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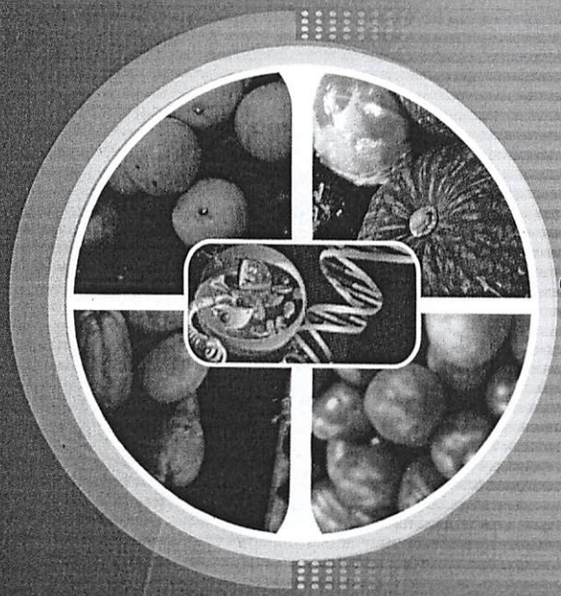
50 UAJY EMAS

PROCEEDING



1st International Seminar on
"Natural Resources Biotechnology: From Local to Global"

September 8th – 9th 2015
Faculty of Biotechnology
Universitas Atma Jaya Yogyakarta

Seminar Committee

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Welcome Speech
Chair of the Seminar Committee

Distinguished Guests,
Honorable Speakers,
Ladies and Gentlemen,

It is a great pleasure to welcome all of you to the International Seminar "Natural Resources: From Local to Global". The Faculty of Biotechnology of Universitas Atma Jaya Yogyakarta runs this seminar to commemorate the 50th Anniversary of the Universitas Atma Jaya Anniversary and the 25th Anniversary of the Faculty of Biotechnology. Your presence is your present for the anniversary of our university and faculty as well.

The Anniversary is not the only reason to run this seminar. A greater reason is behind the seminar. Indonesia is rich in biodiversity. It is a challenge for us, as scientist, to maintain the biodiversity and to develop the potential of the biodiversity for the common good. Through this seminar, the scientific research on Indonesian biodiversity can be shared and probably the finding of the new research can inspire us for further exploration. Therefore, the seminars goal is to facilitate the spread of the research on local potential of biodiversity to the global level. Hopefully, it can attract more researchers to explore the wealth of local biodiversity.

The committee invites speakers who are expertise in the research concerning biodiversity. Our invited speakers are Assoc. Prof. Dr. Michael Murkovic from Graz University of Technology Austria (food scientist), Assoc.Prof. Worawidh Wajjwalku from Kasetsart University Bangkok Thailand (Veterinary disease biotechnology), Dr. Kathryn McMahon from Edith Cowan University Australia (Seagrass biotechnology), Prof. Marco Nemesio E. Montano, PhD from University of the Philippines (Seaweed biotechnology), Prof. Jun Kawabata from Hokkaido University Japan (food biochemist), Endang Semiarti, PhD from Universitas Gadjah Mada, Indonesia (Plant biotechnology), Ign. Pramana Yudha, PhD from Universitas Atma Jaya Yogyakarta (Conservation genetics), Dr Machmud Thohari from Technical Team for Environmental Biosafety, Ministry of Enviroment & Forestry Indonesia (Environmental Biosafety), Dr Harvey Glick from Asia Regulatory Policy & Scientific Affairs Monsanto Company (Regulatory Policy & Scientific Affairs Monsanto). It is a good opportunity to learn from the speakers to enhance and to update our knowledge. I hope this seminar is of benefit to all of us.

In conclusion, I wish you a successful seminar and a pleasant stay in Yogyakarta.

With kind regard
Coordinator of conference program

Dr. rer. nat. Yuliana Reni Swasti, S.TP., MP.

