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Amsterdam, Netherlands

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Day 1 September 14, 2016

07:30-08:30 Registrations

Meeting Place 4&5

conferenceseries.com 08:30-09:00 **Opening Ceremony**

Keynote Forum

09:00-09:10 **Introduction**

09:10-09:55 **Title: Laser acupuncture therapy for temporomandibular disorders**

Wen-Long Hu, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Taiwan

09:55-10:40 **Title: Traditional Chinese Medicine (TCM) for mental diseases and wellbeing: From ancient period to today**

Zhang Zhang-Jin, The University of Hong Kong, Hong Kong

Panel Discussion

Group Photo: 10:40-10:45

Networking and Refreshment Break: 10:45-11:00 @ Pre function area

Sessions: Herbal Medicine
Traditional Chinese Medicine & Acupuncture
Traditional Medicine Today: Clinical and Research Issues
Future Directions of Traditional Medicine

Session Chair: Joshua Dunsky, Dunsky Rehabilitation and Spine Center, USA
Session Co-Chair: Zhang Zhang-Jin, The University of Hong Kong, Hong Kong

Session Introduction

11:00-11:30 **Title: Telomeres and our health**

Joshua Dunsky, Dunsky Rehabilitation and Spine Center, USA

11:30-12:00 **Title: Explore laser acupuncture's role in modern medicine**

Wen-Long Hu, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Taiwan

12:00-12:30 **Title: Binaural beat technology: Can an auditory neurophysiologic technique positively affect the cardiovascular stress response?**

MeLisa Gantt, Landstuhl Regional Medical Center, Germany

12:30-13:00 **Title: American ginseng suppresses colitis and prevents colon cancer in mice: Understanding the mechanisms and the molecules**

Lorne J Hofseth, University of South Carolina, USA

Panel Discussion

Lunch Break: 13:00-14:00 @ Restaurant & Pre function area

14:00-14:30 **Title: Ministerial fire and its clinical applications**

Rebecca Fung, University of East-West Medicine, USA

14:30-15:00 **Title: Protein profile changes among cancer patients after abnormal Savda therapy in traditional Uighur medicine**

Abulizi Abudula, Xinjiang Medical University, PR China

15:00-15:30 **Title: Protective effects of Urtica dioica seed extract in aflatoxicosis: Histopathological and biochemical findings**

Ahmet Uyar, Yuzuncu Yil University, Turkey

15:30-16:00 **Title: Comparative in vitro cytotoxic, anti-inflammatory and anti-microbiological activities of two indigenous Venda medicinal plants**

Muendi T Sigidi, University of Venda, South Africa

Panel Discussion

Networking and Refreshment Break: 16:00-16:15 @ Pre function area

16:15-16:45 **Title: The application of electroacupuncture in temporomandibular disorders**
Aurea Chun-En Kuo, Kaohsiung Chang Gung Memorial Hospital, Taiwan

16:45-17:15 **Title: Histopathological and biochemical investigations of protective role of honey in rats with experimental aflatoxicosis**
Turan Yaman, Yuzuncu Yil University, Turkey

17:15-17:45 **Title: Upper gastrointestinal bleeding, leading to blood and energy deficiency of small intestine and stomach meridians**
Yu-Chiang Hung, Chang Gung University College of Medicine, Taiwan

17:45-18:15 **Title: Decreased interleukin-4 (IL-4), IL-10 and IgE level of type I hypersensitive mice using scopoloetin isolated from noni fruit (Morinda citrifolia L)**
Yufri Aldi, Fakultas Farmasi, Indonesia

Panel Discussion

Day 2 September 15, 2016

Meeting Place 4&5

Keynote Forum

09:00-09:10 **Introduction**

09:10-09:55 **Title: When the east meet the west – Mapping of diagnoses between conventional and traditional Chinese medicine in clinical practice**
Wendy Wong, The Chinese University of Hong Kong, Hong Kong

09:55-10:40 **Title: Restoring women's vaginal health with simple use of essential oils and vegetable oils**
Mara Doljak, Aromara d.o.o., Croatia

Panel Discussion

Networking and Refreshment Break: 10:40-10:55 @ Pre function area

Sessions: Naturopathic Medicine
Entrepreneurs Investment Meet
Toxicology Studies of Plant Products
Drugs from Natural Sources

Session Chair: Domenico V Delfino, University of Perugia, Italy
Session Co-Chair: Wen-Long Hu, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Taiwan

10:55-11:25 **Title: Utilization and validation of therapy with Artocarpus tonkinensis, a tree growing in North Vietnam**
Domenico V Delfino, University of Perugia, Italy

11:25-11:55 **Title: An old and new assessment of frailty and heart failure in the elderly: The correlation between kampo-scores, "the timed 'up and go' test", and indices with echocardiography**
Kazunari Ozaki, Itami City Hospital, Japan

11:55-12:25 **Title: Development and validation of TLC method for determination of mangostin in young and ripe pericarp extract of Garcinia manogstana L. using TLC densitometry**
Dachriyanus, Andalas University, Indonesia

12:25-12:55 **Title: Traditional Japanese medicine (Kampo medicine) could be helpful for control of inflammatory bowel diseases: A case series**
Ryutaro Arita, Tohoku University Hospital, Japan

Panel Discussion

Lunch Break: 12:55-13:55 @ Restaurant & Pre function area

13:55-14:25 **Title: Antipruritic effects of hypothermic and hyperthermic stimulation on acupuncture-point for dermatitis**
Tsai Kao-Sung, China Medical University Hospital, Republic of China

14:25-14:55 **Title: Cytotoxic property of cowanin, isolated compound from the bark of Asam Kadis on T47D breast cancer cell line**
Elidahanum Husni, Andalas University, Indonesia

14:55-15:25 **Title: The study of dichloromethane fraction of fruit rinds of Asam kandis (Garcinia cowa Roxb) on TNF- α level of T47D breast cancer cell line using ELISA method**
Fatma Sri Wahyuni, Andalas University, Indonesia

