





# **TERM OF REFERENCE**

## THE 6<sup>th</sup> ICPAPS -The 3<sup>rd</sup> ASEAN PHARMNET 2019

Royal Ambarrukmo Hotel, Yogyakarta, Indonesia November 14 - 15, 2019



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### **KEYNOTE SPEECH**

Keynote speaker : Prof. Dr. Ali Ghufron Mukti Speech theme : "Exploring the Local Wisdom for Advanced Pharmacy Research and Education"

### PLENNARY SYMPOSIUM

Plenary speaker 1	: Fe-Lin Lin Wu, PhD (Association of School of Pharmacy)
Plenary speaker 2	: Prof. Dr. Taro Kawai, MD (NAIST Japan)
Plenary speaker 3	: Dr. Hanna Engelke (LMU Germany)
Plenary speaker 4	: Prof. Dr. Subagus Wahyuono, MS., Apt (Universitas Gadjah Mada)
Plenary speaker 5	: Assoc. Prof. Surakit Nathisuwan (ASEAN PharmNET Representative)
Plenary speaker 6	: Raymond Tjandrawinata, PhD (Dexa Medica)

Parallel invited speakers:

- a. Pharmacy Education, and Social and Administrative Pharmacy, Clinical Pharmacy (PESC)
- b. Pharmaceutics & Drug Delivery System (PDDS)
- c. Herbal Medicine and Natural Products (HMNP)
- d. Pharmacology, Pharmaceutical Chemistry and Pharmaceutical Biotechnology (PPCP)

Invited speakers are requested from all members of ASEAN PharmNET

### PARTICIPANTS

Participants are expected to come from a variety of backgrounds including academic institutions, pharmaceutical industries, hospitals, community pharmacies from Indonesia and overseas either as active or passive participants. The target number of participants is around 300 people with 100 papers for oral presentation and 80 papers for poster presentation.

### PAPER TOPICS

Accepted papers for oral or poster presentation are those in various topics including:

- Pharmacy Education, and Social and Administrative Pharmacy, Clinical Pharmacy (PESC)
- Pharmaceutics & Drug Delivery System (PDDS)
- Herbal Medicine and Natural Products (HMNP)
- Pharmacology, Pharmaceutical Chemistry and Pharmaceutical Biotechnology (PPCP)

Selected full paper presented in ICPAPS 2019 will be published in Indonesian Journal of Pharmacy (indexed by Scopus), Journal of Management and Pharmacy Practice (nationally accredited), or Traditional Medicine Journal (nationally accredited).

### **TENTATIVE SCHEDULE**

### Day 1, 14 November 2019

Time	Event	Venue
07.00 - 08.30	Registration	
08.30 - 09.30	Opening Ceremony	
09.30 - 10.15	Keynote speaker: Prof. Ali Ghufron Mukti	
10.15 - 10.45	Coffee break	
10.45 - 11.15	Plenary talk 1: Fe-Lin Lin Wu, PhD President of AASP (Asian Association of Schools of Pharmacy)	Main Hall
11.15 – 11.45	Plenary talk 2: <b>Prof. Dr. Taro Kawai, MD</b> Nara Institute of Science and Technology (NAIST Japan)	
11.45 – 12.15	Plenary talk 3: <b>Dr. Hanna Engelke</b> Ludwig-Maximilian-University of Munich <i>(LMU)</i>	
12.15 – 13.30	Lunch break and Opening of Jamu Festival "Menjamu-Dijamu"	