WELCOME SPEECH
DEAN
FACULTY OF BIOTECHNOLOGY
UNIVERSITAS ATMA JAYA YOGYAKARTA

Distinguished Guests,
Honorable Speakers,
Ladies and Gentlemen,

On behalf of the Faculty of Biotechnology, Universitas Atma Jaya Yogyakarta and the Committee of the International Seminar, I would like to first of all to extend our heart-felt thanks for your presence at this Seminar. This seminar is so significant in a sense that it focuses on natural resources with local content but by utilizing biotechnology they will become global and worldwide products and services as well.

Biotechnology has been developed very rapidly and it is believed to be "a new wave in the economic world". Biotechnology has contributed in all aspects of humans' life, such as food production, health, industry, environment, etc. The role of biotechnology for the betterment of human beings, however, is still need to be improved. Indonesia, with its huge biodiversity, has a potency to develop and applied biotechnology nationwide.

The role of biotechnology has increased rapidly. Many are believed that biotechnology has become an integral part of modern industries with high economic values. On the other hand, it needs to be closely managed in order to avoid its negative impacts. The are some example of negative impacts with relate to biotechnology application, such as intellectual property rights, genetically modified organisms (GMOs), environmental degradations, biodiversity issues, indigenous people knowledge, biosafety, etc.

The Seminar covers topics such as: Functional Foods, Food Biotechnology, Biopharmacy, Health/Medical Biotechnology, Environmental Biotechnology, Legal Aspect of Biotechnology, Bioinformatics, and Social-Economic Aspects of Biotechnology. This Seminar will be presented nine (9) invited speakers with different topics and expertise. There will be some papers and posters to be presented also in this Seminar from some participants from the Philippines and Indonesia.

Henceforth, in commemorating its 50th anniversary Universitas Atma Jaya Yogyakarta (UAJY) and 25th anniversary of Faculty of Biotechnology, Universitas Atma Jaya Yogyakarta (UAJY) on September 2015, it is worthy and appropriate to explore the newest innovations in the field of research and development of biotechnology to be applied in many aspects for the betterment of human beings. The Seminar takes this opportunity to discuss and hopefully find ways to solve problems faced by human beings in the world.

I would like to take this opportunity to express my sincere thanks and gratitude to the Committee and in particular to the honorable speakers. Before closing this remarks, allow me to ask the Rector of Universitas Atma Jaya Yogyakarta to open this Seminar officially.

Finally, this is an opportune time for me to wish you all in the two (2) fruitful days of interesting and beneficial programs and hope you have a pleasant stay in Yogyakarta.

Thank you very much and may God bless us all. Amen.

Yogyakarta, 8 September 2015

Dean

Drs. B. Boy Rahardjo Sidharta, M.Sc

Brief Contents

Molecular Aspects of Zinc Intake (Zn) and Selenium (Se) on Glycosylated hemoglobin (HbA1c) in patients with type 2 Diabetes Mellitus (DMT2)

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Abstract

Diabetes mellitus (DM) is a metabolic disease characterized by hyperglycemic. HbA1c is the result of the examination for glycemic control. Zinc and Selenium are metaloenzim factors, play a role in the mechanism and regulation of insulin synthesis. This study aims to explore the relationship between zinc and selenium with HbA1C in patients with type 2 diabetes mellitus. Cross sectional study to patients with type 2 diabetes mellitus. Samples numbered 108 people conducted at several hospitals in Bandung from years 2011 to 2013. The sample was done by purposive sampling. Zinc and Selenium are collected by SQFF. HbA1c is measured by the method of affinity chromatography. Data were analyzed by Fisher's Exact test and Spearman correlation ($p < 0.05$). The study showed that there was a significant relationship between Zinc, Selenium and HbA1c were significantly ($p < 0.001$). There is a relationship between Zinc and Selenium with HbA1c, so the management of diet with intake of Zinc and Selenium is needed in the regulation of patients with type 2 diabetes mellitus.