15:25-15:55 **Title: Integrating TCM and allopathic medicine for global health care**
Hwee-Ling Koh, National University of Singapore, Singapore

Panel Discussion

Networking and Refreshment Break: 15:55-16:10 @ Pre function area

16:10-16:40	**Title: Building global leadership to optimize the future of traditional and alternative medicine** **Phyllis L MacIntyre,** Fairleigh Dickinson University, Canada
16:40-17:10	**Title: Leadership development via critical thinking in healthcare practice: a countermeasure to botox® popularity and global aftermaths?** **Philippe A Souvestre,** NeuroKinetics Health Services, Inc., Canada

17:10-18:00 Poster Presentations TM2016001-TM2016020

Poster Evaluation Judges:Mohammad A Randhawa, Northern Border University, Saudi Arabia
Zhang Zhang-Jin, The University of Hong Kong, Hong Kong

Day 3 September 16, 2016

Sessions: Pharmacognosy and Traditional Medicine
Holistic Medicine
Traditional Pharmaceuticals and Biologic Products
Traditional Medicine & Neurology

Session Chair: Mohammad A Randhawa, Northern Border University, Saudi Arabia
Session Co-Chair: Yibin Feng, The University of Hong Kong, Hong Kong

09:00-09:30	**Title: Neuropsychiatric effects of Nigella sativa (Black seed)** **Mohammad A Randhawa,** Northern Border University, Saudi Arabia
09:30-10:00	**Title: Drug discovery from Chinese medicines: What's new in next?** **Yibin Feng,** The University of Hong Kong, Hong Kong
10:00-10:30	**Title: Simulation training with abdominal simulators in traditional Japanese (Kampo) medicine** **Natsumi Saito,** Tohoku University Hospital, Japan

Panel Discussion

Networking and Refreshment Break: 10:30-10:45 @ Pre function area

10:45-11:15	**Title: Hands-on experience improved students' understanding and evaluation of traditional Japanese Kampo medicine** **Shin Takayama,** Tohoku University Hospital, Japan
11:15-11:45	**Title: Dysautonomia relief by acupressure** **Jung-Nien Lai,** China Medical University, Taiwan
11:45-12:15	**Title: "Lesser Yang disease" in patients with chronic fatigue syndrome/myalgic encephalomyelitis can be treated with traditional herbal (Kampo) medicine: A case series** **Takehiro Numata,** Tohoku University Hospital, Japan
12:15-12:45	**Title: Phenolic contents, antioxidant activity and spectroscopic characteristics of Pterocarpus angolensis DC stem bark fractions** **Afsatou Ndama Traoré,** University of Venda, South Africa
12:45-13:15	**Title: Prescription patterns of Chinese herbal products for patients with fractures in Taiwan: A nationwide population-based study** **Mao-Feng Sun,** China Medical University Hospital, Taiwan

Panel Discussion

Lunch Break: 13:15-14:15 @ Restaurant & Pre function area

14:15-14:45	**Title: Literature documentation about the acupuncture for the intractable disease in Japan** **Soichiro Kaneko,** Tohoku University Hospital, Japan
14:45-15:15	**Title: A case of a functionally cured HIV patient who took herbal medicine** **Willard Mushiwokufa,** Chipinge District Hospital, Zimbabwe
15:15-15:45	**Title: Summary on 100 patterns of pulse in acupuncture for accurate diagnosis and healing** **Sumita Satarkar,** Swasthya Santulan Pvt.Ltd., India
15:45-16:15	**Title: GUNIS-Traditional healers of Rajasthan, India** **Harsh Lata Bookel,** O P Jindal Global University, India
16:15-16:45	**Title: Diet and lifestyle changes and nitric oxide production** **Benjamin Dwumaa Nuako,** Pacific Health Education Centre, USA

Panel Discussion

Thanks giving & Closing ceremony

Networking and Refreshment Break @ Pre function

Yufri Aldi et al., J Tradi Med Clin Natur 2016, 5:2 (Suppl)
http://dx.doi.org/10.4172/2167-1206.C1.002

Decreased interleukin-4 (IL-4), IL-10 and IgE level of type I hypersensitive mice using scopoloetin isolated from noni fruit (*Morinda citrifolia* L)

Yufri Aldi, Elliza Nasrul, Yanwirasti, Dian Handayani and **Dachriyanus**
Fakultas Farmasi, Indonesia

An *in vivo* study of the activity of scopoletin isolated from noni fruit (*Morinda citrifolia* L.) on the level of interleukin-4 (IL-4), IL-10 and IgE in type I hypersensitive male Swiss-Webster mice has been carried out. Scopoletin was isolated from dried noni powder by soxhletation method using dichloromethane, separated by column chromatography using silica gel as stationary phase and n-hexane-ethyl acetate (1:4) as mobile phase, then purified by column chromatography using Sephadex LH20 as stationary phase and methanol as mobile phase. Type I hypersensitive male mice were obtained by ovalbumin sensitization. Animal model were divided into 5 groups: negative control group, positive control group, and scopoletin-treated group (1; 3; and 10 mg/kg). The results showed that scopoletin at doses of 1, 3 and 10 mg/kg decreased the level of IL-4 of type I hypersensitive mice significantly ($p<0.01$). The scopoletin at the dose of 10 mg/kg decreased the serum level of IL-4, IL-10, and IgE ($P<0.01$) to the normal level. The ability of scopoletin to decrease IL-4 and IgE concentration of type I hypersensitive mice to its normal state was shown by dose of 10 mg/kg BW ($p>0.05$), while for IL-10 concentration, the decrease until its normal level was shown by dose of 3 mg/kg BW ($p<0.05$).

Biography

Yufri Aldi is a Lecturer at the Faculty of Pharmacy, University of Andalas. He completed his PhD in 2013 at Andalas University. His research is in the field of Farmaco-Immunology.