Time	Hall 1 PESC	Hall 2 PESC	Room 1 PDD	Room 2 HMNP	Room 3 PPCP	Room 4 PPCP	Poster Hall
13.30 – 13.55	Invited speech: Andi Hermansyah, Ph.D,Apt (Universitas Airlangga)	Invited speech: <b>Prof. Chheang</b> <b>Sena</b> (University of Health Science)	Invited speech: <b>Dr. Muhammad</b> <b>Faiz Othman</b> (Universiti Teknologi Mara)	Invited speech: Assoc. Prof. Dr. Jamia Azdina Jamal (Universiti Kebangsaan Malaysia)	Invited speech: <b>Prof. Yoshihiro</b> <b>Hayakawa, Ph.D.</b> (University of Toyama)	Invited speech: Yulia Yusrini Djabir, Ph.D., Apt. (Hasanuddin University)	
13.55 – 14.20	Invited speech: Assoc. Prof. Tu Anh Nguyen, Ph.D. (Ho Chi Minh University of Medicine and Pharmacy)	Invited speech: Hidayah Kurniawati, M.Sc., Apt. (Universitas Muhammadiyah Surakarta)	Invites speech: <b>Dr. Mahdi Jufri,</b> <b>M.Si.</b> (Universitas Indonesia)	Invited speech: <b>Dr. Raphael Aswin</b> <b>Susilowidodo, M.Si.</b> (PT. Soho Global Health)	Invited speech: Prof. Dr. Mohamed Mansor bin Manan (Universiti Teknologi Mara)	Invited speech: Assoc. Prof. Kusnandar Anggadiredja (Bandung Institute of Technology)	
14.30 - 14.40	PESC-1	PESC-6	PDD-1	HMNP-1	PPCP-1	PPCP-6	
14.40 – 14.50	PESC-2	PESC-7	PDD-2	HMNP-2	PPCP-2	PPCP-7	
14.50 - 15.00	PESC-3	PESC-8	PDD-3	HMNP-3	PPCP-3	PPCP-8	
15.00 - 15.10	PESC-4	PESC-9	PDD-4	HMNP-4	PPCP-4	PPCP-9	
15.10 - 15.20	PESC-5	PESC-10	PDD-5	HMNP-5	PPCP-5	PPCP-10	
15.20 - 15.30	O and A	O and A	O and A	O and A	O and A	Q and A	
15.20 - 15.40	Q anu A	Q and A	Q and A	Q anu A	Q and A	Q and A	

15.40 - 15.50	Coffee Break	Coffee Breek	Coffee Breek	Coffee Break	Coffee Breek	Coffee Break	
15.50 - 16.00	Conee Break						
16.00 - 16.10	PESC-11	PESC-16	PDD-6	HMNP-6	PPCP-11	PPCP-16	
16.10 - 16.20	PESC-12	PESC-17	PDD-7	HMNP-7	PPCP-12	PPCP-17	
16.20 - 16.30	PESC-13	PESC-18	PDD-8	HMNP-8	PPCP-13	PPCP-18	
16.30 - 16.40	PESC-14	PESC-19	PDD-9	HMNP-9	PPCP-14	PPCP-19	
16.40 - 16.50	PESC-15	PESC-20	PDD-10	HMNP-10	PPCP-15	PPCP-20	
16.50 - 16.00	O and A	Q and A	O and A	O and A	Q and A	O and A	
16.00 - 17.10	Q and A	Q and A			Q and A	Q and A	
17.10 - 17.20							Dector Judging
17.20 - 17.30							Poster Judging

17.00 - 18.00	Dean's meeting	
19.30 – 22.00	Welcome Dinner	

Time	Hall 1 PESC	Hall 2 PESC	Room 1 PDD	Room 2 HMNP	Room 3 PPCP	Room 4 PPCP	Poster Hall
08.00 - 08.10	PESC-21	PESC-26	PDD-11	HMNP-11	PPCP-21	PPCP-26	
08.10 - 08.20	PESC-22	PESC-27	PDD-12	HMNP-12	PPCP-22	PPCP-27	
08.20 - 08.30	PESC-23	PESC-28	PDD-13	HMNP-13	PPCP-23	PPCP-28	
08.30 - 08.40	PESC-24	PESC-29	PDD-14	HMNP-14	PPCP-24	PPCP-29	
08.40 - 08.50	PESC-25	PESC-30	PDD-15	HMNP-15	PPCP-25	PPCP-30	
08.50 - 09.00		Q and A	PDD-16	O and A	Q and A	O and A	
09.00 - 09.10	Q and A	Q and A	Q and A	Q and A	Q and A	Q and A	
09.10 - 09.20	Coffee break	Coffee break	Q and A	Coffee break	Coffee break	Coffee break	
09.20 - 09.30	PESC-31	PESC-36	Coffee break	HMNP-16	PPCP-31	PPCP-36	
09.30 - 09.40	PESC-32	PESC-37	Conee break	HMNP-17	PPCP-32	PPCP-37	
09.40 - 09.50	PESC-33	PESC-38	Invited Speech:	HMNP-18	PPCP-33	PPCP-38	
09.50 – 10.00	PESC-34	PESC-39	Rahmat, M.Si., Apt. (Pancasila University)	HMNP-19	PPCP-34	PPCP-39	
10.00 - 10.10	PESC-35	PESC-40	Invited Speech:	HMNP-20	PPCP-35	PPCP-40	
10.10 - 10.20	Q and A	Q and A	Miatmoko, Ph.D., Apt. (Universitas Airlangga)	Q and A	Q and A	PPCP-41	

