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Program and Abstracts

Sciences Go Green

The First International Seminar on Science and Technology

(ISSTEC 2009)

The Challenge of Sciences in a Global Warming Era: Issues and Opportunities for a Better Life

Held from January 24 - 25, 2009

at Kahar Muzakkir Auditorium Universitas Islam Indonesia

Preface

The First International Seminar on Science and Technology (ISSTEC2009) is the scientific meeting of the organized jointly by Faculty of Mathematics and Natural Sciences Universitas Islam Indonesia (UII), Faculty of Sciences and Technology, Universiti Kebangsaan Malaysia (UKM) and Faculty of Sciences and Technology, Universiti Malaysia Terengganu (UMT). Held every two years by a member society of UII, UKM and UMT, the ISSTEC has become a major international meeting of both eminent and upcoming scientists and researchers from all over the world. ISSTEC2009 in hosted by Faculty of Mathematics and Natural Sciences Universitas Islam Indonesia (UII), Indonesia from January 24-25, 2009.

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The Scientific Programme of ISSTEC2009 comprises the following:

1. One (1) Keynotes Speaker
2. Five (8) Invited Speaker
3. A total 342 paper for Parallels Sessions.
   - Mathematics (MATH) — 13 papers
   - Statistics (STAT) — 25 papers
   - Chemistry
     1. Organic Chemistry (Org.Chem.) — 32 papers
     2. Analytical Chemistry (Anal. Chem) — 43 papers
     3. Inorganic Chemistry (Inor.Chem) — 45 papers
     4. Physical Chemistry (Phys.Chem) — 15 papers
     5. Environmental Chemistry (Env.Chem) — 19 papers
     6. Biochemistry (Biochem) — 15 papers
   - Biology (BIO) — 38 papers
   - Pharmacy (PHARM) — 21papers
   - Computer Sciences (CS) — 34 papers
   - Physics (PHYS) — 33 papers

The breakdown of the presentation is as follows:

Session	Oral	Poster	Total
Keynote Speakers	1	0	1
Invited Speakers	8	0	8
MATH	13	0	13
STAT	23	2	25
Org.Chem.	24	8	32
Anal.Chem.	32	11	43
Inor.Chem.	43	2	45
Phys.Chem.	15	0	15
Env.Chem.	19	0	19
Biochem.	10	5	15
BIO	29	9	38
PHARM	13	8	21
CS	34	0	34
PHYS	24	9	33

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PHARM 005
Oral

Activity of Gamavuton-0 on Inflammation and Arthritic Index in Arthritis Rats Induced by Complete Freund's Adjuvant

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Abstract

Rheumatoid arthritis (RA) is a chronic inflammatory joint disease that can affect a lot of people in the world. Gamavuton-0 (GVT-0) was reported has anti-inflammatory activity and relatively nontoxic. This aim of this study was to explore the activity of GVT-0 on inflammation and arthritic index that performed on female Wistar rat as an animal model of RA induced by Complete Freund's Adjuvant (CFA). Rheumatoid arthritis was induced by subplantar injection of a CFA on female Wistar rat's paw on day 0 and day 20. The gradual onset of arthritis normally starts approximately 3 weeks after initial immunization. GVT-0 was suspended in 0.5% CMC and given orally in one daily dose of 10, 20, 40, and 80 mg/kg BW starting on day 21. Methotrexate (0.22 mg/kg BW p.o.) served as a positive control and 0.5% CMC (p.o.) served as a negative control. The clinical severity of arthritis was graded every two days with Smit method based on the changes in swelling and redness of toes, foot pad, and ankle, with a maximum score of 2 per paw. The results of this study demonstrated that treatment with GVT-0 could inhibit paw edema and arthritic index. Administration of GVT-0 dose 80 mg/kg BW induced a significant inhibition of paw edema, with a maximum effect was 50,04%. ED_{50} GVT-0 on inhibition of paw edema was 80,86 mg/kg BW. GVT-0 could suppress arthritic index, with a maximum effect at GVT-0 dose 80 mg/kg BW was 20,06%.

