KEMENTERIAN PENDIDIKAN DAN KEBUDAYAAN
UNIVERSITAS AIRLANGGA
FAKULTAS KEDOKTERAN
PROGRAM STUDI ILMU KEDOKTERAN JENJANG DOKTOR
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Nomor : 342/UN3.1.1/DL/2020
Lamp :
Hal : Penyanggah Ujian Akhir Tahap 2 (Terbuka)

14 Januari 2020
B. Yanti
Arsip Terbuka

Kepada Yth.
Pimpinan Sidang Ujian Akhir Tahap 2 (Terbuka)
Program Studi Ilmu Kedokteran Jenjang Doktor FK UNAIR
Surabaya

Sehubungan dengan Ujian Akhir Tahap 2 (Terbuka) sdr. **Dina Helianti, dr., M.Kes** pada tanggal **20 Januari 2020**, maka dengan ini kami sampaikan nama-nama penyanggah ujian akhir yang bersangkutan untuk diketahui.

Pimpinan sidang ujian akhir terbuka: Prof. Dr. H. Budi Santoso, dr., Sp.OG(K)

Para penyanggah dimaksud adalah :

1. Prof. Soetjipto, dr., MS., Ph.D *) ✓ 1
2. Prof. Dr. Widjiati, drh., M.Si **) ✓ 2
3. Prof. Dr. A. Retno Pudji Rahayu, drg., M.Kes ✓ 3
4. Dr. Soedarsono, dr., Sp.P(K) ✓ 4
5. Supangat, dr., M.Kes., Ph.D., Sp.BA ✓ 5
6. Dr. Tjuk Imam Restiadi, drh., M.Si ✓ 6
7. Dr. Johanes Nugroho Eko Putranto, dr., Sp.JP(K) ✓ 7
8. Dr. Lestari Sudaryanti, dr., M.Kes
9. Prof. Dr. Siswandono, MS., Apt
10. Prof. Dr. H. Budi Santoso, dr., Sp.OG(K)

7 orang luar FK

Demikian dan atas perhatiannya disampaikan terima kasih.

a.n. Dekan
Wakil Dekan I,

Prof.Dr. David S. Perdanakusuma,dr.,Sp.BP-RE(K)
NIP. 196003051989011002

Catatan :
*) Promotor

sdh Proses

DAFTAR HADIR PENYANGGAH

Rapat/Sidang : Ujian Doktor Terbuka *Dina Helianti, dr., M.Kes*
Tanggal : 20 Januari 2020
Pukul : 10.00 – 12.00 Wib
Tempat : Aula Fakultas Kedokteran UNAIR
Acara : Penentuan Predikat Calon Doktor *Dina Helianti, dr., M.Kes*

No	Nama	Instansi	Tanda Tangan	
1.	Prof. Soetjipto, dr., MS., Ph.D		1.	
2.	Prof. Dr. Widjiati, drh., M.Si			2.
3.	Prof. Dr. A. Retno Pudji Rahayu, drg., M.Kes		3.	
4.	Dr. Soedarsono, dr., Sp.P(K)			4.
5.	Supangat, dr., M.Kes., Ph.D., Sp.BA		5.	
6.	Dr. Tjuk Imam Restiadi, drh., M.Si			6.
7.	Dr. Johanes Nugroho Eko Putranto, dr., Sp.JP(K)		7.	
8.	Dr. Lestari Sudaryanti, dr., M.Kes			8.
9.	Prof. Dr. Siswandono, MS., Apt		9.	

DISERTASI

MEKANISME PENCEGAHAN DISFUNGSI ENDOTEL OLEH KAKAO (*Theobroma cacao*) MELALUI ANALISIS F2-ISOPROSTAN PLASMA, EKSPRESI NFκB, CD-34, DAN Flk-1 PADA TIKUS PUTIH *STRAIN Sprague dawley* YANG TERPAPAR ASAP ROKOK

DINA HELIANTI

PROGRAM STUDI ILMU KEDOKTERAN JENJANG DOKTOR
FAKULTAS KEDOKTERAN UNIVERSITAS AIRLANGGA
SURABAYA
2020

DISERTASI

MEKANISME PENCEGAHAN DISFUNGSI ENDOTEL OLEH KAKAO (*Theobroma cacao*) MELALUI ANALISIS F2-ISOPROSTAN PLASMA, EKSPRESI NFκB, CD-34, DAN Flk-1 PADA TIKUS PUTIH *STRAIN Sprague dawley* YANG TERPAPAR ASAP ROKOK

DINA HEIANTI

PROGRAM STUDI ILMU KEDOKTERAN JENJANG DOKTOR
FAKULTAS KEDOKTERAN UNIVERSITAS AIRLANGGA
SURABAYA
2020

MEKANISME PENCEGAHAN DISFUNGSI ENDOTEL OLEH KAKAO (*Theobroma cacao*) MELALUI ANALISIS F2-ISOPROSTAN PLASMA, EKSPRESI NFκB, CD-34, DAN Flk-1 PADA TIKUS PUTIH *STRAIN Sprague dawley* YANG TERPAPAR ASAP ROKOK

DISERTASI

Untuk memperoleh Gelar Doktor
dalam Program Studi Ilmu Kedokteran Jenjang Doktor
pada Fakultas Kedokteran Universitas Airlangga
telah dipertahankan di hadapan
Panitia Ujian Doktor Terbuka

Pada hari : Selasa
Tanggal : 20 Januari 2020
Pukul : 10.00-12.00 WIB

Oleh :

DINA HELIANTI
011317017311

PROGRAM STUDI ILMU KEDOKTERAN JENJANG DOKTOR
FAKULTAS KEDOKTERAN UNIVERSITAS AIRLANGGA
SURABAYA
2020

LEMBAR PENGESAHAN

MEKANISME PENCEGAHAN DISFUNGSI ENDOTEL OLEH KAKAO (*Theobroma cacao*) MELALUI ANALISIS F2-ISOPROSTAN PLASMA, EKSPRESI NFκB, CD-34, DAN Flk-1 PADA TIKUS PUTIH *STRAIN Sprague dawley* YANG TERPAPAR ASAP ROKOK

TELAH DISETUJUI

PADA TANGGAL 20 JANUARI 2020

Oleh:
Promotor

Prof. Soetjipto, dr., MS., PhD
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Kopromotor

Prof. Dr. Widjiati, drh., M.Si
NIP. 1962091519900220001

SUMMARY

THE PREVENTION MECHANISMS OF ENDOTHELIAL DYSFUNCTION BY CACAO (*Theobroma cacao*) THROUGH ANALYSIS OF PLASMA F2-ISOPROSTAN LEVELS, EXPRESSION OF NF-KB, CD-34, AND FLK-1 ON CIGARETTE SMOKING EXPOSED RAT

Cardiovascular disease (CVD) is the main cause of illness and death in the world. In 2008, deaths due to PKV in the world reached 30% of the total deaths at that time, and by 2030 it is estimated to increase to 37%. Smoking habits increase the risk of cardiovascular disease 2-3 times, while the risk of coronary heart disease 2-4 times. Indonesia is the third country with the highest number of smokers in the world (27.6%).