Day 2. 15 November 2019

10.20 – 10.30			Invited Speech: <b>Dr. Fikri Alatas,</b> <b>M.Si Apt.</b> (Jendral Ahmad Yani University)			Q and A	
10.30 - 10.40			-	Invited Speech:			-
10.40 – 10.50	Invited Speech: <b>Prof Dr. Chua</b> <b>Siew Siang</b> (Taylor's University)	Coffee break	Invited Speech: <b>Dr. Dewi</b> <b>Setyaningsih, Apt.</b> (Sanata Dharma University)	Assoc. Prof. Ngoc Van Thi Nguyen, Ph.D. (Can Tho University of Medicine and Pharmacy)	Invited Speech: <b>Dr. Eelco Ruijter</b> (Vrije Universiteit Amsterdam)		
10.50 - 11.00	Invited speech:			Invited speech:	Invited speech:		
11.00 - 11.10	Auliya A. Suwantika, Ph.D. (Universitas Padjadjaran)		PDD-17	<b>Prof. Dr.phil.nat.</b> <b>Sudarsono, Apt.</b> (Universitas Gadjah Mada)	<b>Dr. Ary Yanuar,</b> <b>M.Si.</b> (Universitas Indonesia)	Coffee break	
11.10 - 11.20	PESC-41	PESC-46	PDD-18		Invited Speech:		
11.20 - 11.30	PESC-42	PESC-47	PDD-19	<b>Dr. Oeke Yunita,</b> <b>S.Si., M.Si., Apt.</b> (Universitas Surabaya)	Dr. Nanik Sulistyani, M.Si., Apt. (Universitas Ahmad Dahlan)		
11.30 - 11.40	PESC-43	PESC-48	PDD-20	HMNP-21	PPCP-42	HMNP-26	
11.40 - 11.50	PESC-44	PESC-49	PDD-21	HMNP-22	PPCP-43	HMNP-27	
11.50 - 12.00	PESC-45	PESC-50	O and A	HMNP-23	PPCP-44	HMNP-28	
12.00 - 12.10	Q and A	PESC-51		HMNP-24	PPCP-45	HMNP-29	

12.10 - 12.20	PESC-52	HMNP-25	PPCP-46	HMNP-30	
12.20 - 12.40	Q and A	Q and A	Q and A	Q and A	
12.40 - 12.50	Q and A	Q and A	Q and A	Q and A	Poster Judging
12.50 - 13.00					

13.00 - 14.00	Lunch break	
14.00 - 14.30	Plenary talk 4: <b>Prof. Dr. Subagus Wahyuono, MS., Apt.</b> Universitas Gadjah Mada	
14.30 - 15.00	Plenary talk 5: Assoc. Prof. Surakit Nathisuwan ASEAN PharmNET Representative	Main Hall
15.00 - 15.30	Plenary talk 6: <b>Raymond Tjandrawinata, PhD.</b> Dexa Medica	
15.30 - 16.00	Award presentation and Closing ceremony	

### **ONLINE REGISTRATION**

For registration, please check the following site: http://conference.farmasi.ugm.ac.id/



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Yogyakarta, Indonesia November 14 - 15, 2019

Yogyakarta, August 30, 2019

Subject : Letter of Invitation Ref. number : 36.30.08/IC/Sec./Invi./2019

Dr. Oeke Yunita, S.Si., M.Si., Apt. Faculty of Pharmacy Universitas Surabaya

Dear Dr. Yunita,

We are pleased to inform you that the Faculty of Pharmacy Universitas Gadjah Mada (UGM) will organize the 6<sup>th</sup> International Conference on Pharmacy and Advanced Pharmaceutical Sciences (ICPAPS 2019) in collaboration with the 3<sup>rd</sup> International Conference on Pharmacy Education and Research Network of ASEAN (ASEAN PharmNET) on November 14-15, 2019, in Yogyakarta, Indonesia. The Conference is themed "Exploring the Local Wisdom for Advanced Pharmacy Education and is co-hosted by ASEAN PharmNET member universities in Indonesia.

On behalf of the Organizing Committee, it is with great pleasure to invite you to be one of the invited speakers for the ICPAPS-ASEAN PharmNET 2019 on November 15, 2019. Due to a budget constraint, please be informed that the Organizing Committee will not cover the accommodation and the travel expenses to and from Yogyakarta. We offered 50% waive for the conference fee for each invited speaker.

Enclosed is the term of reference with a tentative program overview for your consideration. Should you have any questions or need further assistance, please do not hesitate to contact us.