Keywords: Intake Zinc, intake Selenium, levels of HbA1c

1. INTRODUCTION

Diabetes Mellitus (DM) is one of the chronic degenerative diseases that the prevalence continues to increase by year to years.[1] DM is also a group of metabolic diseases by characteristies chronic hyperglycemia due to a defect in insulin secretion, insulin or both.[2] The type 2 diabetes pathogenesis based on impaired insulin secretion by pancreatic beta cells and impaired insulin action due to insensitivity (resistance) to insulin target tissues. Shaw showed, the worldwide prevalence of diabetes in the adult population aged 20-70 years was 6.4% in 2010, affected 287 million adults and is expected to increase to 7.7% and affected 439 million adults in 2030.[3] The prevalence of DM in Indonesia is expected to increase from 5.1% in 2000 to 6.3% in the year 2010.[4] Furthermore, Missmanagement could lead to complications and increased morbidity and mortality pasien.[5] Glycosylated hemoglobin or (HbA1c) is one of the laboratory tests for blood sugar control.[6] Persistent hyperglycemia causes glycosylation of the protein hemoglobin. It is estimated by the percentage of glycosylated hemoglobin glycation of hemoglobin (HbA1c), which are used clinically since 30 years ago to assess the degree of chronic hyperglycemia in patients with mild severe of DM.[7] Its value indicates the

average level of sugar in the period of 3 months; disglycemia helpful to know the characteristics of the study population because it is simple compared to oral glucose tolerance test (OGTT). In diabetes, one percent increase in HbA1c associated with 20-30% that it would lead to increase in mortality and morbidity of the cardiovascdiseasular.[7,8]

DM management is necessary to seek the way the blood sugar levels closely to normal. The main pillars is a medical nutrition therapy. Medical nutrition therapy, or better known as diet or meal arrangements for persons with DM is a very important factor in controlling blood sugar. [9] Dietary management generally still rarely pay attention to the availability and adequacy of the trace elements and bioactives food. Dieticians tend more priority to macro-nutrients such as carbohydrates, fats and proteins .Trace minerals are important for the body, specifically in patients with type 2 diabetes. Dietary management generally still rarely pay attention to the availability and adequacy of the trace element minerals and bioactive food.

Minerals such as Zinc and Selenium including types of trace minerals, in the body there is a small amount, but it has a play very vital role.[10] This mineral belongs to a group of minerals that works as an antioxidant metaloenzim which can prevent free radicals, increase insulin receptor sensitivity, thereby potentially preventing the degenerative disease.[11]

Zinc for example is an element essential for the synthesis, storage and secretion of insulin. It is a component of several enzymes. Zinc has also an important role in maintaining the balance function of multiple networks and have an important role in modulating system imun.[12] Body's ability to synthesize and secrete insulin is affected by zinc in the body, because it is involved in the mechanism of regulation and synthesis of insulin receptors.[13]

Selenium serves as part of a protein known as Selenoprotein. Selenoproterin plays a role as a defensive mechanism to oxidative stress, to regulation of thyroid hormone activity, and for the redox status of vitamin C and other molecules. However, note that the "therapeutic window" Se limited, and the adverse effects on health may occur due to excessive intake of Se (supra nutritional) or below the level required to toxicity.[14] Selenium acts as an antioxidant and contributes in regulating cell membrane integrity and lowering the risk of oxidative damage.[16] High-Se diet can stimulate the release of glucagon, promotes hyperglycemia, or can cause excess of gluthathion peroxidase-1 and other antioxidants Selenoprotein resulting in insulin resistance and obesitas.[15] This study aims to explore the relationship between zinc and selenium with $HbA1_C$ in patients with type 2 diabetes mellitus.

2. METHODS AND MATERIALS

This study is cross sectional study design, which was implemented in January 2011 to December 2013. The experiment was conducted at several hospitals in Bandung. Research was used all patients by type 2 diabetes who did endocrine outpatients clinic at Hospital in Bandung and incorporated Diabetes Association Members (Persadia). The samples was taken as many as 108 patients. They were obtained by purposive sampling with the following inclusion criterias: Patients with type 2 diabetes who have a history of results of HbA1c, age <65 years, did not have a blood disorder,

has been getting nutrition education, without the complications of the disease, not pregnant and was willing to be the subject of research by signing informed consent.