Keywords: rheumatoid arthritis, arthritic index, GVT-0, inflammation, CFA

PHARM 006
Oral

Gamavuton-0 Suppressed Cytokine IL-1β Level in Joints Tissue of Arthritis Rats Model Induced by Complete Freund's Adjuvant

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Abstract

Rheumatoid arthritis (RA) is an inflammation disease in joints that it's cause still unclearly known. Some recently studies has proven that there is elevation of cytokines level including TNF-α and IL-1β especially in RA joints synovium. Many medicines are used for RA therapy, but there are still no satisfying. Gamavuton-0 (GVT-0) was reported has anti-inflammatory activity and relatively nontoxic. This study was undertaken to know whether the GVT-0 could suppress IL-1β level contributing to RA. The research has done by inducing female Wistar rats with Complete Freund's Adjuvant (CFA) to get arthritic rats. After arthritis inducing, the rats perorally administrated with GVT-0 with 10, 20, 40 and 80 mg/kg BW for 21 days and then joints tissue of the rats analyzed by Enzyme Linked-Immuno-Sorbent Assay (ELISA) method to measure IL-1β level. The joints level of IL-1β with GVT-0 treatment is compared with normal rats, negative controls (perorally administered with 0,5% Na-CMC), and positive controls (perorally administered with Metotrexate dose 0,223 mg/kg BB) The research results show that 80 mg/kg BW of GVT-0 decreased IL-1β in joints tissue by 79,65%. GVT-0 have anti rheumatoid arthritis activity that described as % decreasing of IL-1β (%PKI) with ED_{50} of 12,38 mg/kg BW.

Keywords: Rheumatoid Arthritis (RA), Complete Freund's Adjuvant (CFA), Interleukin-1β (IL-1β), Gamavuton-0 (GVT-0)

Pharmacy

Activity of Gamavuton-0 as Anti Rheumatoid Arthritis on Female Wistar Rats Induced by Complete Freund's Adjuvant with Parameter Suppression of Cytokine Il-1β Level in Joints Tissue

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Abstract

Rheumatoid arthritis (RA) is an inflammation dissease in joints that it's cause still unclearly known. In the some recently study has proven that there is elevation of sitokines level including TNF-α and IL-1β especially in RA joints synovium. Many kind of medicines is used for RA therapy, but thereare still no satisfy result yet and had advers effects to the gastric especially non-steroidal anti-inflammatory drugs (NSAID) that alot used for RA therapy.

This study was undertaken to know in vivo activity of Gamavuton-0 (GVT-0) in RA with joints level of IL-1β as parameter. The research has done by inducing female Wistar rats with Complete Freund's Adjuvant (CFA) to get arthritic rats. After arthritis inducing, the rats perorally administrated with GVT-0 with 10, 20, 40 and 80 mg/kg BW for 21 days and then joints tissue of the rats analyzed by Enzyme Linked-Immuno-Sorbent Assay (ELISA) method to establish IL-1β. The joints level of IL-1β with GVT-0 treatment is compared with normal rats, negative controls (perorally administration with 0,5% Na-CMC), and positive controls (perorally administration with Metotrexate dose 0,223 mg/kg BB)

The research resulting that 80 mg/kg BW of GVT-0 decrease IL-1β in joints tissue by 79,65%. GVT-0 have anti rheumatoid arthritis activity that described as % decreasing of IL-1β (%PKI) with ED_{50} by 12,38 mg/kg BW.

Keywords: *Rheumatoid Arthritis (RA), Complete Freund's Adjuvant (CFA), Interleukin-1β (IL-1β), Gamavuton-0 (GVT-0)*

Introduction

Rheumatoid Arthritis (RA) is a common form of arthritic disease that suspected about 1% of population or 2.1 million people in USA [1]. RA is an inflammatory disease involving small joints of the extremities, particularly of the fingers, as well as larger joints including shoulders, elbows, knees, and ankles. There are rheumatoid factor that usually found in serum. Numerous cytokines, including IL-1, IL-8, TNF, and IFN-γ, have been detected in the synovial (joint) fluid [2].