Cigarette smoke contains nicotine, CO, tar, as well as many types and amounts of oxidants that can help with various pathological effects, especially on the endothelium. The increase in ROS due to cigarette smoke causes lipid peroxidation in the endothelial cell membrane with the final product F2-isoprostane which can be used as an early indicator of the atherogenesis process. Cigarette smoke also causes an inflammatory process through the activation of Nuclear Factor kappa B (NFκB) which triggers an increase in pro-inflammatory cytokines and further causes activated endothelium which affects the expression of adhesion molecules such as ICAM-1, and VCAM-1 so that the anti-adhesive properties of the endothelium decrease which is a sign of endothelial dysfunction. Besides causing endothelial damage, cigarette smoke also interferes with the regeneration and maintenance of endothelium. Endothelial progenitor cells (EPCs) play a role in the process of endothelial regeneration either through the paracrine system (including Vascular Endothelial Growth Factor, Fibroblast Growth Factor, IL-6, IL-8, IL-11) or differentiate into endothelial cells. EPC markers that are often used are Cluster of differentiation 133+ (CD133 +), CD34 + and Vascular Endothelial Growth Factor Receptor 2+ (VEGFR2 +)/Fetal Liver Kinase-1 (Flk-1).

Epidemiological data suggest that regular intake of certain herbal plants can reduce the risk of CVD. Cocoa (Theobroma cacao) or chocolate is a food ingredient that has been shown to be beneficial for cardiovascular health. A study by Bayard et al., 2007 of residents of Kuna India off the coast of Panama who used to consume cocoa every day showed lower mortality from cardiovascular disease compared to citizens of other countries (9.2 ± 3.1 versus 83.4 ± 0.7 age-adjusted deaths per 100′000).

In vivo studies on the mechanism of cocoa administration on the prevention of endothelial dysfunction due to smoking, in this case, the increase in ICAM-1 and VCAM-1 has not been widely carried out, while research data on the effect of cocoa in smokers on EPC levels in the blood circulation have been reported. This study intends to investigate further the mechanisms for preventing endothelial dysfunction by cocoa due to cigarette smoke, particularly the relationship between oxidative stress, inflammation, and EPC activation with the recency of the immunohistochemical increase in EPC in the injured area, in this case, arteria coronaria. The oxidative stress pathway used an indicator of plasma F2-isoprostane levels, the inflammatory pathway by the expression of the NFkB coronary artery, and the EPC activation pathway by the expression of CD34 and Flk-1 coronary artery, while the endothelial dysfunction used the indicators ICAM-1 and VCAM-1.

This research was conducted in 2 phase. Phase 1 to determine the effective dose of cacao in reducing plasma F2-isoprostane levels; and phase 2 to analyze the mechanisms of preventing endothelial dysfunction by cacao on cigarette smoke exposure. In the first phase

of study, 3 doses of cacao were used. This type of phase 1 is an experimental laboratory with a post-test-only control group design model. The experimental animals used were 30 rattus norvegicus strains of Sprague Dawley, males, aged 3 months, weight 200-300 g grouped randomly into 5 treatment groups. The normal control group (K0) received 2 ml of aqua bidest and given air exposure once a day; the cigarette control group (K1) received 2 ml of aqua bidest and given exposure to cigarette smoke once a day. In the treatment group, each group was given exposure to cigarette smoke and given cocoa powder that had been dissolve in aqua bidest. Cacao group 1 was given a dose of 1206 mg/kg BW/day (P1), cacao group 2 was given a dose of 2411 mg/kg BW/day (P2), and cacao group 3 was given a dose of 3616 mg/kg BW/day (P3). Each group was treated for 14 days. On the 15th day, the experimental animals were terminated and F2-isoprostane was examined using the ELISA method, then was selected one of the three doses of cacao was the most effective in reducing plasma F2-isoprostane levels.

The result of phase 1 showed that the effective dose of cacao in reducing plasma F2-isoprostane levels was 1205 mg/kg BW/day. Furthermore, the cacao treatment group with a dose of 1205 mg/kg BW/day in the second phase of the study was called the treatment group (P), together with the K0 and K1 groups, the NFκB, CD34, Flk-1, VCAM-1 and ICAM-1 were examined. The results of examinations in phases 1 and 2 showed that cacao decreased the expression of NFκB, VCAM-1, and ICAM-1 arteria coronaria and increased the expression of CD34 and Flk-1 coronary artery in rats exposed to cigarette smoke. The result of the path analysis test showed that there was a relationship between cacao in the condition of exposure to cigarette smoke with an increase in CD34 and a decrease in ICAM-1. In addition, there is also a relationship between cacao and a decrease in NFκB and a decrease in VCAM-1.

New in this study, presenting cacao to Rattus norvegicus exposed to cigarette smoke can prevent endothelial dysfunction in 2 ways: the pathway of increasing EPC and an inflammatory pathway with a decrease in NFκB as an inflammatory mediator. The results of this study can be used as a basis for knowledge of prevention disease due to cigarette smoke by using cacao which can be applied daily.

ABSTRACT

The Prevention Mechanisms of Endothelial Dysfunction by Cacao (Theobroma Cacao) Through Analysis of Plasma F2-Isoprostan Levels, Expression of NF-kB, CD-34, and Flk-1 on Cigarette Smoking Exposed Rat

Dina Helianti

Background: Smoking has known as causative factor of cardiovascular disease that was started with endothelial dysfunction. Polyphenols has known significantly prevent endothelial dysfunction. Cacao is a rich source of polyphenols. This study was designed to evaluate the cardioprotective effects of cocoa that mediated through the anti-oxidant effect, and was measured by plasma F2-isoprostane level, anti-inflammatory effect by expression of NFκB, and Endothelial Progenitor Cell (EPC) activation by expression of CD-34 and Flk-1 in coronary arteries. The condition of endothelial dysfunction was measured by expression of ICAM-1 and VCAM-1 in coronary arteries.

Material and Methods: These research was conducted in 2 phases: the first phase determined the efective dose of cocoa in reducing plasma F2-isoprostane level and the second phase analyzed the preventing mechanism of endothelial dysfunction by cocoa on cigarette smoke exposure. This study using cocoa powder. In the first phase, 3 doses of cocoa were used. This study subjected rats, divided into five groups: the normal control group (2 ml of aquabidest, air exposure); the cigarette control group (2 ml of aquabidest, cigarette smoke); cacao group 1 (1205 mg/kg BW/day, cigarette smoke); cocoa group 2 (2410 mg/kg BW/day, cigarette smoke); cacao group 3 (3615 mg/kg BW/day, cigarette smoke). Each group was treated for 14 days. In the second phase of the study using the optimal dose of cacao, based on the results from the first phase. NFkB, CD34, Flk-1, VCAM-1 and ICAM-1 were measured by immunohistochemistry.