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Notes:

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THE SCOPOLETIN STUDY OF FRUIT NONI (*Morinda citrifolia* L.) AS DRUG HYPERSENSITIVITY TYPE I.

Yufri Aldi, Elliza Nasrul, Yanwirasti, Dian Handayani dan Dachriyanus
Fakultas Farmasi Universitas Andalas Indonesia

ABSTRACT

Type I hypersensitive is an excessive and unexpected immune response because it would cause a damage to certain tissue immediately after the allergen exposed and entered the body. Type 1 hypersensitive reaction invoked IL-4, IL-10 and IgE.

The evaluation of scopoletin effect from mengkudu fruit (*Morinda citrifolia Linn.*) to IL-4, IL-10 and IgE in type I hypersensitive mice has been conducted. Mice were injected with ovalbumin 250 mg/kg BW intraperitoneally to induce type I hypersensitive and on the 3rd day, they were re injected subcutaneously with the same dose. Mice with type I hypersensitive reaction would be seen on the 7th day with the reddish colour on its skin after ovalbumin administration subcutaneously with dose 250 mg/kg BW.

Scopoletin was administered orally on 7th day after the appearance of type I hypersensitive reaction with dose of 1, 3, and 10 mg/kg BW for treatment group, while for control group they were administered with Physiological NaCl. On the 8th day, the serum was collected and its amount of IL-4, IL-10, and being IgE were determined by using ELISA method.

Scopoletin administration with dose of 1, 3, and 10 mg/kg BW was actually could decrease the amount of IL-4, IL-10, and IgE ($P<0,01$). The ability of scopoletin to decrease IL-4 and IgE concentration of type I hypersensitive mice to its normal state was shown by dose of 10 mg/kg BW ($p>0,05$), while for IL-10 concentration, the decrease until its normal level was shown by dose of 3 mg/kg BW ($p<0,05$).

Key Word: Mengkudu, Scopoletin, Type I Hypersensitive, IL-4, IL-10 dan IgE.

THE SCOPOLETIN STUDY OF FRUIT NONI (*Morinda citrifolia* L.) AS DRUG HYPERSENSITIVITY TYPE I.

INTRODUCTION

Originator of hypersensitivity type I reactions including protein, pollen, food, cold and dry air, dust, smoke, animal, medicine, fungi, viruses, chemicals and industrial products, and stress. Allergens can cause a wide variety of hypersensitivity type I reactions, such as bronchial asthma, allergic rhinitis, atopic dermatitis, anaphylactic shock and any others (Janeway, 2001; Dipiro, 2008).

The entry of allergens into the body caused an immune response with the formation of immunoglobulin-E (IgE) and subsequently the IgE bound on the surface of mast cells and basophil cells (Janeway, 2001; Kindt, 2007). Allergen exposure process begins with phagocytosis by macrophages. Macrophage cells will break the allergen into peptide fragments and then the fragments were ligated by mayor histocompatibillity complex (MHC) class II and carried to macrophages cell surface and subsequently presented to Th_0 cells (helper naive). Macrophage cells will release several cytokines such as interleukin-1 (IL-1) and tumor necrosis factror- α (TNF-α). T helper cell (Th) which receive signals from macrophages undergo differentiation and proliferation into Th1 and Th2 cells. Allergens also phagocyted by mastcell and basophils, then these cells will release IL-4. High levels of IL-4 caused the proliferation and differentiation of Th_0 cells toward Th2 cells. Th2 cells will release several cytokines such as IL-4 , IL-5, IL-10 and IL-13 (Burtis *et al.*, 2006). IL-4 has a direct effect on lymphocytes B and these cells differentiate and proliferate into plasma, which in turn produces IgE (Karlsson, 2994; Maizels 2005).

IL-10 is a cytokine produced by Th2 cells, CD8 T cells, lymphocytes B and macrophages. IL-10 has ability to inhibit inflammation, inhibit the process of antigen recognition by macrophages and cells dendrit with suppression of expression of MHC class II and inhibit the production of Th1 cells cytokines. IL-10 also inhibit TCD4 cell proliferation into Th1 cells, so that the higher process of proliferation to Th2 cells (Burtis *et al.*, 2006).

Two main functions of IL-10 are inhibit the production of several cytokines (TNF, IL-1, chemokines and IL-12) and inhibit the function of macrophages in helping T cell activation. Macrophage function barriers occurs because IL-10 suppress the expression of MHC class II on macrophages and reduces the expression of co-stimulatory. The final impact of the IL-10 activity is inhibit the non-specific and specific inflammatory reaction mediated by T cells, so that IL-10 also known as cytokine synthesis inhibitor factor and anti-inflammatory cytokines (Burtis, 2006; Dharma, 2015).

Repressing of IL-10 synthesis caused Th1 cells will increase INFγ production and cell proliferation and differentiation of Th1 and Th2 cells will be balance. The amount of IL-4 will decrease. INFγ also can inhibit the binding of IL-4 to its receptor on the cell plasma so the product can be inhibited IgE (Burtis *et al.*, 2006).

Previous research has been conducted against hypersensitivity type I shown scopoletin isolated from noni fruit may inhibit active cutaneous anaphylaxis reaction (Aldi *et al.*, 2010) and decrease IgE levels (Aldi *et al.*, 20012). Scopoletin was able to reduce levels of IL-4 from the male white mice who had hypersensitivity type I (Aldi *et al.*, 2015). Besides, it was also reported that scopoletin can inhibit the production of PGE2 (prostaglandin E2), TNF-α, IL-1β, IL-6 and suppresses COX-2 (Moon *et al.*, 2007; Hyung *et al.*, 2006) and hepatoprotective (Kang *et al*, 1999).