RA progression is associated with elevated levels of tumour necrosis factor-α (TNF-α) and interleukin (IL)-1β produced by macrophages and dendritic cells, an imbalance of Th1/Th2 and overproduction of antigenspecific immunoglobulins [3]. The biologic efffects of IL-1 are similar to TNF and depend on the quantity of cytokine produced. When secreted at low concentrations, IL-1 functions as a mediator of local inflammation. It acts on endothelial cells to increase expression of surface molecules that mediate leukocyte adhesion. When IL-1 was secreted in larger quantities, IL-1 enter the blood stream and exerts endocrine effects. Systemic IL-1 shares with TNF the ability to cause fever, to induce synthesis of acute-phase plasma proteins by the liver, and to initiate metabolic wasting [2]. Amount of IL-1 increased appropriate with incidence level of RA. Because of that, level of IL-1 (specially IL-1β, most of the IL-1 found in the circulation is IL-1β [2]) can be used as parameter of the incidence. If there are large amount of IL-1 in joint tissue,so the occurrence of AR also increased [4].

Most of drugs were used for RA treatment have adverse effects specially for nonsteroidal anti-inflammatory drugs (NSAIDs) that may caused Gastric ulcer. So there are needs discovering for new drugs in order to solve RA with minimum of adverse effects. Gamavuton-0 (GVT-0) or 1,5-*bis(*4'-hidroksi-3'-metoksifenil)1,4-pentadien-3-on is an analouge of curcumine that reported have anti-inflammatory effect. Anti-inflammatory effect of GVT-0 is higher than curcumin by 40mg/kgBW [5]. Wahyuni [6] reported that no ulcer was caused by curcumin in rat's gastric. So GVT-0 has high potency for treatment of RA. Because of that, an appropriate research was needed in order to knew activity of GVT-0 as anti rheumatoid arthritis on female wistar rats induced by complete freund's adjuvant with parameter suppression of cytokine IL-1β level in joints tissue.

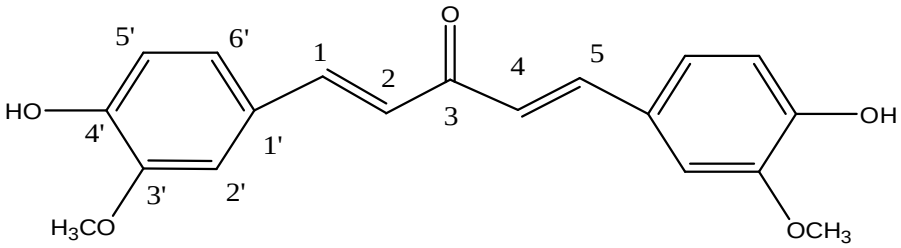

Figure 1. Structure of Gamavuton-0 (1,5-bis(4'-hydroxy-3'-methoxyphenyl)-1,4-pentadiene-3-one

Experimental

Materials

Materials were used are: GVT-0 (Synthesised by Nugroho *et al*, 2004), Complete Freund's Adjuvant (CFA) (Gibco BRL, Grand Island, NY, USA), *sodium-carboxymethylcellulosa* (CMC-Na) 0,5% in aquadest, methotrexate (Lederle®), lysis buffer

(Potassium phosphate), reagents were included in ELISA kit: standard of IL-1β, standard diluent buffer, control of IL-1β, IL-1β biotin conjugates, streptavidin-peroksidase (HRP), washing buffer, tetrametilbenzidin (TMB), stop solution (BioSource International, Inc., California, USA).

Animals

Female Wistar rats (good healthy, 200-220g, 2-3months) were housed in cages under standard laboratory conditions of temperature (27 ± 2^0C) and 12:12-h light-dark cycle.