Results: Cocoa 1205 mg/kg/day significantly decreases plasma F2-isoprostane level, NFkB, ICAM-1 and VCAM-1 expression of coronary arteries in cigarette smoking exposed rat ($p<0,05$). There was not a significant increases CD-34 but there was a significant increases in Flk-1 expression ($p<0,05$).

Conclusions: Cocoa in cigarette smoke-exposed rats can prevent endothelial dysfunction in 2 ways: the pathway of increasing EPC and an inflammatory pathway with a decrease in NFκB as an inflammatory mediator. The results of this study can be used as a basis for preventing endothelial dysfunction due to cigarette smoke by using cocoa.

Keywords: cigarette smoke exposure, cacao, F2-isoprostane, EPC, endothelial dsyfunction

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SURAT TUGAS
Nomor :4839 /UN3.1.1/DL/2020

Wakil Dekan I Fakultas Kedokteran Universitas Airlangga dengan ini menugaskan :

1.	Prof. Dr. I Ketut Sudiana, Drs.,M.Si	Ketua
2.	Prof. Dr. Teddy Ontoseno, dr., Sp.A(K)., Sp.JP.FIHA	Anggota
3.	Prof. Dr. Achmad Basori, Drs., Apt., MS	Anggota
4.	Dr. Sri Endah Rahayuningsih, dr.,Sp.A(K)	Anggota
5.	Dr. Reny I'tishom., M.Si	Anggota
6.	Dr. Hari Basuki Notobroto, dr., M.Kes	Anggota
7.	Dr. Johanes Nugroho Eko P, dr., Sp. JP(K),FIHA, FASCC,FICA, FESC	Anggota
8.	Dr. Arifa Mustika, dr.,M.Si	Anggota

Sebagai Ketua / Anggota Panitia Ujian Tahap Pertama (Tertutup) Program Doktor Fakultas Kedokteran Universitas Airlangga atas nama I Ketut Alit Utamayasa, dr.,Sp.A(K) peserta Program Doktor Program Studi Ilmu Kedokteran angkatan tahun 2016/2017 yang diselenggarakan pada tanggal 23 Oktober 2020.

Surat tugas ini diterbitkan sementara untuk menunggu keluarnya Surat Keputusan dari Dekan Fakultas Kedokteran Universitas Airlangga.

Surabaya, 16 Oktober 2020
a.n. Dekan
Wakil Dekan I,

Dr. Achmad Chusnu Romdhoni,dr.,Sp.THT-KL(K).,FICS
NIP. 197609022008011009

KEMENTERIAN PENDIDIKAN DAN KEBUDAYAAN
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Nomor : 4838 /UN3.1.1/DL/2020
Lamp : 1 Berkas
Hal : Mohon Kesediaan untuk menjadi Panitia Penguji Disertasi

16 Oktober 2020

Yth.
1. Prof. Dr. I Ketut Sudiana, Drs.,M.Si
2. Prof. Dr. Teddy Ontoseno, dr., Sp.A(K)., Sp.JP.FIHA (Ketua)
3. Prof. Dr. Achmad Basori, Drs., Apt., MS
4. Dr. Sri Endah Rahayuningsih, dr.,Sp.A(K)
5. Dr. Reny I'tishom., M.Si
6. Dr. Hari Basuki Notobroto, dr., M.Kes
7. Dr. Johanes Nugroho Eko P, dr., Sp. JP(K),FIHA, FASCC,FICA, FESC
8. Dr. Arifa Mustika, dr.,M.Si

Dengan hormat,

Sehubungan dengan selesainya penulisan disertasi peserta Program Doktor angkatan tahun 2016/2017,

Nama : I Ketut Alit Utamayasa, dr.,Sp.A(K)
NIM : 011617017329 ELPT : 557
Judul : PERBEDAAN DAN MEKANISME ANTARA PEMBERIAN ACE INHIBITOR DAN VALSARTAN UNTUK PENCEGAHAN PROGRESIVITAS GAGAL JANTUNG PADA PENYAKIT JANTUNG BAWAAN PIRAU KIRI KE KANAN MELALUI ANALISIS NT-proBNP, TROPONIN-T, SOD DAN KATALASE

Promotor : Prof. Dr. Teddy Ontoseno, dr., Sp.A(K)., Sp.JP.FIHA
Ko-Promotor : Prof. Dr. Achmad Basori, Drs., Apt., MS

Ujian Disertasi rencananya diselenggarakan :

Hari, Tanggal : Jum'at, 23 Oktober 2020
Pukul : 08.30 – 11.30 WIB
Tempat : Menguji secara online menggunakan aplikasi zoom

Maka dengan ini mohon kesediaan Saudara untuk menjadi Ketua / Anggota panitia Penguji Disertasi tersebut, terlampir kami sampaikan pernyataan kesediaan untuk diisi dan dilampirkan pada kami dalam waktu yang tidak terlalu lama guna diproses lebih lanjut.

Demikian atas perhatian Saudara, kami ucapkan terima kasih.

a.n Dekan
Wakil Dekan I

Dr. Achmad Chusnu Romdhoni,dr.,Sp.THT-KL(K).,FICS
NIP. 197609022008011009

Tindasan :
- KPS Ilmu Kedokteran Program Doktor
- Kepala Sub. Bagian Akademik

KEMENTERIAN PENDIDIKAN DAN KEBUDAYAAN
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DAFTAR HADIR UJIAN

Hari, Tanggal : Jum'at, 23 Oktober 2020
Pukul : 08.30 – 11.30 WIB
Ujian : Tertutup an. I Ketut Alit Utamayasa, dr.,Sp.A(K) Mahasiswa Program Studi Ilmu Kedokteran Jenjang Doktor FKUA

NO	NAMA	TANDA TANGAN
1.	Prof. Dr. I Ketut Sudiana, Drs.,M.Si	1. Hadir online
2.	Prof. Dr. Teddy Ontoseno, dr., Sp.A(K)., Sp.JP.FIHA	2. Hadir online
3.	Prof. Dr. Achmad Basori, Drs., Apt., MS	3. Hadir online
4.	Dr. Sri Endah Rahayuningsih, dr.,Sp.A(K)	4. Hadir online
5.	Dr. Reny I'tishom., M.Si	5. Hadir online
6.	Dr. Hari Basuki Notobroto, dr., M.Kes	6. Hadir online
7.	Dr. Johanes Nugroho Eko P, dr., Sp. JP(K),FIHA, FASCC,FICA, FESC	7. Hadir online
8.	Dr. Arifa Mustika, dr.,M.Si	8. Hadir Online
9.		9.
10.		10.
11.		11.
12.		12.
13.		13.
14.		14.