Based on this background, we tried to prove the effect of scopoletin from noni fruit (*Morinda citrifolia L.*) on levels of IL-10 in male white mice with hypersensitivity reaction type I. This study is an advanced of previous research about scopoletin effects on levels of IgE (Aldi *et al.*, 2012), and the levels of IL-4 (Aldi *et al.*, 2015) of mice with hypersensitivity type I.

MATERIAL AND METHODS

Tools and materials

The tool used were a measuring cup, animal scales, needles oral, analytical balance, mortar and stamfer, surgical scissors, a set of centrifuges, HPLC (Detector: Prominence DAD SPD-M20A, Coloumn: RP C18-Shimadzu) and a spectrophotometer IR (Perkin Elmer). Materials used were scopoletin (Aldi *et al*, 2015), distilled water, physiological saline, Na CMC, ovalbumin (Brand No. Lot.20HO763 A-5253) and Platinum Mouse IL-10 ELISA kit (eBioscience, BMS 614/2, No. 887 904).

Preparation of hypersensitivity type I animals technique

Healthy mice with 20-25 g weight were injected intraperitoneally with 250 mg/kg BW ovalbumin. On the third day, ovalbumin administrated again with the same dose given subcutaneously. Animal declared sensitive if on the seventh day given 250 mg/kg BW ovalbumin subcutaneously raised reddish color in place of injection (Aldi *et al.*, 2015).

Determination of scopoletin purity level

Extrasynthese (France) as standard compound and scopoletin isolated from noni fruit was diluted with methanol. To create a calibration curve, standard compound (Extrasynthese France) was made in different concentration of 3 mg/mL, 6 mg/mL, 12 mg mL, 24 mg/mL, 48 mg/mL.

Each sample was filtered first before it is injected into the HPLC, 20 mL of the sample were injected to the HPLC. Eluent used was methanol: aquabidest (9: 1) with a flow rate of 0.5 mL / min at room temperature, using a detector at a wavelength of 345 nm.

Administration of test compound

The treatment group consisted of five groups, namely: Group I was a normal animal, group II was mice with hypersensitivity type I (positive control) given only normal saline, group III was given 1 mg/kg BW scopoletin, group IV was given 3 mg/kg BW scopoletin and Group V was given 10 mg/kg BW scopoletin. Scopoletin directly given at the visible signs of redness place of injection.

Determination of the IL-4 levels

Levels of IL-4 was determined by Enzyme Linked Immunosorbent Assay (ELISA) method using a Platinum Mouse IL-4 ELISA kit.

Determination of the IL-10 levels

Levels of IL-10 was determined by Enzyme Linked Immunosorbent Assay (ELISA) method using a Platinum Mouse IL-10 ELISA kit.

RESULTS AND DISCUSSION

Scopoletin used in this study was isolated from previous studies (Aldi *et al.*, 2015) and gained as much as 0.01% scopoletin from noni fruit. According to the Indonesian Herbal Pharmacopoeia first edition (2008) scopoletin in noni fruit simplesia (powder) not less than 0.02%. This may be

due to differences in the place grows on plants and processes. the scopoletin obtained are still relatively small.

Scopoletin used in this study has same Rf value with scopoletin comparator (Exrtasynthase France) with the eluent n-hexane: ethyl acetate (1.5: 3.5) is 0.56 (Fig. 1).

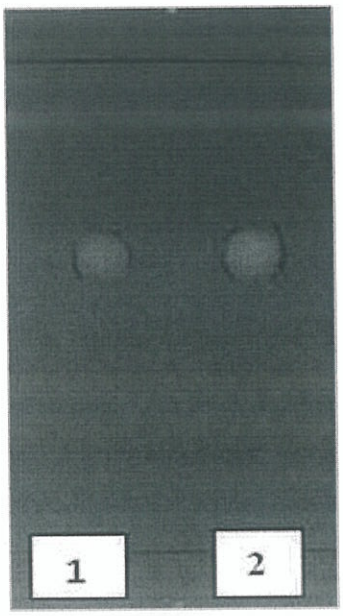

Fig. 1. Thin-layer chromatograms of scopoletin under the uv light 365 nm (1. Scopoletin isolated from noni fruit; 2. Scopoletin comparator compound (Exrtasynthase French)

Spectrum of ultraviolet data of scopoletin in Fig. 2. Scopoletin in this study proved equal to the comparator (Exrtasynthase France).

IR spectrum Examination showed scopoletin isolated from noni fruit has the same spectrum with scopoletin from Extrasyntese France and spectrum can be seen Fig. 3 and Fig. 4.

In this study, purity of scopoletin determined by HPLC, which measure the area under the curve. Scpoletin was detected at retention time (Rt) about 6.05 minutes. HPLC chromatogram

of scopoletin shown in Fig. 5. area measurement of a standard scopoletin (Extrasynthese, France) at several concentrations obtained calibration curve as shown in Fig. 6.