Induction of RA

Female Wistar rats, aged 2-3 months at the start of the experiments, were immunized subplantar at right-hind footpad with 0,1 ml CFA (Gibco BRL, Grand Island, NY, USA). Arthritis will be developing gradually and on day 20 (from first injection) all rats were boosted with an subplantar injection of 0,05 ml CFA (subplantar at right-hind footpad).

Treatment with GVT-0

The next day after boosted, rats were selected and divided into seven groups, which each contained four rats. The control negative group were treated orally with 0.5% Na-CMC, the control positive group were treated orally with methotrexate 0.223 mg/kg BW, the GVT-0 were suspended in 0.5 % Na-CMC and given orally at the doses 10, 20, 40 and 80 mg/kg BW for 21 days. The gradual onset of arthritis normally starts approximately 3 weeks after initial immunization. The progression arthritic were evaluated macroscopically every 2 days at right-hind footpad and IL-1β was measured on day 42 by ELISA.

Measurement of IL-1β levels in mouse ankles

IL-1β was measured using commercially available ELISAs for IL-1β (BioSource International, Inc., California, USA) according to the manufacturer's recommendations. For measuring the cytokine production, peeled joint tissues from the upper portion of ankle to the middle of the paw were ground by homogenizer in the equal volume of the lysis buffer (100 mmol/l potassuim phosphate, pH 7.8). The tissue lysates were used to measure the level of IL-1β. IL-1β production was standardized as amount of IL-1β per ml of lysates.

Statistical analysis

Statistical evaluation were carried out using the SPSS with One Way ANOVA test then Post Hoc Test LSD method. Data were expressed as means and standard errors of the means. $P \leq 0.05$ was considered statistically significant for α.

Results and discussion

The objective of this research was to measure cytokine IL-1 β level in the rats joint tissue in order to knew activity of GVT-0 as anti AR. IL-1β is potent proinflammatory protein and is important in the pathogenesis of RA [7]. IL-1β is known to be present in large quantities in affected synovial fluid. There was needed a standard curve to established IL-1β level in rats joint tissue that performed by ELISA method. The principal of ELISA method were spesific binding between antigenes (IL-1β) with antibody (antiIL-1β) that was followed colloring by an enzyme.ELISA resulted absorption of standard IL-1β that made by some concentration (0, 31.2, 62.5, 125, 250, 500, 1000, and 2000 pg/ml).Standard IL-1β absorption data were plotted on curve between standard IL-1β level (x) and it's absorption (y) so we got the standard curve for IL-1β,

the equation was y = 6,049.10^{-4}x + 0,076 (r = 0,999 and R^2 = 99,7%). Standard IL-1β curve were shown in figure 2.

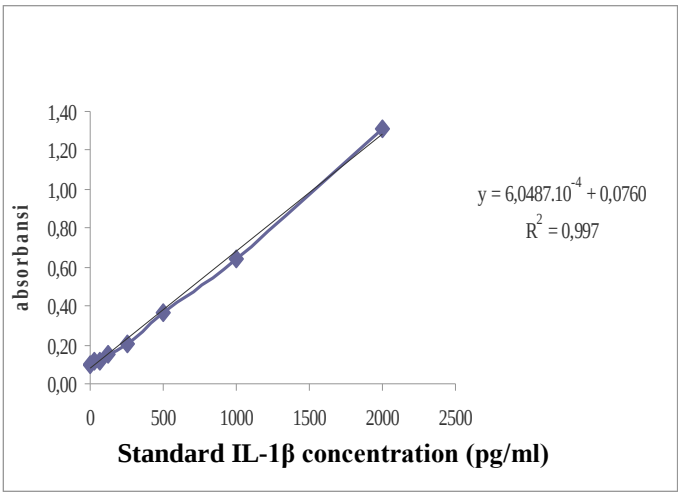

Figure 2. Standard IL-1β curve.