We are very much looking forward to welcoming you in Yogyakarta.

Sincerely,



Professor Zullies Ikawati, Ph.D., Pharmacist Chair of the ICPAPS-ASEAN PharmNET 2019 Organizing Committee

### THE SECRETARIAT

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### Faculty of Pharmacy Universitas Gadjah Mada

With high appreciation presents

## Certificate

to

Ceke Yunita

as Presenter

ùn.

### THE 6<sup>th</sup> INTERNATIONAL CONFERENCE ON PHARMACY AND ADVANCED PHARMACEUTICAL SCIENCES & THE 3<sup>rd</sup> INTERNATIONAL CONFERENCE ON PHARMACY EDUCATION AND RESEARCH NETWORK OF ASEAN

Accredited by Indonesian Pharmacist Association (PP IAI No. 126/SK-SKP/PP.IAI/IV/2019): Participant: 10 credits; Presenter: 3 credits; Speaker: 4.5 credits; Moderator: 1.5 credits; Committee: 1.5 credits

Prof. Dr. Zullies Ikawati, Apt. Chair of the ICPAPS-ASEAN PharmNET 2019 Organizing Committee

Yogyakarta, November 14 - 15, 2019

Prof. Dr. Agung Lindro Nugroho, M.Si., Apt. Dean of Faculty of Pharmacy Universitas Gadjah Mada

### Signaling Pathways-based Approach for Identifying Mechanisms of Herbal Medicines

### Oeke Yunita

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### Abstract

Indonesian Herbal Medicine (IHM) has been recognized as one of the most important strategies in complementary and alternative medicine. In Indonesia, many of this herbal knowledge were passed down from one generation to the next through oral tradition and daily rituals. Nowadays, IHM is developed to meet the requirement of Indonesian Healthcare System. However, understanding its mechanism of action in the treatment of disease remains unknown due to its numerous complex compound mixtures that often bound transiently to multiple therapeutic targets. Investigating the mechanism of action of the IHM formula is key to the modernization of IHM. Identifying which are the active compound(s) of IHM formulas, which biological entities they target, and through which signaling pathway(s) they act to modify disease symptoms, can be studied with multiple approaches including network pharmacology, pharmacogenomics, proteomics, and metabolomics. The concept of network pharmacology is built on the belief that targeting multiple nodes in interconnected molecular systems rather than individual molecules, which could lead to better efficacy and fewer adverse effects. A network pharmacology approach can integrate prediction of ingredients, target exploration, network construction, module partition and pathway analysis. This approach successfully helped to identify several active ingredients of IHM, interacting with several important key targets. Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis indicated that IHM-regulated pathways were mainly classified into several systems. The present work may help to illustrate the mechanism(s) of action of IHM, and it may provide a better understanding of herbal formula effects.

Keywords: action mechanism, Indonesian Herbal Medicine, pathways analysis, targets prediction

### Introduction

Herbs' complexity as biological systems with a wealth of chemical compounds that can work in concert with different therapeutic target proteins gives them an advantage in disease therapy. Understanding the molecular and system-level mechanisms of herbal activity can be challenging due to the complexity of the chemical components found in herbs (Huang et al., 2013; Liu et al., 2013).

Physical and functional interactions govern biological systems, which in turn excite and coordinate molecules in a network to allow the organism to react to its surroundings. The medication should be able to restore the network to its pre-disrupted state because the sickness can do so. In biological systems, network analysis is a crucial method because it can map intricate relationships in cells, tissues, and biological systems, which can then be utilized as a foundation for the development of new medications, particularly when examining pharmacological reactions (Tatonetti et al., 2009; Engin et al., 2014).

Systems pharmacology is a method that combines pharmacology and systems biology to advance the knowledge and discovery of medicinal processes. Protein-active chemical interactions can explain how herbal medicines work and open up new avenues for the development of therapeutic approaches (Tatonetti et al., 2009; Huang et al., 2013; Liu et al., 2013). The "multiple targets, multicomponent therapeutics" paradigm, which replaces the "one target, one drug" trend in herbal pharmacology, offers a thorough and integrated examination of the effects of herbal therapies based on network analysis (Liu et al., 2013; Ru et al., 2014).