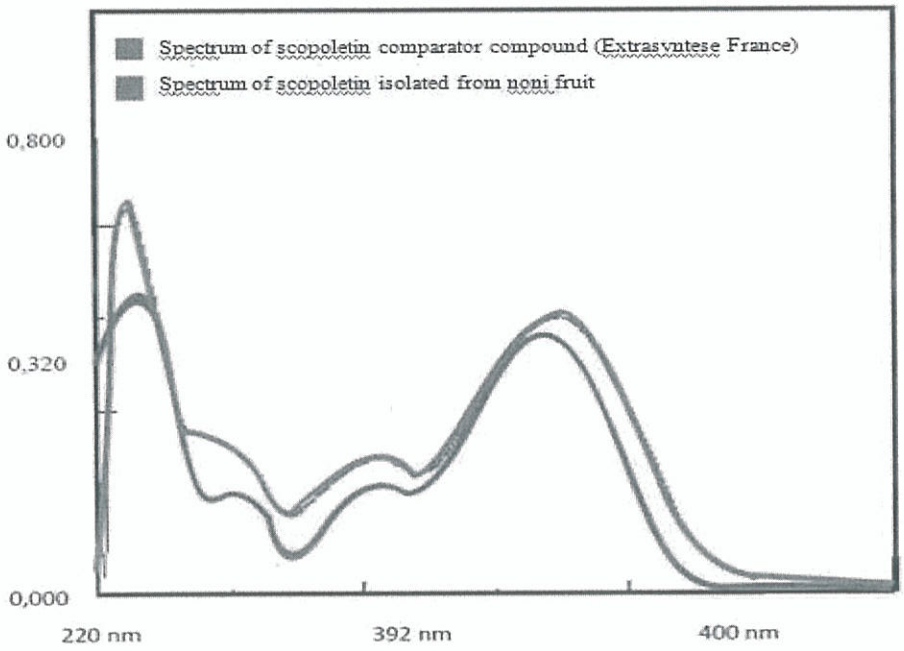

Fig. 2. UV spectrum of scopoletin isolated from noni fruit and scopoletin comparator compound (Extrasyntese France) (Aldi, 2015)

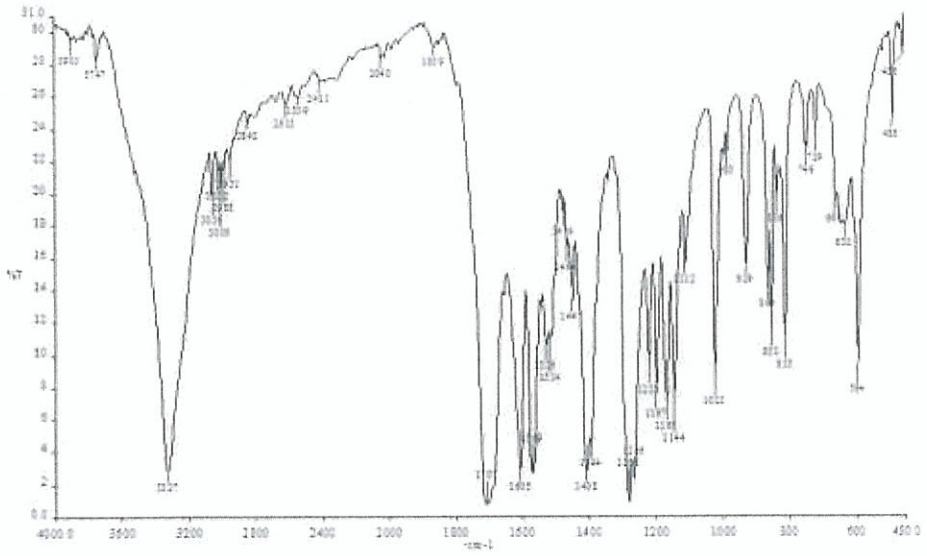

Fig. 3. IR spectrum of scopoletin isolation from noni fruit (Aldi, 2015)

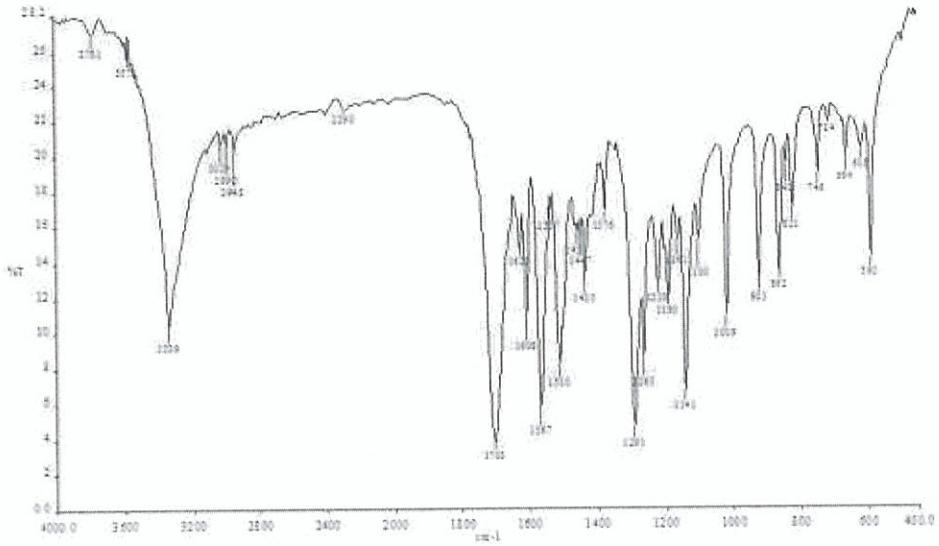

Fig. 4. IR spectrum of scopoletin comparator compound (Extrasyntese France) (Aldi, 2015)