KEMENTERIAN RISET, TEKNOLOGI, DAN PENDIDIKAN TINGGI
UNIVERSITAS AIRLANGGA
FAKULTAS KEDOKTERAN
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Nomor : 5921/UN3.1.1/PPd/2019 6 Agustus 2019
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Hal : Penyanggah Ujian Akhir Tahap 2 (Terbuka)

Kepada Yth.
Pimpinan Sidang Ujian Akhir Tahap 2 (Terbuka)
Program Studi Ilmu Kedokteran Jenjang Doktor FK UNAIR
Surabaya

Sehubungan dengan Ujian Akhir Tahap 2 (Terbuka) sdr. **Dyana Sarvasti, dr., Sp.JP(K)** pada tanggal **14 Agustus 2019**, maka dengan ini kami sampaikan nama-nama penyanggah ujian akhir yang bersangkutan untuk diketahui.

Pimpinan sidang ujian akhir terbuka: Prof.Dr. Soetojo, dr., Sp.U(K)

Para penyanggah dimaksud adalah :

1. Prof. Dr. Rochmad Romdoni, dr., Sp.PD., Sp.JP(K) FIHA., FASCC *)
2. Dr. Anwar Santoso, dr., Sp.JP(K) **)
3. Prof. Dr. Teddy Ontoseno, dr., Sp.A(K)., Sp.JP.FIHA
4. Prof. Dr. Toeti Melani Widjoseno Gardjito, drg., MS., Sp.Pros(K)
5. Prof. Dr. Hening Laswati Putra, dr., Sp.RM(K)
6. Dr. Yudi Her Oktaviono, dr., Sp.JP(K)
7. Dr. Johanes Nugroho Eko Putranto, dr., Sp.JP(K)
8. Muhammad Miftahussurur, dr., M.Kes., Ph.D., Sp.PD., FINASIM
9. Prof. Dr. Aryati, dr., MS., Sp.PK(K)
10. Prof. Dr. Soetojo, dr., Sp.U(K)

Demikian dan atas perhatiannya disampaikan terima kasih.

a.n. Dekan
Wakil Dekan I,

Prof.Dr. David S. Perdanakusuma,dr.,Sp.BP-RE(K)
NIP. 196003051989011002

Catatan :
*) Promotor
**) Ko-Promotor I
***) Ko-Promotor II

KEMENTERIAN RISET, TEKNOLOGI, DAN PENDIDIKAN TINGGI
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Nomor : 5849/UN3.1.1/PPd/2019 2 Agustus 2019
Lampiran :
Hal : Penyanggah Ujian Akhir Tahap 2 (Terbuka)

Dengan hormat,

Dengan ini kami mengharap kehadiran Saudara sebagai **Penyanggah** Ujian Akhir Tahap 2 (Terbuka) Prodi Ilmu Kedokteran Jenjang Doktor atas nama **Dyana Sarvasti, dr., Sp.JP(K)** yang akan diselenggarakan pada :

Hari, tanggal : Rabu, 14 Agustus 2019
Pukul : 10.00 – 12.00 WIB
Tempat : Aula Fakultas Kedokteran UNAIR.

Demikian untuk diketahui dan atas perhatian Saudara kami sampaikan terima kasih.

a.n.Dekan
Wakil Dekan I,

Prof. Dr. David S. Perdanakusuma, dr.,Sp.BP-RE(K)
NIP. 19600305 1989011002

Catatan
- Dimohon hadir pukul:09.45 WIB
- Pakaian : Guru Besar mohon membawa toga

DAFTAR HADIR PENYANGGAH

Rapat/Sidang : Ujian Doktor Terbuka *Dyana Sarvasti, dr., Sp.JP(K)*
Tanggal : 14 Agustus 2019
Pukul : 10.00 – 12.00 Wib
Tempat : Program Studi Ilmu Kedokteran Univ. Airlangga Surabaya
Acara : Penentuan Predikat Calon Doktor *Dyana Sarvasti, dr., Sp.JP(K)*

No	Nama	Instansi	Tanda Tangan	
1.	Prof. Dr. Rochmad Romdoni, dr., Sp.PD., Sp.JP(K)., FIHA., FASCC		1.	
2.	Dr. Anwar Santoso, dr., Sp.JP(K)			2.
3.	Prof. Dr. Teddy Ontoseno, dr., Sp.A(K)., Sp.JP.FIHA		3.	
4.	Prof. Dr. Toeti Melani Widjoseno Gardjito, drg., MS., Sp.Pros(K)			4.
5.	Prof. Dr. Hening Laswati Putra, dr., Sp.RM(K)		5.	
6.	Dr. Yudi Her Oktaviono, dr., Sp.JP(K)			6.
7.	Dr. Johanes Nugroho Eko Putranto, dr., Sp.JP(K)		7.	
8.	Muhammad Miftahussurur, dr., M.Kes., Ph.D., Sp.PD., FINASIM			8.
9.	Prof. Dr. Aryati, dr., MS., Sp.PK(K)		9.	
10.	Prof. Dr. Soetojo, dr. Sp.U(K)			10.

Diterbitkan untuk Ujian Akhir Tahap II (Terbuka)

DISERTASI

MEKANISME PROTEKSI KARDIOVASKULAR LATIHAN FISIK INTERVAL INTENSITAS TINGGI PADA PASIEN PENYAKIT JANTUNG KORONER STABIL PASCAIMPLANTASI STENT KORONER

(Evaluasi *flow-mediated dilatation* melalui jalur adrenalin, noradrenalin, eNOS, dan aktivitas SOD ekstraselular)

DYANA SARVASTI

PROGRAM STUDI ILMU KEDOKTERAN JENJANG DOKTOR
FAKULTAS KEDOKTERAN UNIVERSITAS AIRLANGGA SURABAYA
2019

LEMBAR PENGESAHAN

DISERTASI

MEKANISME PROTEKSI KARDIOVASKULAR LATIHAN FISIK INTERVAL INTENSITAS TINGGI PADA PASIEN PENYAKIT JANTUNG KORONER STABIL PASCAIMPLANTASI STENT KORONER
(Evaluasi *flow-mediated dilatation* melalui jalur adrenalin, noradrenalin, eNOS, dan aktivitas SOD ekstraselular)

TELAH DISETUJUI
PADA TANGGAL 16 JULI 2019

Oleh
Promotor

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NIP. 19490712 197703 1001

Ko promotor

Dr. Anwar Santoso, dr., Sp.JP(K)
NIP. 19520720 198403 1001

Mengetahui
Koordinator Program Studi Ilmu Kedokteran Jenjang Doktor
Fakultas Kedokteran Universitas Airlangga

Prof. Dr. H. Joewono Soeroso, dr., M.Sc., Sp.PD-KR
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ABSTRACT

MECHANISM OF CARDIOVASCULAR PROTECTION OF HIGH-INTENSITY INTERVAL TRAINING IN STABLE CORONARY ARTERY DISEASE PATIENTS AFTER CORONARY STENTING
(Evaluation of flow-mediated dilatation through adrenaline, noradrenaline, eNOS, and extracellular SOD activities)

Background: High-intensity interval training (HIIT) has been shown to improve aerobic capacity compared with moderate-intensity continuous training (MICT). Unfortunately, little data on the mechanism of HIIT is available.