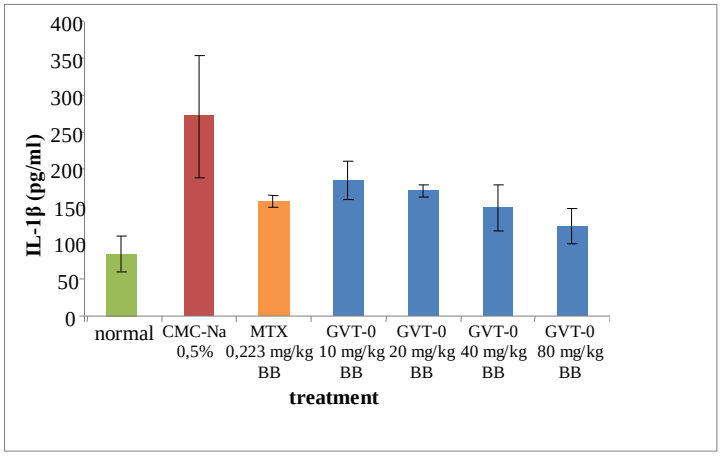

Figure 3. Histogram of IL-1β concentration in sample from rats joint tissue (normal rats, negative control rats were treated orally with 0.5% Na-CMC, positive control rats were treated orally with methotrexate 0.223 mg/kg BW, rats were treated with GVT-0 given orally at the doses 10, 20, 40 and 80 mg/kg BW for 21 days. each of group consist of 4 rats.

We can calculate IL-1β concentration in sample by include sample absorption in to standard curve equation. Histogram of IL-1β concentration in sample was shown in figure3. As shown in figure3, the level of IL-1β were all significantly reduced by treatment with MTX and GVT-0 compared with control rats treated with vehicle (0.5% Na-CMC, *P< 0.05*).

According to figure 3, MTX was proved can decrease IL-1β in arthritic rats joint tissue, so we can used MTX as positive control of GVT-0 activity. These results suggest that GVT-0 inhibits the production of cytokine IL-1β in the affected paws of RA rats. The dose of 80 mg/kg BW give the highest supression effect on IL-1β compared to others dose of GVT-0 and MTX dose 0.223 mg/kg BW. The histogram shown that decreasing of IL-1β adequate (sesuai) with increasing of GVT-0 doses, so there are sugested that treatment with higher doses of GVT-0 can decrease IL-1β untill reach normal level in joint tissue. GVT-0 activity decrease IL-1β level was assumed by it's activity as antiinflammatory, rallated with radical scavanging so inhibits

prostaglandines production.In an arthritis animal model, IL-1ß is increased by inflammatory stimulation, and IL-1ß induces COX-2 transcription in inflammatory cells [8]. At the same time, increased IL-1ß in inflammation upregulate the IL-6 expression [9]. Decreasing of IL-1β also can caused by apoptosis [10] that may stimullated by GVT-0.

GVT-0 activity in decrease IL-1β was described as % decrasing of IL-1β (%PKI) that shown decreasing of IL-1β in treatment rats joint tissue compare to IL-1β level in negative control rats joint tissue (peroral treatment with CMC-Na 0.5%). Histogram of %PKI was shown in figure 4.