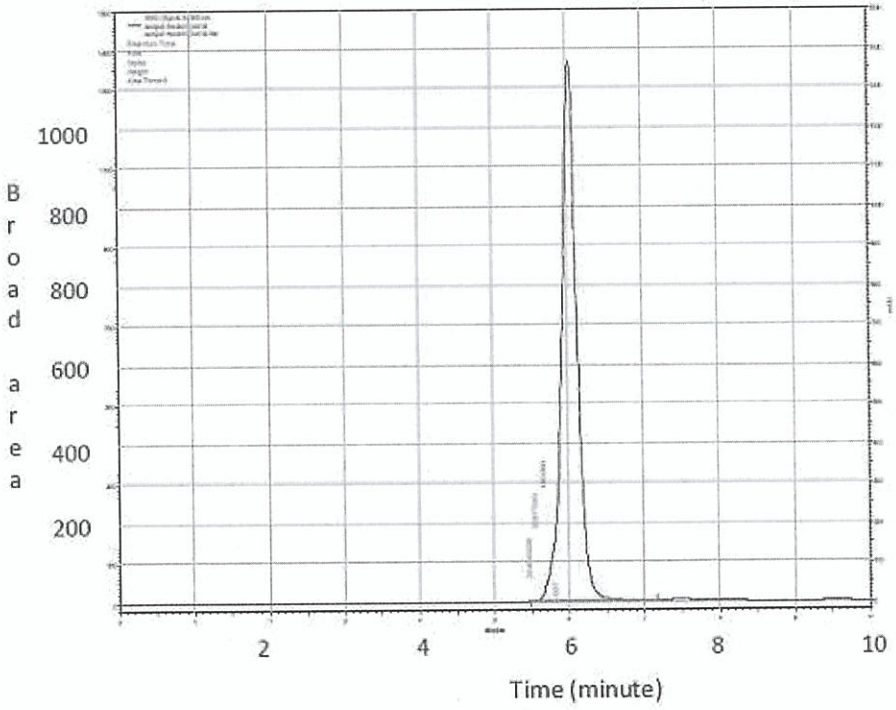

Fig. 5. The curve of scopoletin injected as much as 20 mL with methanol : aquabidest eluent (9: 1) flow rate 0.5 mL/min at room temperature, using a detector on 345 nm wavelength.

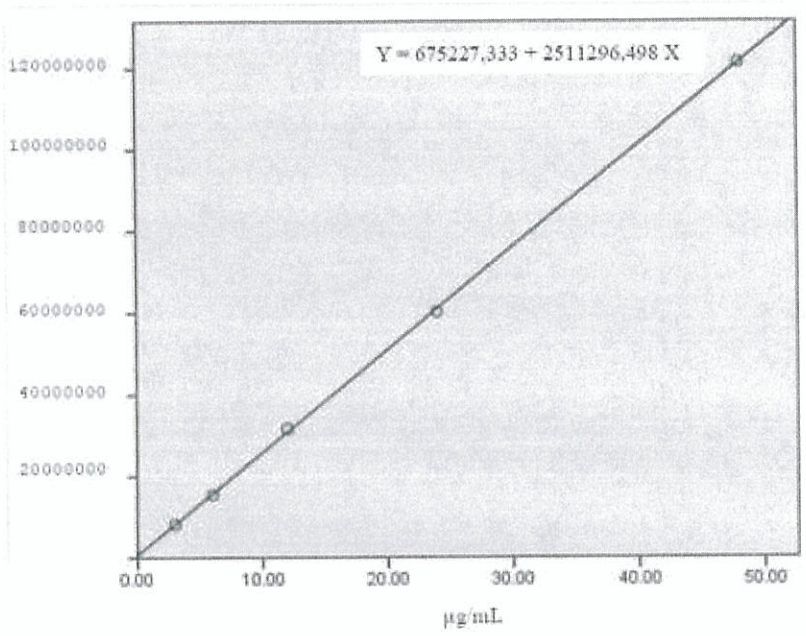

Fig. 6. The calibration curve of scopoletin standard compound (Extrasynthese, France).

Linear equation of the calibration curve of scopoletin standard with a linear equation Y = 675227,333 + 2511296,498 X. Using this equation, obtained the purity of scopoletin isolated from noni fruit is 104.22%.

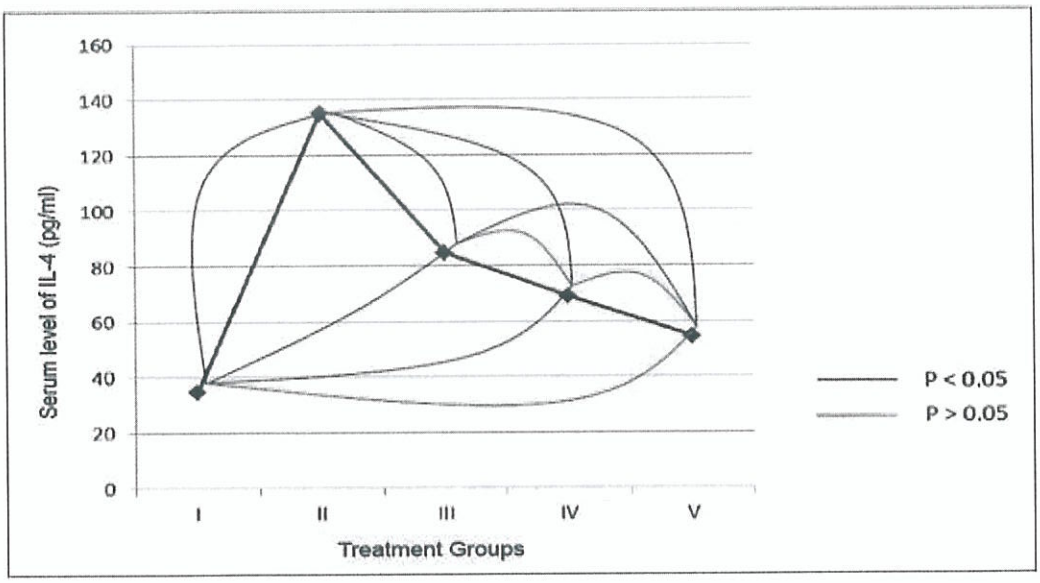

Fig. 7. Relationship between doses of scopoletin isolated from noni fruit and serum levels of IL-4 in type I hypersensitive mice.

The major function of IL-4 is in the regulation of the immune response mediated by IgE and mastocyte or eusinophil cells. The activity of IL-4 is not limited on B cells only, but also on T cells, macrophages, granulocytes, mastocytes, erythrocyte precursors and megakaryocytes. IL-4 acts as a stimulator of Th2 cells and inhibits the activity of macrophages, but this effect can be countered by the INFγ .Increased level of IL-4 in animals experiencing type I hypersensitivity reactions will affect the activity of CD4 T cells to undergo cell proliferation and differentiation toward Th2 cells and subsequently increase the production of IL-4. Furthermore, IL-4 has receptors on the plasma cells that will be

IL-10 measurement in mice hypersensitivity type I serum used Platinum Mouse IL-10 ELISA kit (eBioscience, BMS 614/2, No. 887 904). To determine levels of IL-10, first standard curve of IL-10 was made used a standard compound in the kit at a wavelength of 450 nm. The standard curve of IL-10 in the blood serum of mice can be seen in Fig. 7.

