Microvasculature Improvement of Heart in Diabetic Rat with Curcumin Supplementation

Vipavee Anupunpisit PhD*,
Hattaya Petpiboolthai MSc*, Wipapan Khimmaktong PhD**

** Department of Anatomy, Faculty of Medicine, Srinakharinwirot University, Bangkok, Thailand*
*** Department of Anatomy, Faculty of Science, Prince of Songkla University, Songkhla, Thailand*

Objective: *To investigate the effect of curcumin supplementation on the improvement of heart microvasculature in Streptozotocin -induced diabetic rat.*
Material and Method: *Streptozotocin (STZ: 60 mg/kg BW) was applied into rat to induce diabetic condition. Male rats were divided into three groups, control (C), diabetic (DM) and diabetic rats supplemented with curcumin (DMC) (200 mg/kg BW). After 8 and 12 weeks of experiments, heart microvasculature was investigated under vascular corrosion cast technique with scanning electron microscope (SEM).*
Results: *Destruction of heart microvasculature of DM group was observed at 8 and 12-week experiments. Five important categories of heart vessels and related veins and venules were examined respectively: right coronary arteries (RCA), medium arteries (MA), small arteries (SA), arterioles, and capillaries. RCA, cardiac arteries and veins demonstrated abnormality. Atypical patterns of vessels were presented, including shrinkage of artery vessels, capillary dropout, constriction and tortuousity of small cardiac vein and venules, and microaneurysm. At 12-week experiment, vascular lesion of DM group increased in complicated signs, including arterial constrictions and stenosis, arterial blind endings, capillary dropout and shrinkage. In addition, severity of microaneurysm dilatation of arterial branch of RCA, arterial tortuosity, coiled and twisting arteries were investigated. The diameters of vessels of all DM groups were evidently decreased. Subsequent to curcumin supplementation, typical and healthy heart microvasculatures were restored and redeveloped. The diameter sizes of DMC vessels have nearly increased back to normal situations, especially at artery, arteriole, and capillary levels.*
Conclusion: *Efficiency of curcumin treatment beneficially repaired and recovered heart microvascular diabetic complications. This evidence suggests that potential anti-diabetic effect of curcumin is meaningful about the ongoing therapeutic consequences, owing to the improvement and recovery of heart blood vessels.*

Keywords: *Diabetes mellitus, Streptozotocin, Curcumin, Microvasculature, Heart vessels, Vascular corrosion cast, Scanning electron microscope*

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Micro- and macrovascular complications and atherosclerosis are seriously associated with diabetes mellitus, conducting to cardiovascular dysfunction, leading to damage many body tissues such as nephropathy, retinopathy, neuropathy, fatty liver, pancreatitis, cardiomyopathy and coronary vasculature[1-6]. The malfunctions of these vascular complications are related with the hyperglycemic metabolic alteration, endothelial dysfunction and increased oxidative stress and inflammation. Definitely, athrosclerosis and ischemic heart disease in diabetes seriously constitute the significant morbidity and mortality[7,8]. Therefore, many therapeutic modalities have been explored in order to battle with diabetic vascular complication, especially at cardiovascular system. Concerning the abnormality of blood vessels, the characteristic of shrinkage, constriction, tortuousity, stenosis and microaneurysm are typically identified by vascular corrosion cast/Scanning Electron Microscope (SEM).

Curcumin, a naturally active yellow compound of turmeric (*Curcuma longa*), has been illustrated for diabetic treatments in traditional Indian and Chinese for thousands of years. However, curcumin has been scientifically declared as a potential therapeutic agent for diabetic treatments in both animal models and patients for only a few centuries. The potential beneficial gigantic effectiveness of curcumin can be

Correspondence to:
Anupunpisit V, Department of Anatomy, Faculty of Medicine, Srinakharinwirot University, Sukhumvit 23, Wattana, Bangkok 10110, Thailand.
Phone: +66-2-2606195, Fax: +66-2-2601532
E-mail: vipavee19@gmail.com

summarized as anti-hyperglycemia, anti-hyperlipidemia, anti-tumor, anti-inflammatory and antioxidant properties[9].

The potential effect of curcumin has been enormously established for treatment in diabetes and its complication, including glycemia, liver disorders, adipocyte dysfunction, diabetic neuropathy, vascular diseases, and pancreatic beta cell dysfunction[9-12]. In vascular condition, curcumin revealed protective property to control the balance levels of endothelial nitric oxide synthase (eNOS) and inducible nitric oxide synthase (iNOS) levels, and endothelin-1. These effects were beneficial to decrease oxidative DNA and protein damage. Diabetes-induced endothelial cell dysfunction was recovered owing to antioxidant activity and protein kinase C (PKC) inhibition of curcumin efficiency[9,13]. However, the straight approach of curcumin effect on amelioration of cardiovascular architecture in diabetic model has not been explored yet.