The eating habits questionnaire was colledted by Food Frequency Questionnaire (FFQ). This data were analyzed by Nutri survey. Nutrition intake of trace minerals such Zn, Se was collected by Food Frequency Questionnaire (FFQ). HbA1c was measured by affinity chromatography method. Processing and analysis the data was used by computer software with a significance level of $p < 0.05$ and 95% confidence level. Data were analyzed in univariate and bivariate format. The corelation between independent variables and the dependent variable was analyzed by non-parametric statistical analysis the Fisher Exact, Spearman correlation ($p < 0.05$). This study has approved by ethical clearance.

3. RESEARCH RESULT

3.1 Characteristics of Samples

The study sample characteristics include age, educational background, employment, and others in this study it is presented in Table 1.

Table 1. Distribution of the characteristics of the study sample by gender

Samples Characteristics	Category by Sex					
	Boy		Girl		Total	
	n	%	n	%	N	%
Age						
<50 years	5	11,6	7	12,7	12	11,1
≥50 years	38	88,4	48	87,3	96	88,9
Education level						
Elementary	8	18,6	52	80,0	60	55,5
Higher	35	81,4	13	20,0	48	44,5
Occupation						
Work	23	53,5	64	98,5	87	80,6
Unemploy	20	46,5	1	1,5	21	19,4
Family DM History						
Yes	25	58,1	23	35,9	48	44,4
No	18	41,9	42	64,6	60	55,6
Duration suffer DM						
<5 year	19	44,2	31	47,7	50	46,3
≥5 year	24	55,8	34	52,3	58	53,7
Medical therapy						
Yes	39	90,7	59	90,8	98	90,7
No	4	9,3	6	9,2	10	9,3
Exercise (Sport)						
Yes	15	34,9	11	90,8	26	24,1
No	28	65,1	54	9,2	82	75,9
Nutritional Status						
Normal	25	58,1	28	43,1	53	49,1
Malnutrition	18	41,9	37	49,2	55	50,9

3.2 Intake of Zinc, Selenium and levels of HbA1c samples

Based on finding, Zinc intake showed it achieved at a mean of 8.3 ± 2.62 mg, with a minimum intake value of 5.2 and a maximum of 18 mg. The recommended dietary allowance level (RDA) of less than 80% by 56 (61.5%). The intake of selenium showed on the average position of 74.62 ± 15.46 ug with a minimum intake value of 41 and a maximum of 104 ug that can be seen in Table 2. The findings suggest that most of the patients were in the intake of zinc is not ideal to meet the recommended nutrient required by RDA.

Table 2. Distribution of the intake of zinc, selenium intake and levels of HbA1c samples.

Variabel	Statistical analysis		
	χ± SD	Min	Max
Zinc Intake (mg)	8,3 ± 2,62	5,2	18
Baik (≥80% RDA)	35 (38,5%)		
Kurang (80%RDA)	56 (61,5%)		
Selenium Intake (µg)	74,62 ± 15,46	41	104
Good (≥80% RDA)	91(100%)		
Less (<80%RDA)	0(0%)		
HbA1c Level (%)	8,4 ± 2,17	5,7	15,4
Controlled (≤7%)	32(35,2%)		
Uncontrolled (> 7%)	59 (64,8%)		

Based on the study of HbA1c levels showed that it achieved at the mean of 8.4 ± 2, 17 percent which the achievement of a minimum value of 5.7 and a maximum of 15.4 percent. This showed that the majority of patients are at high HbA1c levels or uncontrolled regulation.

3.3 Relationship intake of zinc and selenium intake with levels of HbA1c

Based on the data analysis of the relationship intake zinc, selenium with HbA1c levels obtained the data as it is presented in Table 3 below.

Table 3. Relationship intake of zinc and selenium intake with levels of HbA1c

Variabel	n	r	P
Zinc intake and HbA1c level	108	-0,482	0,001*
Selenium intake and HbA1c level	108	-0,863	0,001*

*) *Korelasi Spearman p<0,05*

Results of correlation analysis on samples of zinc intake patients with type 2 diabetes showed that zinc intake was significantly associated with HbA1c levels (r = -0.482, p <0.01). The present invention provided an indication of improvement zinc intake which meets the nutritional adequacy (RDA) can reduce HbA1c levels in patients with

type 2 diabetes. Selenium intake also showed significantly association with HbA1c levels ($r = -0.863$, $p < 0.05$). Results of this analysis indicated that an increased intake of selenium in accordance with the level of adequacy of the advice showed a decrease of the levels of HbA1c.