IL-10 Levels in the serum of hypersensitivity type I mice after administration of scopoletin was determined using a calibration curve (Fig. 7). The results of IL-10 serum levels on five treated groups can be seen in Table 1.

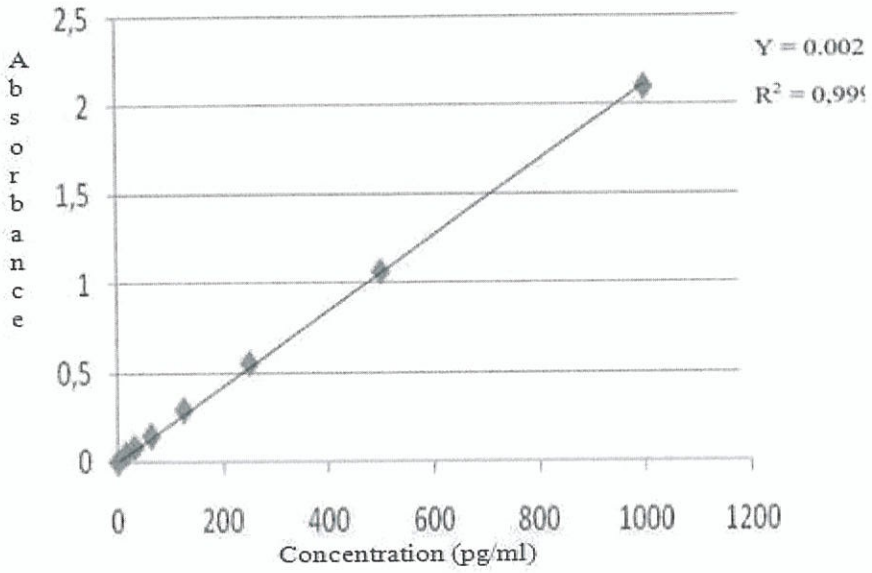

Fig. 8. The standard curve of IL-10 in the blood serum of mice on 450 nm wavelength.

Table 1. IL-10 serum levels on male white mice with hypersensitivity type I after administration of scopoletin from noni fruit.

No.	Group	IL-10 levels (pg/ml)					Rate of IL-10 levels (pg/ml)
		1	2	3	4	5	
1	I	229,00	228,00	189,00	220,00	275,00	228,20 ± 30,80
2	II	364,00	381,00	427,00	413,00	427,00	402,40 ± 28,53
3	III	338,00	279,00	364,00	346,00	306,00	326,60 ± 33,90
4	IV	313,00	236,00	267,00	323,00	309,00	289,60 ± 36,82

5	V	267,00	232,00	263,00	379,00	291,00	286,40 ± 55,86

I = normal animals, II = positive control animals (NaCMC solution), III = hypersensitivity type I animals with 1 mg/kg BW dose, IV = hypersensitivity type I animals with 3 mg/kg BW dose, V = hypersensitivity type I animals with 10 mg/kg BW dose.

Administration of the scopoletin at doses of 1, 3 and 10 mg / kg bw in mice with hypersensitivity type I reaction was to decreased levels of IL-10 after analyzed statistically by analysis of variance in one direction was able to reduce the levels of IL-10 very significantly ($p < 0.01$).

Statistical analysis followed by Bonferroni test to determine differences of each dose ability in decreasing the IL-10 levels. Results of Benferroni statistical test can be seen in Fig. 8. Administration of scopoletin at 1 mg/kg BW dose to hypersensitivity type I mice have not decreased IL-10 levels significantly ($p > 0.05$) when compared with IL-10 levels of the positive control group. After administration 3 mg/kg BW and 10 mg/kg BW dose significant decreassing IL-10 levels was happened ($p < 0.05$). that means the dose of 1 mg / kg BW had no effect and the effect seen at a dose of 3 mg / kg and 10 mg / kg BW. But statistically, scopoletin ability to decrease of IL-10 levels provided by 1 mg/kg BW a dose was same with 3 mg/kg BW dose and 10 mg/kg BW dose. While the ability of a dose of 3 mg/kg BW for the lower levels of IL-10 from mice hipersensitivity type have been able to get to the levels of IL-10 normal animals ($p > 0.05$).

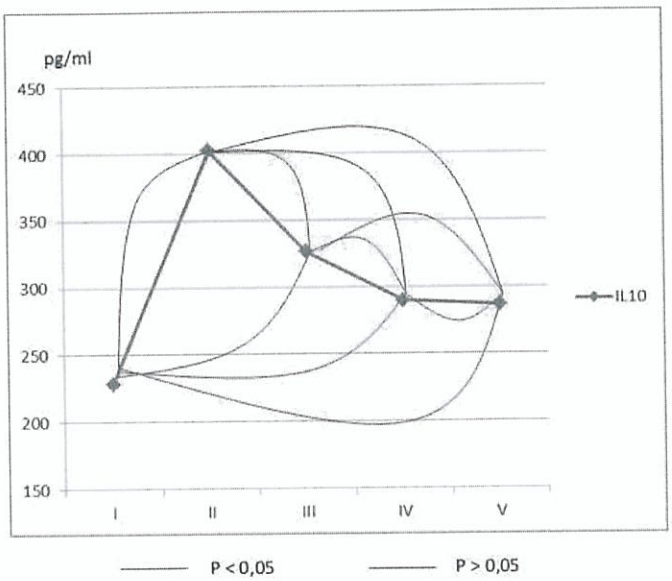

Fig. 8. The relationship between the dose of scopoletin compound given to male white mice with hypersensitivity type I to IL-10 levels. I = normal animals, II = positive control animals (NaCMC solution), III = hypersensitivity type I animals with 1 mg/kg BW dose, IV = hypersensitivity type I animals with 3 mg/kg BW dose, V = hypersensitivity type I animals with 10 mg/kg BW dose.