Objective: This study aimed to compare and determine the mechanism of cardiovascular protection variables in MICT dan HIIT in stable coronary heart disease (CHD) patients after coronary stenting.

Methods: This experimental study used the same subject and cross-over design. Eleven stable CHD patients after coronary stenting were randomly divided into two groups, MICT (29 min at 50-60% heart rate reserve) and HIIT (4x4 min intervals at 60-80% heart rate reserve, each followed by 3 min of active recovery at 40-50% heart rate reserve), three times a week for two weeks. The patients performed adrenaline, noradrenaline, endothelial nitric oxide synthase (eNOS) concentration, extracellular superoxide dismutase (EC-SOD) activity, and flow-mediated dilatation (FMD) examination, before and after treatment was completed.

Results: HIIT significantly increased noradrenaline and eNOS compared to MICT ($p<0.05$). HIIT was better to preserve EC-SOD activity and FMD compared to MICT ($p <0.05$). HIIT through the noradrenalin pathway had a direct and significant effect on eNOS ($p <0.05$). MICT through the noradrenaline pathways had a direct and significant effect on eNOS ($p<0.05$), and through the EC-SOD activity pathways had a direct and significant effect on FMD ($p <0.05$). MICT reduced EC-SOD activity, which results in a decrease in FMD value.

Conclusion: HIIT is superior to MICT in increasing cardiovascular protection through the increment of noradrenalin and eNOS concentration and preserves EC-SOD activity and FMD in stable CHD patients after coronary stenting.

Keywords: Coronary heart disease, high-intensity interval training, catecholamine, eNOS, SOD, FMD.

Promotor,

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KEMENTERIAN PENDIDIKAN DAN KEBUDAYAAN
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Nomor : 342/UN3.1.1/DL/2020
Lamp :
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14 Januari 2020
B. Yanti
Arsip Terbuka

Kepada Yth.
Pimpinan Sidang Ujian Akhir Tahap 2 (Terbuka)
Program Studi Ilmu Kedokteran Jenjang Doktor FK UNAIR
Surabaya

Sehubungan dengan Ujian Akhir Tahap 2 (Terbuka) sdr. **Dina Helianti, dr., M.Kes** pada tanggal **20 Januari 2020**, maka dengan ini kami sampaikan nama-nama penyanggah ujian akhir yang bersangkutan untuk diketahui.

Pimpinan sidang ujian akhir terbuka: Prof. Dr. H. Budi Santoso, dr., Sp.OG(K)

Para penyanggah dimaksud adalah :

1. Prof. Soetjipto, dr., MS., Ph.D *) ✓ 1
2. Prof. Dr. Widjiati, drh., M.Si **) ✓ 2
3. Prof. Dr. A. Retno Pudji Rahayu, drg., M.Kes ✓ 3
4. Dr. Soedarsono, dr., Sp.P(K) ✓ 4
5. Supangat, dr., M.Kes., Ph.D., Sp.BA ✓ 5
6. Dr. Tjuk Imam Restiadi, drh., M.Si ✓ 6
7. Dr. Johanes Nugroho Eko Putranto, dr., Sp.JP(K) ✓ 7
8. Dr. Lestari Sudaryanti, dr., M.Kes
9. Prof. Dr. Siswandono, MS., Apt
10. Prof. Dr. H. Budi Santoso, dr., Sp.OG(K)

7 orang luar FK

Demikian dan atas perhatiannya disampaikan terima kasih.

a.n. Dekan
Wakil Dekan I,

Prof.Dr. David S. Perdanakusuma,dr.,Sp.BP-RE(K)
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Catatan :
*) Promotor

sdh Proses

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Rapat/Sidang : Ujian Doktor Terbuka *Dina Helianti, dr., M.Kes*
Tanggal : 20 Januari 2020
Pukul : 10.00 – 12.00 Wib
Tempat : Aula Fakultas Kedokteran UNAIR
Acara : Penentuan Predikat Calon Doktor *Dina Helianti, dr., M.Kes*

No	Nama	Instansi	Tanda Tangan	
1.	Prof. Soetjipto, dr., MS., Ph.D		1.	
2.	Prof. Dr. Widjiati, drh., M.Si			2.
3.	Prof. Dr. A. Retno Pudji Rahayu, drg., M.Kes		3.	
4.	Dr. Soedarsono, dr., Sp.P(K)			4.
5.	Supangat, dr., M.Kes., Ph.D., Sp.BA		5.	
6.	Dr. Tjuk Imam Restiadi, drh., M.Si			6.
7.	Dr. Johanes Nugroho Eko Putranto, dr., Sp.JP(K)		7.	
8.	Dr. Lestari Sudaryanti, dr., M.Kes			8.
9.	Prof. Dr. Siswandono, MS., Apt		9.	

DISERTASI

MEKANISME PENCEGAHAN DISFUNGSI ENDOTEL OLEH KAKAO (*Theobroma cacao*) MELALUI ANALISIS F2-ISOPROSTAN PLASMA, EKSPRESI NFκB, CD-34, DAN Flk-1 PADA TIKUS PUTIH *STRAIN Sprague dawley* YANG TERPAPAR ASAP ROKOK

DINA HELIANTI

PROGRAM STUDI ILMU KEDOKTERAN JENJANG DOKTOR
FAKULTAS KEDOKTERAN UNIVERSITAS AIRLANGGA
SURABAYA
2020

DISERTASI

MEKANISME PENCEGAHAN DISFUNGSI ENDOTEL OLEH KAKAO (*Theobroma cacao*) MELALUI ANALISIS F2-ISOPROSTAN PLASMA, EKSPRESI NFκB, CD-34, DAN Flk-1 PADA TIKUS PUTIH *STRAIN Sprague dawley* YANG TERPAPAR ASAP ROKOK

DINA HEIANTI

PROGRAM STUDI ILMU KEDOKTERAN JENJANG DOKTOR
FAKULTAS KEDOKTERAN UNIVERSITAS AIRLANGGA
SURABAYA
2020

MEKANISME PENCEGAHAN DISFUNGSI ENDOTEL OLEH KAKAO (*Theobroma cacao*) MELALUI ANALISIS F2-ISOPROSTAN PLASMA, EKSPRESI NFκB, CD-34, DAN Flk-1 PADA TIKUS PUTIH *STRAIN Sprague dawley* YANG TERPAPAR ASAP ROKOK

DISERTASI

Untuk memperoleh Gelar Doktor
dalam Program Studi Ilmu Kedokteran Jenjang Doktor
pada Fakultas Kedokteran Universitas Airlangga
telah dipertahankan di hadapan
Panitia Ujian Doktor Terbuka

Pada hari : Selasa
Tanggal : 20 Januari 2020
Pukul : 10.00-12.00 WIB

Oleh :