Two network levels—the compound-target protein (compound-target network) and the target protein-pathway (target-pathway network)—can be used to study and map the mechanism of action of herbs (Huang et al., 2013; Liu et al., 2013). The graph mining concept, which finds subgraphs as a result of data reduction and comprises representative data, is actually implemented in network analysis. In addition, this idea can be used to spot trends in a graph. The analysis results display can indicate the presence of nodes and edges, where the nodes can be plants, plant chemical content in the herbal network, clinical symptoms in the phenotypic network, or genes and gene products in the biomolecular network. Numerous factors are displayed by network topology, including closeness, which displays the average length of the shortest paths to reach every other node in the network, betweenness, which displays the number of shortest paths through the node,

and connectivity degree, which displays the number of interactions between a node and its directly neighboring nodes. Figure 1 provides a clearer picture of this structures (Huang *et al.*, 2013; Shao & Bo, 2013).



Figure 1. Some terms and measurements in network analysis (Shao & Bo, 2013)

Several herbal activity mechanisms have been studied using a systems pharmacology approach, starting from a single herb, namely licorice (*Glycyrrhiza glabra*) for cough suppressant and immunomodulator (Ru et al., 2014), Indian ginseng (*Withania somnifera*) for immunomodulator (Chandran & Patwardhan, 2017), or a combination of several herbs (polyherbals) for example Ginseng, *Codonopsis pilosula*, *Panax quinquefolium*, *Radix pseudostellariae*, *Radix astragali*, *Rhizoma atractylodis macrocephalae*, *Dioscorea opposita*, and *Radix glycyrrhiz* resp. in the formula as well as *Radix paeoniae alba*, *Angelica sinensis*, *Polygonum multiflorum*, and *Rehmannia glutinosa* in the formula (Liu et al., 2013); *Hypericum perforatum* and *Semen nelumbinis* (Huang et al., 2013).

In this research, network pharmacology analysis was carried out on herbal ingredients combined in a formula from Indonesian Herbal Medicine, called as Scientific Jamu for treating gastric pain or dyspepsia. This formula consists of 4 herbal medicines such as ginger (*Zingiber* 

officinale), sembung (Blumea balsamifera), black seed (Nigella sativa), and turmeric (Curcuma domestica).

### **Research Method**

### **Network-Pharmacology Analysis**

Network development was carried out using metabolite profile data from metabolite characterization as well as several databases related to compounds in plants (PubChem, Universal Natural Products Database), databases related to target proteins (UniProt, ChEMBL), databases related to reaction pathways related to the immune system (Kyoto Encyclopedia of Genes and Genomes' KEGG pathway database (KEGG)), as well as the protein interaction database (STRING) adapted from Chandran and Patwardhan (2017). Network construction was carried out with Cytoscape 3.5.0 software. with the concept of graph mining. The construction results show the topology parameters of the nodes, which include connectivity degree, betweenness centrality, and closeness centrality.

### **Result and Discussions**

In our initial experiments, we choose one formula from Indonesian Herbal Medicine, called as Scientific Jamu for treating gastric pain or dyspepsia. This formula consists of 4 herbal medicine such as ginger (jahe), sambong (sembung), black seed (Jintan hitam), and turmeric (kunyit) (Figure 2).



Figure 2. Indonesian scientific jamu formula for treating gastric pain or dyspepsia (Kementerian Kesehatan RI, 2016)

This approach successfully helped to identify 33 active ingredients of herbal component in the formula, in the yellow box, interacting with 89 important key targets, in the blue box, which contributed in 120 kind of diseases, in the red box, as seen in Figure 3. Several compounds in plants contributed significantly in interaction with several protein targets, while most of these proteins contributed in paraganglioma and gastrointestinal stromal tumor.



Figure 3. Result analysis on Indonesian scientific jamu formula for treating gastric pain or dyspepsia

According to Online Mendelian Inheritance in Man (OMIM) database, Gastrointestinal stromal tumors are mesenchymal tumors found in the gastrointestinal tract that originate from the interstitial cells. This finding can help us to predict the new effect of this formula for being an anticancer, not only for treating gastric pain.

For further enrichment analysis, we use Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway. Figure 3 shows that EPO or Erythropoietin is one of target protein which contribute to Paraganglioma and gastrointestinal stroma tumor, and based on pathway of malignant paraganglioma from KEGG, this protein is involved in this pathway for regulation of erythrocyte proliferation, that's useful for cancer cell. EPO may also bind EPO R expressed on the surface of

cancer cells and may elicit tumor growth via cell proliferation, protection from apoptosis, and/or angiogenesis.

#### Conclusions

Network pharmacology approach successfully helped to identify several active ingredients of herbal formula, interacting with several important key targets. This approach may help to illustrate the mechanism(s) of action of herbal formula, and it may provide a better understanding of herbal formula effects. This approach can also help to predict new effect of the herbal formula.

### Reference

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