IL-10 levels in normal group of mice was 228.20 ± 30.80 pg/ml. if mice had hypersensitivity type I reaction with unannounced test compound (positive control), the IL-10 levels increase up to 176% of normal levels). Increasing of IL-10 levels hypersensitivity type I mice was not as high when compared with the levels of IL-4 (Aldi *et al.*, 2015)

Increasing of IL-10 levels in hypersensitivity type I mice also affects the activity of CD4 T and IL-4. it will undergo cell proliferation and differentiation to Th2 cells (Kang *et al.*, 2005). Besides, IL-10 also has capability to inhibit the production of cytokines by Th1 cells and inhibit the function of monocytes or macrophages (Kearly *et al.*, 2005). Decreassing of IL-10 levels in hypersensitivity type I mice will improve the balance of proliferation and differentiation of CD4 T cells and then production of IL-4 by Th2 cells will be decreased.

The increase of IL-10 levels in mice with hypersensitivity was not so high when compared with the increase of IL-4 levels (Aldi *et al.*, 2015) and as well as decreased levels of IL-10 caused by scopoletin was also weak. Ability decreassing of IL-10 on hypersensitivity type

I mice with 1 mg/kg BW scopoletin was not significant ($p > 0.05$) when compared with hypersensitivity type I mice were not given the test compounds.

When compared the effects of compound scopoletin on levels of IL- 4 , IL - 10 and IgE type I hypersensitivity mice there was a correlation , where the decline in the levels of IL - 4 and IL - 10 , the IgE levels will also go down . When seen with the effect of each dose levels of IL - 4 and IgE levels were the same , which can already be significantly lowered in a dose of 1 mg / kg bw and at a dose of 10 mg / kg bw has been able to reduce levels of IL-

4 and IgE levels to the normal animals .

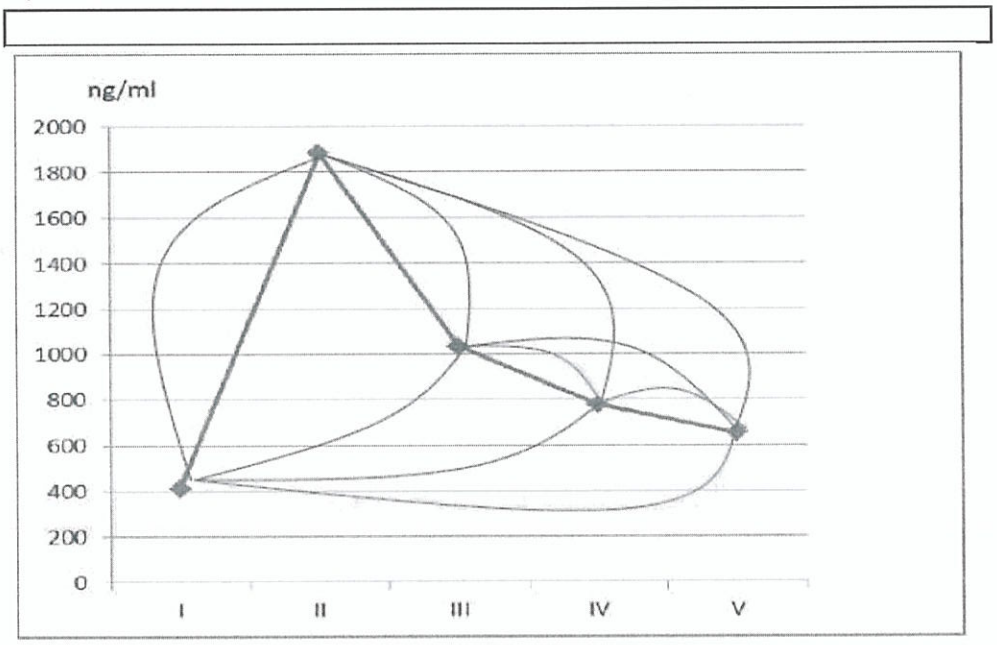

Fig.9 The relationship between the dose of compound scopoletin from noni fruit given to male white mice against type I hypersensitivity IgE levels.

Description: I. Animal normal.

II. Animals positive control (NaCMC solution).

III. Animal type I hypersensitivity dose of 1 mg / kg bw.

IV. Animal type I hypersensitivity dose of 3 mg / kg bw.

V. Animal type I hypersensitivity dose of 10 mg / kg bw.

In mice who had type I hypersensitivity reaction turned out to be the increase in IgE levels were the highest of 456.30 % , followed by IL-4 levels are 388.17 % and the smallest gains are increased levels of IL - 10 is 176 %. This proves that the type I hypersensitivity reaction that is important is to set IgE and cytokine IL - 4 (Kikuchi , et al. , 2006) . Decreased levels of IL - 4 , is expected through a reduction in the activity of Th2 cells, activities through the suppression of macrophage cells or eosinophil cell activity , because all these cells produce IL- 4 . Suppression activity of macrophage cells could be directly against the production of IL - 4 , but it could be through suppression of production of IL - 1 , since IL - 1 also plays an important role in cell differentiation Tho become Th2 and Th1 cells .

CONCLUSION

These results indicate that administration of scopoletin with dosege of 1, 3, and 10 mg/kg of body weight can decrease serum IL-4, IL-10 and IgE mice with type I hypersensitivity. Scopoletin at the dose of 10 mg/kg can decrease the serum level of IL-4 and IgE in type I hypersensitive mice to the normal level. The decrease of serum IL-10 in mice with type 1 hypersensitivity scopoletin given a dose of 3 mg / kg BW can reduce IL-10 to the normal range.

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