulation by Phorbol myristate acetate (PMN), Professional phagocytes including PMNs will release Myeloperoxidase (MPO) enzyme. This enzyme is abundantly expressed in phagocyte cells, which catalyze the production of hypochlorous acid (HClO) as microbicidal agent. Various diseases are always related with high activity of this enzyme including chronic inflammation.[18] Therefore, suppressing the release of MPO is advantageous for the treatment of inflammation. MPO activity assay was conducted to investigate the effect of LME on activity of this enzyme. Indomethacin was used as positive control due to its significant effect in inhibiting the release of MPO.[19] In this study, LME enabled to inhibit the MPO activity and might be used as immunosuppression.

Respiratory burst is an essential step in phagocytosis. Reactive Oxygen Species (ROS) produced during this activity plays an important role to eliminate pathogen. However, over production of oxidative stress may cause inflammation. Thus, it is important to find the alternative that can inhibit ROS production. In this study, the production of ROS was stimulated with Serum Opsonized Zymosan (SOZ). Due to the small molecular weight, luminol was used as a probe to detect intracellular ROS.[20] According to previous work, acetylsalicylic acid enabled to inhibit luminol-amplified chemiluminescene was selected as a positive control. Moreover, the agent is the most potent of drug in inhibiting ROS production of human phagocytes.[21] The results obtained indicated that LME are able to inhibit the production of oxygen species during respiratory burst. According to previous study, it has been reported that LME also significantly reduced nitrate production in macrophage RAW 254.7.[22] This result also corresponded with MPO activity assay, whereas the ability of LME in inhibiting MPO activity could reduce ROS production of stimulated phagocyte cells. It has been suggested that the inhibition of MPO enable to suppress the production of intracellular ROS.[23]

Recently, the use of natural compounds has been confirmed beneficial for the treatment several ailments including inflammation. Naphtoquinone is a group of natural product found in plant kingdom. This compound has displayed strong anti-inflammatory effect by modulate innate immune response. Previous study from Pinho and colleagues showed the potential of diosquinone to reduce NO production. This compound also caused a decrease of pro-inflammatory cytokines, such as TNFα and IL-6.[24] Besides, plumbagin, a quinone from *Plumbago zeylanica* enabled to inhibit activation of NFκB in lymphocytes.[25] In recent study, Dong and team reported that shikonin isolated from *Onosma paniculatum* demonstrate good anti-inflammatory activity by inhibiting NO production of macrophage RAW 264.7 cells.[26] In our study, semi synthetic nahptoquinone named LME possessed significant effect to inhibit at three different steps of phagocytosis. The results indicated that LME has potency as anti-inflammatory substance by regulate innate response of human phagocytes. Moreover, this study is the first report immunosuppression effect of LME on human phagocytes.

CONCLUSION

In conclusion, LME was able to suppress phagocytosis of human phagocytes. This compound contributed for the inhibition of chemotactic activity of PMNs towards chemoattractant and suppressing the activity of MPO enzyme system which in turn reducing ROS production. These results provide an insight that LME has a potential to be anti-inflammatory agents. Nevertheless, further investigations are still needed to confirm other mechanism of actions.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

ROS: Reactive Oxygen Species; **MPO:** Myeloperoxidase; **LME:** Lawsone methylether; **PMNs:** Polymorpho Nuclear Cells.