3.4 Effect of intake of zinc, selenium on HbA1c

Based on regression analysis of the effect of the intake of zinc, selenium against HbA1c levels of data obtained as follows: Levels of HbA1c = 13.6 - 0.44 (zinc intake) - 3.03 (selenium intake), with coefficient R = 0.773 or 77.3% HbA1c is determined by the intake of zinc and selenium, rest influenced by other factors, namely obedience berdiit, drug consumption, exercise, heredity, habits and eating patterns ($p < 0.001$).

4. DISCUSSION

This study has shown a significantly association between the intake of zinc with HbA1c levels, despite a weak negative relationship ($r = -0.4$). This study also showed a statistically significant association between the intake of Selenium with HbA1c levels ($p < 0.001$). These results were consistent with research conducted by Jayawardena *et al.*, 2012, that the better grades of zinc in the blood, then the individual will be in the regulatory status of DM were better, but lower when compared with the regulations on the individual non DM.[16] Song study, patients with type 2 diabetes who given pro-z (flour and zinc) for 3 months was able to reduce HbA1c levels in bermakna.[17]

Zinc (Zn) is an essential micronutrient that is needed for more than 300 different cellular processes, including DNA, protein synthesis, enzyme activity, and intracellular signaling. Require compartmentalization of cellular homeostasis Zn into intracellular organelles, which are closely regulated through the integration of transport mechanism.[18] Zinc works as an antioxidant to protect intracellular oxidation process produces free radicals which will also work as a synthesizer, storing and secreting a protective role insulin.[19] Zinc affect on damage pancreatic beta cells. Lack of zinc affects the beta cells of the pancreas in response to the call of the body to produce and secrete insulin, lowers insulin secretion and improve insulin resistance.[20] If the pancreas does not produce and secrete enough insulin in the body's glucose levels remain high, so that with continued high levels of glucose in the body of the regulation of blood sugar is not good.[21]

The role of zinc as an antioxidant is inhibition of ROS via the reduction of glucose toxicity by Zn. Zinc stimulates transcription of metallothionein. Metallothionein itself have antioxidant effects. Zinc provides protection against free radical attack immune mediators (immune-mediated free radical attack) to protect sulfhydryl groups (SH) against oxidation. Also participation in the inhibition of the production of free radicals (Haber Weiss cycle) to compete with the transition metal. Zinc contributes to stabilizing SH by protecting proteins from oxidation. It also reduces direct and radical $^{\cdot}O_2$ $^{\cdot}OH^{-}$, H_2O_2, and the level of xanthine oxidase, thereby improving mitochondrial function. This radical decline decrease lead to lipid peroxidation. Zinc also stimulates the activity of insulin promoter PDX-1, and inhibits the activity of xanthine oxidase, thus reducing lipid peroxidation. [22]