DINA HELIANTI
011317017311

PROGRAM STUDI ILMU KEDOKTERAN JENJANG DOKTOR
FAKULTAS KEDOKTERAN UNIVERSITAS AIRLANGGA
SURABAYA
2020

LEMBAR PENGESAHAN

MEKANISME PENCEGAHAN DISFUNGSI ENDOTEL OLEH KAKAO (*Theobroma cacao*) MELALUI ANALISIS F2-ISOPROSTAN PLASMA, EKSPRESI NFκB, CD-34, DAN Flk-1 PADA TIKUS PUTIH *STRAIN Sprague dawley* YANG TERPAPAR ASAP ROKOK

TELAH DISETUJUI

PADA TANGGAL 20 JANUARI 2020

Oleh:
Promotor

Prof. Soetjipto, dr., MS., PhD
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Kopromotor

Prof. Dr. Widjiati, drh., M.Si
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SUMMARY

THE PREVENTION MECHANISMS OF ENDOTHELIAL DYSFUNCTION BY CACAO (*Theobroma cacao*) THROUGH ANALYSIS OF PLASMA F2-ISOPROSTAN LEVELS, EXPRESSION OF NF-KB, CD-34, AND FLK-1 ON CIGARETTE SMOKING EXPOSED RAT

Cardiovascular disease (CVD) is the main cause of illness and death in the world. In 2008, deaths due to PKV in the world reached 30% of the total deaths at that time, and by 2030 it is estimated to increase to 37%. Smoking habits increase the risk of cardiovascular disease 2-3 times, while the risk of coronary heart disease 2-4 times. Indonesia is the third country with the highest number of smokers in the world (27.6%).

Cigarette smoke contains nicotine, CO, tar, as well as many types and amounts of oxidants that can help with various pathological effects, especially on the endothelium. The increase in ROS due to cigarette smoke causes lipid peroxidation in the endothelial cell membrane with the final product F2-isoprostane which can be used as an early indicator of the atherogenesis process. Cigarette smoke also causes an inflammatory process through the activation of Nuclear Factor kappa B (NFκB) which triggers an increase in pro-inflammatory cytokines and further causes activated endothelium which affects the expression of adhesion molecules such as ICAM-1, and VCAM-1 so that the anti-adhesive properties of the endothelium decrease which is a sign of endothelial dysfunction. Besides causing endothelial damage, cigarette smoke also interferes with the regeneration and maintenance of endothelium. Endothelial progenitor cells (EPCs) play a role in the process of endothelial regeneration either through the paracrine system (including Vascular Endothelial Growth Factor, Fibroblast Growth Factor, IL-6, IL-8, IL-11) or differentiate into endothelial cells. EPC markers that are often used are Cluster of differentiation 133+ (CD133 +), CD34 + and Vascular Endothelial Growth Factor Receptor 2+ (VEGFR2 +)/Fetal Liver Kinase-1 (Flk-1).

Epidemiological data suggest that regular intake of certain herbal plants can reduce the risk of CVD. Cocoa (Theobroma cacao) or chocolate is a food ingredient that has been shown to be beneficial for cardiovascular health. A study by Bayard et al., 2007 of residents of Kuna India off the coast of Panama who used to consume cocoa every day showed lower mortality from cardiovascular disease compared to citizens of other countries (9.2 ± 3.1 versus 83.4 ± 0.7 age-adjusted deaths per 100′000).

In vivo studies on the mechanism of cocoa administration on the prevention of endothelial dysfunction due to smoking, in this case, the increase in ICAM-1 and VCAM-1 has not been widely carried out, while research data on the effect of cocoa in smokers on EPC levels in the blood circulation have been reported. This study intends to investigate further the mechanisms for preventing endothelial dysfunction by cocoa due to cigarette smoke, particularly the relationship between oxidative stress, inflammation, and EPC activation with the recency of the immunohistochemical increase in EPC in the injured area, in this case, arteria coronaria. The oxidative stress pathway used an indicator of plasma F2-isoprostane levels, the inflammatory pathway by the expression of the NFkB coronary artery, and the EPC activation pathway by the expression of CD34 and Flk-1 coronary artery, while the endothelial dysfunction used the indicators ICAM-1 and VCAM-1.

This research was conducted in 2 phase. Phase 1 to determine the effective dose of cacao in reducing plasma F2-isoprostane levels; and phase 2 to analyze the mechanisms of preventing endothelial dysfunction by cacao on cigarette smoke exposure. In the first phase

of study, 3 doses of cacao were used. This type of phase 1 is an experimental laboratory with a post-test-only control group design model. The experimental animals used were 30 rattus norvegicus strains of Sprague Dawley, males, aged 3 months, weight 200-300 g grouped randomly into 5 treatment groups. The normal control group (K0) received 2 ml of aqua bidest and given air exposure once a day; the cigarette control group (K1) received 2 ml of aqua bidest and given exposure to cigarette smoke once a day. In the treatment group, each group was given exposure to cigarette smoke and given cocoa powder that had been dissolve in aqua bidest. Cacao group 1 was given a dose of 1206 mg/kg BW/day (P1), cacao group 2 was given a dose of 2411 mg/kg BW/day (P2), and cacao group 3 was given a dose of 3616 mg/kg BW/day (P3). Each group was treated for 14 days. On the 15th day, the experimental animals were terminated and F2-isoprostane was examined using the ELISA method, then was selected one of the three doses of cacao was the most effective in reducing plasma F2-isoprostane levels.

The result of phase 1 showed that the effective dose of cacao in reducing plasma F2-isoprostane levels was 1205 mg/kg BW/day. Furthermore, the cacao treatment group with a dose of 1205 mg/kg BW/day in the second phase of the study was called the treatment group (P), together with the K0 and K1 groups, the NFκB, CD34, Flk-1, VCAM-1 and ICAM-1 were examined. The results of examinations in phases 1 and 2 showed that cacao decreased the expression of NFκB, VCAM-1, and ICAM-1 arteria coronaria and increased the expression of CD34 and Flk-1 coronary artery in rats exposed to cigarette smoke. The result of the path analysis test showed that there was a relationship between cacao in the condition of exposure to cigarette smoke with an increase in CD34 and a decrease in ICAM-1. In addition, there is also a relationship between cacao and a decrease in NFκB and a decrease in VCAM-1.

New in this study, presenting cacao to Rattus norvegicus exposed to cigarette smoke can prevent endothelial dysfunction in 2 ways: the pathway of increasing EPC and an inflammatory pathway with a decrease in NFκB as an inflammatory mediator. The results of this study can be used as a basis for knowledge of prevention disease due to cigarette smoke by using cacao which can be applied daily.

ABSTRACT

The Prevention Mechanisms of Endothelial Dysfunction by Cacao (Theobroma Cacao) Through Analysis of Plasma F2-Isoprostan Levels, Expression of NF-kB, CD-34, and Flk-1 on Cigarette Smoking Exposed Rat

Dina Helianti

Background: Smoking has known as causative factor of cardiovascular disease that was started with endothelial dysfunction. Polyphenols has known significantly prevent endothelial dysfunction. Cacao is a rich source of polyphenols. This study was designed to evaluate the cardioprotective effects of cocoa that mediated through the anti-oxidant effect, and was measured by plasma F2-isoprostane level, anti-inflammatory effect by expression of NFκB, and Endothelial Progenitor Cell (EPC) activation by expression of CD-34 and Flk-1 in coronary arteries. The condition of endothelial dysfunction was measured by expression of ICAM-1 and VCAM-1 in coronary arteries.