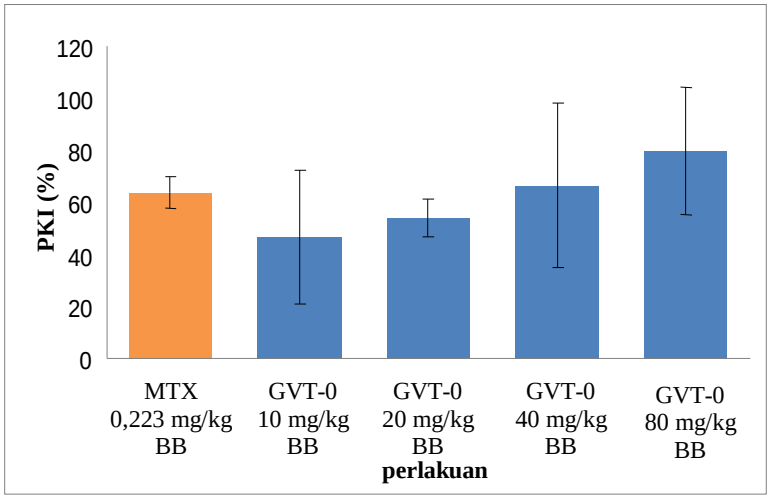

Figure 4. Histogram of %PKI (positive control rats were treated orally with methotrexate 0.223 mg/kg BW, rats were treated with GVT-0 given orally at the doses 10, 20, 40 and 80 mg/kg BW for 21 days. each of group consist of 4 rats).

%PKI of MTX was high (63,71 ± 5,87%), it means that MTX (positive control) proved has high activity to decrease IL-1β. According to figure 4 (%PKI), GVT-0 activity was increased in corellation with increasing of it's doses. MTX activity almost the same with dose 40 mg/kgBW of GVT-0 activity (66,38 ± 31,5%). MTX is one of disease modifying antirheumatic drugs (DMRADs) that have a long onset [11]. Response to MTX usually in 3-6 weeks after first treatment [12]. Treatment for artrhritis rats were 21 days (3 weeks), so the response that caused by peroral treatment of MTX (dose 0.223mg/kgBW) shown the activity in decrease IL-1β level. Statistical analysis (one way ANOVA) for %PKI shown the difference of treatment with all doses of GVT-0 and MTX was no significant ($p \leq 0.05$).this statistic means that all doses of GVT-0 and also MTX have activity that almost the same for decreasing IL-1β in arthritis rats joint tissue.

After each doses GVT-0 activty has known, we can get ED_{50} value of GVT-0 by make a rellation curve betwen GVT-0 doses with it's activity (%PKI). The curve was shown in figure 5. GVT-0 can decrease IL-1β levels with ED_{50} was 12.38 mg/kg BW in per oral.

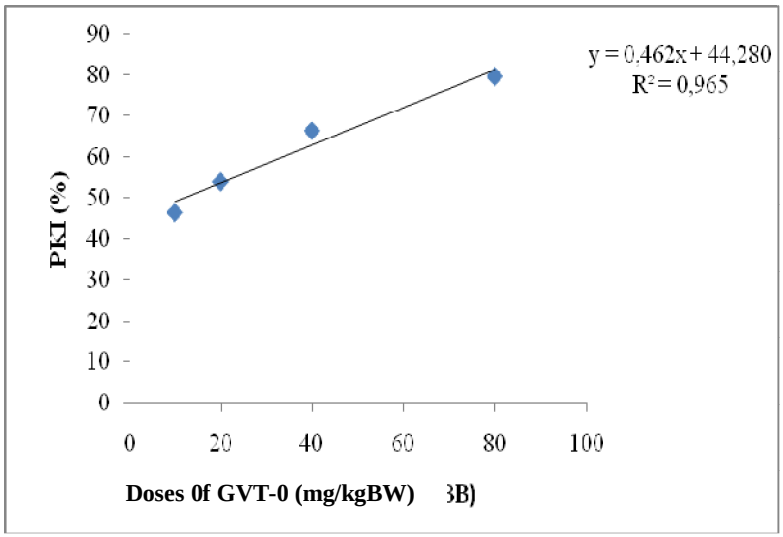

Figure 5. activity curve of GVT-0 (%PKI) by doses of GVT-0 (r = 0,982, r_{table} = 0,878)

Conclusions

These results suggest that GVT-0 suppressed cytokine IL-1β level in joints tissue and the effect of GVT-0 in the inhibition of inflammatory diseases may be partially associated with the down-regulation of IL-1β.

Acknowledgements

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