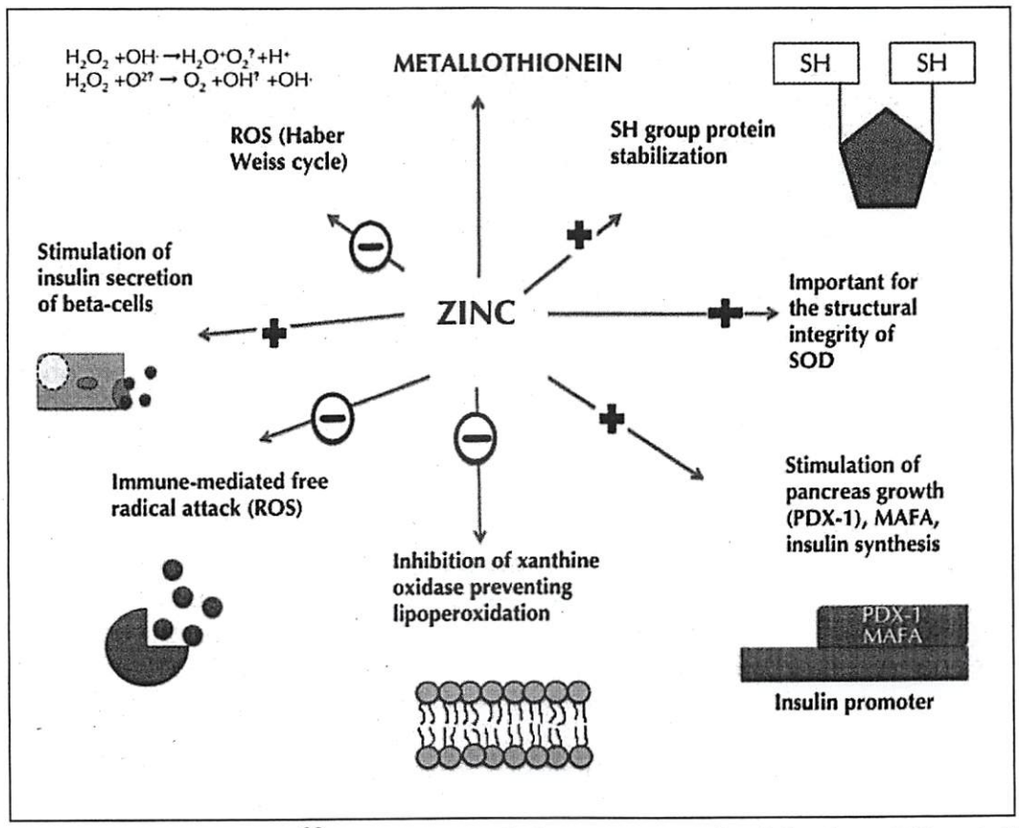

Figure 1. (Modified by [22]): The role of zinc as an antioxidant; +: Stimulation pathways.; -: Inhibition track

Research on intake of selenium (Se) in patients with diabetes, previous findings indicated that contrary to the possibility of a relationship between the level of control of diabetes and changes in the levels of this mineral. Se intake in this study was measured and the relationship between the intake and the metabolic control of diabetes, as determined by glycosylated hemoglobin (HbA1c). A negative correlation between the intake of Se and HbA1c was found. Some studies show lower serum selenium levels in the diabetic group compared with the non diabetes.[23] Subjects of research data showed that selenium plays a role in regulation of beta cell-specific target genes and potentially push the overall improvement in the function of the island Langerhans.[24] On the other hand, has shown that high levels of selenium are associated with the prevalence of diabetes.

In addition due to the intake of zinc and selenium that already meet adequacy, HbA1c levels were also influenced by other factors, including the use of pharmacological therapy. The results showed that nearly all of the samples (90%) using the pharmacologic therapy. Oral hypoglycemic drugs and injection drug given to patients with diabetes mellitus can reduce HbA1c between 05 to 3.5% .25

5. CONCLUSIONS AND RECOMMENDATIONS

This study showed an association between the intake of zinc and selenium with HbA1c levels in patients with type 2 diabetes mellitus (T2DM). It is suggested that the management of diet in patients with type 2 diabetes that it needed to pay attention to

the intake of zinc and Se in sufficiency recommended with respect to obtain a controlled HbA1c levels. Futher research It is needed to be examined gluthathion peroxidase-1 and selenoproteins other antioxidants such as Copper (cu) which resulted in insulin resistance and obesity.

6. ACKNOWLEDGEMENT

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7. AUTHOR CONTRIBUTIONS

All authors participated in data collection, participated in the study design, statistical analysis and preparation of the manuscript. All authors gave final approval for publication. There is no conflect interest with any company in this research.

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CERTIFICATE

This certificate is awarded to

Dr. dr. Indranila K.S., Sp.PK(K)

In recognition of their valuable contribution as

ORAL PRESENTER

In The 1st International Seminar on
"Natural Resources Biotechnology: From Local to Global"
organized by Faculty of Biotechnology, Universitas Atma Jaya Yogyakarta on
September 8-9th, 2015 in Yogyakarta, Indonesia.

Rector,

Dr. G. Sri Nurhartanto, SH., LLM.

Chief of Organizing Committee,

Dr. rer.nat. Yuliana Reni Swasti, S.TP., MP.