Material and Methods: These research was conducted in 2 phases: the first phase determined the efective dose of cocoa in reducing plasma F2-isoprostane level and the second phase analyzed the preventing mechanism of endothelial dysfunction by cocoa on cigarette smoke exposure. This study using cocoa powder. In the first phase, 3 doses of cocoa were used. This study subjected rats, divided into five groups: the normal control group (2 ml of aquabidest, air exposure); the cigarette control group (2 ml of aquabidest, cigarette smoke); cacao group 1 (1205 mg/kg BW/day, cigarette smoke); cocoa group 2 (2410 mg/kg BW/day, cigarette smoke); cacao group 3 (3615 mg/kg BW/day, cigarette smoke). Each group was treated for 14 days. In the second phase of the study using the optimal dose of cacao, based on the results from the first phase. NFkB, CD34, Flk-1, VCAM-1 and ICAM-1 were measured by immunohistochemistry.

Results: Cocoa 1205 mg/kg/day significantly decreases plasma F2-isoprostane level, NFkB, ICAM-1 and VCAM-1 expression of coronary arteries in cigarette smoking exposed rat ($p<0,05$). There was not a significant increases CD-34 but there was a significant increases in Flk-1 expression ($p<0,05$).

Conclusions: Cocoa in cigarette smoke-exposed rats can prevent endothelial dysfunction in 2 ways: the pathway of increasing EPC and an inflammatory pathway with a decrease in NFκB as an inflammatory mediator. The results of this study can be used as a basis for preventing endothelial dysfunction due to cigarette smoke by using cocoa.

Keywords: cigarette smoke exposure, cacao, F2-isoprostane, EPC, endothelial dsyfunction

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2.	Prof. Dr. Teddy Ontoseno, dr., Sp.A(K)., Sp.JP.FIHA	Anggota
3.	Prof. Dr. Achmad Basori, Drs., Apt., MS	Anggota
4.	Dr. Sri Endah Rahayuningsih, dr.,Sp.A(K)	Anggota
5.	Dr. Reny I'tishom., M.Si	Anggota
6.	Dr. Hari Basuki Notobroto, dr., M.Kes	Anggota
7.	Dr. Johanes Nugroho Eko P, dr., Sp. JP(K),FIHA, FASCC,FICA, FESC	Anggota
8.	Dr. Arifa Mustika, dr.,M.Si	Anggota

Sebagai Ketua / Anggota Panitia Ujian Tahap Pertama (Tertutup) Program Doktor Fakultas Kedokteran Universitas Airlangga atas nama I Ketut Alit Utamayasa, dr.,Sp.A(K) peserta Program Doktor Program Studi Ilmu Kedokteran angkatan tahun 2016/2017 yang diselenggarakan pada tanggal 23 Oktober 2020.

Surat tugas ini diterbitkan sementara untuk menunggu keluarnya Surat Keputusan dari Dekan Fakultas Kedokteran Universitas Airlangga.

Surabaya, 16 Oktober 2020
a.n. Dekan
Wakil Dekan I,

Dr. Achmad Chusnu Romdhoni,dr.,Sp.THT-KL(K).,FICS
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Lamp : 1 Berkas
Hal : Mohon Kesediaan untuk menjadi Panitia Penguji Disertasi

16 Oktober 2020

Yth.
1. Prof. Dr. I Ketut Sudiana, Drs.,M.Si
2. Prof. Dr. Teddy Ontoseno, dr., Sp.A(K)., Sp.JP.FIHA (Ketua)
3. Prof. Dr. Achmad Basori, Drs., Apt., MS
4. Dr. Sri Endah Rahayuningsih, dr.,Sp.A(K)
5. Dr. Reny I'tishom., M.Si
6. Dr. Hari Basuki Notobroto, dr., M.Kes
7. Dr. Johanes Nugroho Eko P, dr., Sp. JP(K),FIHA, FASCC,FICA, FESC
8. Dr. Arifa Mustika, dr.,M.Si

Dengan hormat,

Sehubungan dengan selesainya penulisan disertasi peserta Program Doktor angkatan tahun 2016/2017,

Nama : I Ketut Alit Utamayasa, dr.,Sp.A(K)
NIM : 011617017329 ELPT : 557
Judul : PERBEDAAN DAN MEKANISME ANTARA PEMBERIAN ACE INHIBITOR DAN VALSARTAN UNTUK PENCEGAHAN PROGRESIVITAS GAGAL JANTUNG PADA PENYAKIT JANTUNG BAWAAN PIRAU KIRI KE KANAN MELALUI ANALISIS NT-proBNP, TROPONIN-T, SOD DAN KATALASE

Promotor : Prof. Dr. Teddy Ontoseno, dr., Sp.A(K)., Sp.JP.FIHA
Ko-Promotor : Prof. Dr. Achmad Basori, Drs., Apt., MS

Ujian Disertasi rencananya diselenggarakan :

Hari, Tanggal : Jum'at, 23 Oktober 2020
Pukul : 08.30 – 11.30 WIB
Tempat : Menguji secara online menggunakan aplikasi zoom

Maka dengan ini mohon kesediaan Saudara untuk menjadi Ketua / Anggota panitia Penguji Disertasi tersebut, terlampir kami sampaikan pernyataan kesediaan untuk diisi dan dilampirkan pada kami dalam waktu yang tidak terlalu lama guna diproses lebih lanjut.

Demikian atas perhatian Saudara, kami ucapkan terima kasih.

a.n Dekan
Wakil Dekan I

Dr. Achmad Chusnu Romdhoni,dr.,Sp.THT-KL(K).,FICS
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Tindasan :
- KPS Ilmu Kedokteran Program Doktor
- Kepala Sub. Bagian Akademik

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Hari, Tanggal : Jum'at, 23 Oktober 2020
Pukul : 08.30 – 11.30 WIB
Ujian : Tertutup an. I Ketut Alit Utamayasa, dr.,Sp.A(K) Mahasiswa Program Studi Ilmu Kedokteran Jenjang Doktor FKUA

NO	NAMA	TANDA TANGAN
1.	Prof. Dr. I Ketut Sudiana, Drs.,M.Si	1. Hadir online
2.	Prof. Dr. Teddy Ontoseno, dr., Sp.A(K)., Sp.JP.FIHA	2. Hadir online
3.	Prof. Dr. Achmad Basori, Drs., Apt., MS	3. Hadir online
4.	Dr. Sri Endah Rahayuningsih, dr.,Sp.A(K)	4. Hadir online
5.	Dr. Reny I'tishom., M.Si	5. Hadir online
6.	Dr. Hari Basuki Notobroto, dr., M.Kes	6. Hadir online
7.	Dr. Johanes Nugroho Eko P, dr., Sp. JP(K),FIHA, FASCC,FICA, FESC	7. Hadir online
8.	Dr. Arifa Mustika, dr.,M.Si	8. Hadir Online
9.		9.
10.		10.
11.		11.
12.		12.
13.		13.
14.		14.

