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1ST INTERNATIONAL CONFERENCE, EXHIBITION, & BUSINESS MEETING ON

# AGROMEDICINE & TROPICAL DISEASES

Optimizing The Role of Agromedicine and Tropical Diseases in Human Life

PROCEEDING

NOVEMBER 5TH, 2016

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# Medical Faculty University Of Jember

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ICATD 2016

*Optimizing the Role of Agromedicine and  
Tropical Diseases in Human Life*

Proceeding

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Medical Faculty University Of Jember  
Jember

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## PROGRAM

TIME	ACTIVITIES	VENUE
07:30-08:00	Registration	Auditorium, dean building second floor
08:00-08:30	Opening Ceremony	
08:00-08:10	Opening Dance	
08:10-08:20	Report Speech by chairman of ICATD	
08:20-08:30	Welcome speech and officially opened the conference by Dean of Medical Faculty University of Jember	
08:30-09:15	<b>Session I : Keynote Speaker</b>	
	Speaker : Susan Alison Brumby, Ph.D: <b><i>Role Agromedicine for Human Life in the Near Future</i></b> Moderator : dr. Laksmi Indreswari, Sp.B	
09.15-09.45	Discussion	
09.45-10.00	Coffee Break	
10:00-11:20	<b>Session II : Plenary Speakers (invited speakers)</b> Moderator : dr. Dwita Aryadina R, M. Kes	
10:00-10:20	Al Munawir, Ph.D: <b><i>Epidemiology, Clinical Case and Experimental Research of Jellyfish Sting in Indonesia</i></b>	
10:20-11:05	Angel Anne Yanagihara, Ph.D: <b><i>New Experiments Determine Effective Treatments for Box Jellyfish Sting</i></b>	
11:05-11:35	Discussion	
11:35-13:00	<b>Session III Plenary Speakers (invited speakers)</b> Moderator: dr. Bagus Hermansyah, M. Biomed	
11:35-12:10	Kim Euikyung, Ph.D: <b><i>Perspective of Nomurai Jellyfish for Human Life</i></b>	
12:10-12:30	DR.RER.BIOL.HUM dr. Erma Suiistiyaningsih,MSI : <b><i>Parasitological Infection in Agriculture Population</i></b>	
12.30-13:00	Discussion	
13.00-13:45	<b>Lunch</b>	Tramed building, first floor
	<b>Poster session</b>	
13:45-14:45	Parallel session presentation (divided in to 2 groups)	
15:00	<b>Closing ceremony</b>	Auditorium, dean building second floor

# THE COMBINATION THERAPY OF ANTIRETROVIRAL AND *PHYLLANTHUS NIRURI* EXTRACT FOR HIV PATIENTS

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## Abstract

Some in vitro researches reported that application of *Phyllanthus niruri* extract exhibited HIV reverse transcriptase enzyme inhibitor and immunostimulator effects. A quasi-experimental trial with a pretest-posttest control group design, a combination of antiretroviral therapy (ART) and capsules of *Phyllanthus niruri* extract (contained 50 mg dried powdered extracts of *P. niruri*) were administered to 15 HIV patients in the intervention group, while ART and placebo capsules (contained 50 mg dried powdered extracts of *Amylum manihot*) were administered to 13 HIV patients in the control group from a teaching hospital in Surabaya, Indonesia and a teaching hospital in Sidoarjo, East Java, Indonesia.

After six months of therapy, results from paired t-test revealed the treatment group achieved higher absolute CD4 cell count than the control group ( $p < 0.001$ ). Therefore, the combination of antiretroviral and *Phyllanthus niruri* extract is more effective to increase CD4 cells count on HIV patients.

## INTRODUCTION

HIV infection and AIDS are a global problem. Indonesia was one of five countries in the South-East Asia Region, which accounts for the majority of HIV burden (World Health Organization, 2013). The HIV-positive adult prevalence in Indonesia is stable at 0.3% regionally, but sub regional epidemic is still rising (Ministry of Health of the Republic of Indonesia, 2016).

Up to the present time, the management of patients with HIV and AIDS in Indonesia is concentrated in clinical therapy by using a combination of antiretroviral therapy (ART) to optimize efficacy and reduce the likelihood of developing a drug resistance (Ministry of Health of the Republic of Indonesia, 2016).



There has not been any published research on ART cost carried out in Indonesia, however providing free ART during lifetime of each HIV-infected individual requires a huge amount of funding. In addition, large sections of population especially in developing countries still rely on a broader, safer and also cheaper repertoire of herbal medicine (Wachtel-Galor and Benzie, 2011).

Since the ancient past, the Indonesian traditional herbal medicines, or *jamus*, have been known and practiced in the Indonesian community to maintain good health and to treat diseases (Elfahmi et al., 2014).

Of many *Phyllanthus* species from Euphorbiaceae family that are widely distributed in most tropical countries, only a few have been studied and indicated to possess potential benefits in clinical practice (Dirjomuljono and Tjandrawinata, 2011).