REFERENCES

1. Viladomiu M, Hontecillas R. Bassaganya-Riera, Modulation of inflammation and immunity by dietary conjugated linoleic acid. Eur J Pharmacol. 2016;785:87-95.
2. Sprague AH, Khalil RA. Inflammatory cytokines in vascular dysfunction and vascular disease. Biocham Pharmacol. 2009;78(6):539-52.
3. Kobayashi SD, Voyich JM, DeLeo FR. Regulation of the neutrophil-mediated inflammatory response to infection. Microbes Infect. 2003;5(14):1337-44.
4. Buetler B. Innate immunity: an overview. Mol Imunol. 2004;40(12):845-59.
5. Jantan I, Harun NH, Septama AW, Murad S, Mesaik MA. Inhibition of chemiluminescence and chemotactic activity of phagocytes *in vitro* by the extracts of selected medicinal plants. J Nat Med. 2011;65(2):400-5.
6. Newman DJ, Cragg GM. Natural products as sources of new drugs over the 30 years from 1981 to 2010. J Nat Pro. 2012;75(3):311-35.
7. Fürst R, Zündorf I. Plant-derived anti-inflammatory compounds: hopes and disappointments regarding the translation of preclinical knowledge into clinical progress. Mediat Inflamm. 2014;1-9.
8. Farnssworth NR, Bunyapraphatsara N. Thai medicinal plant recommended for primary health care system. Bangkok: Prachachon. 1992.
9. Little JE, Sproston T, Foote MW. Isolation and antifungal action of naturally occurring 2-methoxy-1,4-naphthoquinone. J Bio Chem. 1948;174(1):335-42.
10. Sritrairat N, Nukul N, Inthasame P, Sansuk A, Prasirt J, Leewatthanakorn T, *et al.* Antifungal activity of lawsone methyl ether in comparison with chlorhexidine. J Oral Pathol Med. 2011:40(1);90-6.
11. Reanmongkol W, Subhadhirasakul S, Panichayupakaranant P, Kim KM. Anti-allergic and antioxidative activities of some compounds from Thai medicinal plants. Pharm Biol. 2003;41(8):592-7.
12. Panichayupakaranant P, Reanmongkol W. Evaluation of chemical stability and skin irritation of lawsone methyl ether in oral base. Pharm Biol. 2002;40(6):429-32.
13. Gmelig-Meyling F, Waldman TA. Separation of human blood monocytes and lymphocytes on a continuous percoll gradient. J Immunol Method. 1980;33(1):1-9.
14. Koko WS, Mesaik MA, Yousaf S, Galal M, Choundary MI. *In vitro* immunomodulating properties of selected Sudanese medicinal plants. J Ethnopharmacol. 2008;118(1):26-34.
15. Foster TJ. Immune evasion by Staphylococci. Nat Rev Microbiol. 2005;3(12):948-58.
16. Spisani S, Gabriella V, Serena T. Inhibition of human leucocytes locomotion by anti-inflammatory drugs. Experientia. 1978;35(6):803-4.
17. Oku H, Ishiguro K. Cyclooxygenase-2 inhibitory 1,4-Naphthoquinones from *Impatiens balsamina* L. Biol Pharm Bull. 2002;25(5):658-60.
18. Tabart J, Franck T, Kevers C, Pincemail J, Serteyn D, Defraigne JO. Antioxidant and anti-inflammatory activities of *Ribes nigrum* extracts. Food Chem. 2012; 131(4):1116-22.
19. Nève J, Parij N, Moguilevsky N. Inhibition of the myeloperoxidase chlorinating activity by non-steroidal anti-inflammatory drugs investigated with a human recombinant enzyme. Eur J Pharmacol. 2001;417(1-2):37-43.
20. Rathakrishnan C, Tiku ML. Lucigenin-dependent chemiluminescence in articular chondrocytes. Free Radical Bio Med. 1993:15(2);143-9.

21. Parij N, Nagy AM, Pondu P, Neve J. Effects of non-steroidal anti-inflammatory drugs on the luminol and lucigenin amplified chemiluminescence of human neutrophils. Eur J Pharmacol. 1998;352(2-3):299-305.
22. Dahlgren C, Stendahl O. Role of myeloperoxidase in luminol-dependent chemiluminescence of polymorphonuclear leukocytes. Infect Immun. 1983;39(2):736-41.
23. Klebanoff SJ. Myeloperoxidase: friend and foe. J Leukoc Biol. 2005;77(5):598-625.
24. Pinho BR, Sousa C, Valentoa P, Andrade PB. Is nitric oxide decrease observed with naphthoquinones in LPS stimulated RAW 264.7 macrophages a beneficial property?. PLoS One. 2011;6(8):e24098.
25. Checker R, Sharma D, Sandur SK, Khanam S, Poduval TB. Anti-inflammatory effects of plumbagin are mediated by inhibition of NF-kappaB activation in lymphocytes. Int J Immunopharmacol. 2009;9(7-8):949-58.
26. Dong M, Liu D, Li YH, Chen XQ, Luo K, Zhang YM, *et al.* Naphthoquinones from *Onosma paniculatum* with potential anti-inflammatory activity. Planta Med. 2017;83(07):631-5.

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