KEMENTERIAN RISET, TEKNOLOGI, DAN PENDIDIKAN TINGGI
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Program Studi Ilmu Kedokteran Jenjang Doktor FK UNAIR
Surabaya

Sehubungan dengan Ujian Akhir Tahap 2 (Terbuka) sdr. **Dyana Sarvasti, dr., Sp.JP(K)** pada tanggal **14 Agustus 2019**, maka dengan ini kami sampaikan nama-nama penyanggah ujian akhir yang bersangkutan untuk diketahui.

Pimpinan sidang ujian akhir terbuka: Prof.Dr. Soetojo, dr., Sp.U(K)

Para penyanggah dimaksud adalah :

1. Prof. Dr. Rochmad Romdoni, dr., Sp.PD., Sp.JP(K) FIHA., FASCC *)
2. Dr. Anwar Santoso, dr., Sp.JP(K) **)
3. Prof. Dr. Teddy Ontoseno, dr., Sp.A(K)., Sp.JP.FIHA
4. Prof. Dr. Toeti Melani Widjoseno Gardjito, drg., MS., Sp.Pros(K)
5. Prof. Dr. Hening Laswati Putra, dr., Sp.RM(K)
6. Dr. Yudi Her Oktaviono, dr., Sp.JP(K)
7. Dr. Johanes Nugroho Eko Putranto, dr., Sp.JP(K)
8. Muhammad Miftahussurur, dr., M.Kes., Ph.D., Sp.PD., FINASIM
9. Prof. Dr. Aryati, dr., MS., Sp.PK(K)
10. Prof. Dr. Soetojo, dr., Sp.U(K)

Demikian dan atas perhatiannya disampaikan terima kasih.

a.n. Dekan
Wakil Dekan I,

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NIP. 196003051989011002

Catatan :
*) Promotor
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Nomor : 5849/UN3.1.1/PPd/2019 2 Agustus 2019
Lampiran :
Hal : Penyanggah Ujian Akhir Tahap 2 (Terbuka)

Dengan hormat,

Dengan ini kami mengharap kehadiran Saudara sebagai **Penyanggah** Ujian Akhir Tahap 2 (Terbuka) Prodi Ilmu Kedokteran Jenjang Doktor atas nama **Dyana Sarvasti, dr., Sp.JP(K)** yang akan diselenggarakan pada :

Hari, tanggal : Rabu, 14 Agustus 2019
Pukul : 10.00 – 12.00 WIB
Tempat : Aula Fakultas Kedokteran UNAIR.

Demikian untuk diketahui dan atas perhatian Saudara kami sampaikan terima kasih.

a.n.Dekan
Wakil Dekan I,

Prof. Dr. David S. Perdanakusuma, dr.,Sp.BP-RE(K)
NIP. 19600305 1989011002

Catatan
- Dimohon hadir pukul:09.45 WIB
- Pakaian : Guru Besar mohon membawa toga

DAFTAR HADIR PENYANGGAH

Rapat/Sidang : Ujian Doktor Terbuka *Dyana Sarvasti, dr., Sp.JP(K)*
Tanggal : 14 Agustus 2019
Pukul : 10.00 – 12.00 Wib
Tempat : Program Studi Ilmu Kedokteran Univ. Airlangga Surabaya
Acara : Penentuan Predikat Calon Doktor *Dyana Sarvasti, dr., Sp.JP(K)*

No	Nama	Instansi	Tanda Tangan	
1.	Prof. Dr. Rochmad Romdoni, dr., Sp.PD., Sp.JP(K)., FIHA., FASCC		1.	
2.	Dr. Anwar Santoso, dr., Sp.JP(K)			2.
3.	Prof. Dr. Teddy Ontoseno, dr., Sp.A(K)., Sp.JP.FIHA		3.	
4.	Prof. Dr. Toeti Melani Widjoseno Gardjito, drg., MS., Sp.Pros(K)			4.
5.	Prof. Dr. Hening Laswati Putra, dr., Sp.RM(K)		5.	
6.	Dr. Yudi Her Oktaviono, dr., Sp.JP(K)			6.
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Diterbitkan untuk Ujian Akhir Tahap II (Terbuka)

DISERTASI

MEKANISME PROTEKSI KARDIOVASKULAR LATIHAN FISIK INTERVAL INTENSITAS TINGGI PADA PASIEN PENYAKIT JANTUNG KORONER STABIL PASCAIMPLANTASI STENT KORONER

(Evaluasi *flow-mediated dilatation* melalui jalur adrenalin, noradrenalin, eNOS, dan aktivitas SOD ekstraselular)

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2019

LEMBAR PENGESAHAN

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ABSTRACT

MECHANISM OF CARDIOVASCULAR PROTECTION OF HIGH-INTENSITY INTERVAL TRAINING IN STABLE CORONARY ARTERY DISEASE PATIENTS AFTER CORONARY STENTING
(Evaluation of flow-mediated dilatation through adrenaline, noradrenaline, eNOS, and extracellular SOD activities)

Background: High-intensity interval training (HIIT) has been shown to improve aerobic capacity compared with moderate-intensity continuous training (MICT). Unfortunately, little data on the mechanism of HIIT is available.

Objective: This study aimed to compare and determine the mechanism of cardiovascular protection variables in MICT dan HIIT in stable coronary heart disease (CHD) patients after coronary stenting.

Methods: This experimental study used the same subject and cross-over design. Eleven stable CHD patients after coronary stenting were randomly divided into two groups, MICT (29 min at 50-60% heart rate reserve) and HIIT (4x4 min intervals at 60-80% heart rate reserve, each followed by 3 min of active recovery at 40-50% heart rate reserve), three times a week for two weeks. The patients performed adrenaline, noradrenaline, endothelial nitric oxide synthase (eNOS) concentration, extracellular superoxide dismutase (EC-SOD) activity, and flow-mediated dilatation (FMD) examination, before and after treatment was completed.

Results: HIIT significantly increased noradrenaline and eNOS compared to MICT ($p<0.05$). HIIT was better to preserve EC-SOD activity and FMD compared to MICT ($p <0.05$). HIIT through the noradrenalin pathway had a direct and significant effect on eNOS ($p <0.05$). MICT through the noradrenaline pathways had a direct and significant effect on eNOS ($p<0.05$), and through the EC-SOD activity pathways had a direct and significant effect on FMD ($p <0.05$). MICT reduced EC-SOD activity, which results in a decrease in FMD value.

Conclusion: HIIT is superior to MICT in increasing cardiovascular protection through the increment of noradrenalin and eNOS concentration and preserves EC-SOD activity and FMD in stable CHD patients after coronary stenting.

Keywords: Coronary heart disease, high-intensity interval training, catecholamine, eNOS, SOD, FMD.

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