Scientific studies have showed that extracts and purified isolated compounds of *Phyllanthus niruri* possessed antiviral effects against herpes simplex virus (HSV), dengue virus (DENV), hepatitis B and HIV reverse transcriptase enzyme (Naik and Juvekar, 2003; Ogata et al., 1992). In addition, *Phyllanthus niruri* exhibited immunostimulator (Bagalkotkar et al., 2006; Choudhari et al., 2011), and hepatoprotector (Chatterjee and Sil, 2006; Harish and Shivanandappa, 2006; Velusami et al., 2011) effects. Therefore, this study aimed to determine the effectiveness of a combination between the first line of ART and *Phyllanthus niruri* extract, compared to ART only in HIV patients.

## METHODS

This study was a quasi-experimental trial on 28 stage 2 and 3 treatment naïve HIV patients at Dr. Ramelan Naval Hospital, Surabaya and Sidoarjo General Hospital, Sidoarjo, East Java Province, Indonesia. The study was carried out from September 2013 to March 2015.

The research ethics approvals were acquired from the Human Research Ethics Committee at Hang Tuah University (No. 04/M/DU/KEPUHT/IX/2013) and Dr. Ramelan Naval Hospital, Surabaya (No. 65/EC/KERS/2013).

The purpose, procedure and conditions of the study were explained beforehand to the patients who met the inclusion criteria. All study participants agreed not to take



any vitamin or other herbal medicine during the study period. A written consent was obtained from each patient who agreed to participate voluntarily in the study.

The absolute CD4 cells count and CD4 percentage were measured with immunofluorescence analysis using flow-cytometry (World Health Organization, 2007) using BD FACSCalibur™ (Fluorescence Activated Cell Structure) count. The liver function tests were carried out according to the International Federation of Clinical Chemistry (IFCC) recommendation using Dimension® RxL® Max, Siemens. All laboratory tests were performed at the Clinical Pathology Laboratory, Dr. Soetomo General Hospital, Surabaya. The demographic characteristics and adherence to therapy were evaluated using questionnaire.

The intervention group was provided with a combination of the first-line ART and capsules of *Phyllanthus niruri* extract for six months, while the control group was provided with the first-line ART and placebo for six months. The intervention group took two capsules of *Phyllanthus niruri* extract (each contained 50 mg extract of *Phyllanthus niruri*) three times a day, 15 – 30 minutes after meal, before taking ART. The control group took two capsules of placebo contained 50 mg of *Amylum manihot* three times a day. The *Phyllanthus niruri* extract and placebo capsules were produced by the same company and provided in the same weight, shell color, and bottle.

## RESULTS

**Table 1 – Comparison of clinical and laboratory tests between intervention and control groups**

Characteristics		Intervention n = 15	Control n = 13	Test results (2-sided)
		No (%)	No (%)	
Absolute CD4 cells count	before treatment	229.7 (66.9)	216.2 (57.7)	Indep t-test, p = 0.576
	after 6 months	315.9 (101.3)	241.7 (60.9)	Indep t-test, p = 0.030

Twenty-eight HIV patients were participated in this study. The mean of age in the control group was significantly older than that in the treatment group (2-sided independent t-test, p = 0.039). There was not any other significant difference in demographic characteristics, clinical, adherence to therapy, and laboratory test



results before treatment between intervention and control groups (Table 1 and Table 2).

The absolute CD4 cells count data were normally distributed and had a homogenous variance. The 2-sided independent t-tests showed there were differences in absolute CD4 cells count ( $p = 0.030$ ) after six months of therapy between intervention and control groups. The intervention group significantly had higher mean of absolute CD4 cells count (315.9 cells/ $\mu\text{L}$ ) compared to control group (241.7 cells/ $\mu\text{L}$ ), and had higher CD4% (19.5%) compared to control group (12.7%) after six months of therapy.

## DISCUSSION

This was the first report of the effectiveness of a combination of the first line ART and *Phyllanthus niruri* extract for HIV patients. The increase of absolute CD4 cell counts in the intervention group was due to immunostimulator and reverse-transcriptase inhibitory effects of *Phyllanthus niruri*. Several active phytochemicals in *Phyllanthus niruri* were flavonoids, alkaloids, terpenoids, lignans, polyphenols, tannins, coumarins and saponins. Coumarins and repandusinic acid (hydrolysable tannins) inhibited the reverse-transcriptase enzyme and HIV-1 replication (Kostova et al., 2006; Ogata et al., 1992).

Phenolic compounds were known to demonstrate inhibitory action in the HIV replication, from fusion, adsorption, reverse-transcription, integration and protein cleavage (Hassan Khan and Ather, 2007). Terpenoid compounds were known to have anti-HIV activity (Chinsembu and Hedimbi, 2009), while flavonoids showed immunostimulator effect by increasing the phagocytosis activity of macrophage and stimulating activation of effector cells such as lymphocytes and macrophages to release cytokines, interleukins and tumor necrosis factor alpha (TNF-alpha) (Zalizar, 2013).

Although herbal medicinal products are widely considered to be of lower risk compared to synthetic drugs, they are not completely excluded from the possibility of having toxic or other adverse effects (De Smet, 2004). Deficiencies such as under-reporting of adverse reactions, lack of toxicological information on herbs, and the

quality of the reported information present challenges when signals of safety concern arise (Asare et al., 2011).

We suggested a randomized clinical trial with bigger sample size to be carried out with the same purpose as this study.

## CONCLUSION

The combination of the first line of ART and *Phyllanthus niruri* extract was more effective in increasing the absolute CD4 cells count compared to the administration of ART alone in HIV patients.

## ACKNOWLEDGEMENTS

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