Therefore, the effort of this work will study the effect of curcumin in diabetic animal model on cardiovascular improvement, particularly at coronary blood vessels and related microvascular networks.

Material and Method

Induction of diabetes

Male Wistar rats (200-250 g) obtained from National Laboratory Animal Center of Mahidol University were induced by intravenous injection of streptozotocin (STZ) (Sigma, St. Louis, MO, USA) (60 mg/kg BW) dissolved in 0.9% normal saline. Diabetic rats were classified with blood sugar level higher than 250 mg/dl within three days. The rats were divided into three groups (10 rats/group): control group (C), diabetic group (DM), and diabetic-supplemented with curcumin (DMC; curcumin 99.99% pure, sigma, St, Louis, MO, USA) at a dose of 200 mg/kg BW in corn oil diet at 3 ml/kg BW by oral intragastric feeding. C and DM groups received only corn oil diet 3 ml/kg BW. At the end of 8- and 12-week experiments, the heart microvasculature were performed and investigated by vascular corrosion cast/SEM. The protocol of animal research was followed and supervisored by Srinakarinwirot University Medical Center Animal Care Committee.

Experimental animal protocol

The animals were anaesthetized and then thoracic cavity was exposed by transverse incision in the subcostal region. Chest flaps were clamped and retracted to demonstrate the heart. The animals were suddenly injected with heparin solution (Leo, 5,000 IU/ml) into the left ventricle and allowed to circulate for 2 minutes. The thoracic ascending aorta was cannulated by a blunt No. 18 gauge needle, which passed through the left ventricle[14].

Vascular corrosion cast technique

The experimental rats were perfused with 500 ml of 0.9% NaCl solution through the left ventricle, flowing into ascending aorta and distributing through the circulatory system, in order to flush out the blood from the vessels. The blood and solution returned to the heart through superior vena cava and inferior vena cava, then were flushed out at the leaked atrium. Immediately after the perfusion, the Batson's No. 17 plastic mixture was infused into blood circulation of rats and was performed as same as the NaCl solution procedure. The plastic injected-animals were left at room temperature for 30 minutes and immersed in hot water (80°C) for 3 hours to complete plastic polymerization. After polymerization, the heart was isolated, and then was digested and corroded with 10% KOH solution at room temperature for 30-40 days. The heart vascular cast was rinsed in slow running tap water and finally cleaned in distilled water to remove the corroded elements. Then, the heart corrosion casts were prepared air-dried at room temperature, mounted on a metal stub with double glue tape and carbon paint before being coated with gold on sputtering apparatus. Finally, the heart casts were observed under SEM (JEOL JSM-5400) at accelerating voltage of 10 KV.

Statistical analysis

The diameter of heart blood vessels were measured by SemAfore computer software program. The results were expressed as mean $\pm$ standard error of the mean. Statistical analysis was performed by using ANOVA followed by Bonferroni posttest. The value of $p<0.05$ was considered to indicate statistical significance.

Results

SEM of heart corrosion casts revealed clearly the different microvascular characteristics among three groups of rats: control group (C); diabetic groups (DM): and diabetic groups with curcumin supplementation (DMC) and between 8- and 12- week intervals. The SEM micrographs evidently illustrated that cardiovascular vessels could be classified into five categories regarding their larger to smaller sizes respectively: 1) Coronary arteries (CA), 2) Medium arteries (MA), 3) Small arteries (SA), 4) Arterioles and

5) Capillaries. Because of higher magnification of SEM, the obvious destruction and abnormalities of each type of blood vessels could be further clearly identified, including shrinkage, tortuousity, irregular caliber, twisted vessels, and microaneurysm dilatation. Not only cardiovascular qualifications were evaluated, but the quantitative analysis of the diameters of each type of cardiovascular vessels were also measured and compared among each animal group and at different experimental time intervals. All of the following data would be compared among C, DM, and DMC groups, according the aspects of five categories of cardiovascular vessels and the different time intervals of experiments.

Cardiovascular characteristics of right coronary artery (RCA) at 12 weeks

In control group at 12-week experiment, the normal whole heart vascular cast was observed together with the right coronary artery (RCA) at the anterior view of the heart (Fig. 1A). Definitely, RCA was the important vessel that supplied the major blood circulation for the anterior part the heart. On the contrary, the posterior descending artery (PDA), which branched off from RCA, took responsibility the posterior part of heart (Fig. 1B).

Comparison of right coronary artery (RCA) and branching vessels among C, DM, and DMC at 8 and 12 weeks

Regarding C groups of 8- and 12-week time intervals, healthy large right RCA were obviously observed consisting of branching medium vessels, small vessels, arterioles and finally massive capillary networks respectively (Fig. 2A,B). In comparison to C group, the noticeable lesions of diabetic vessels were identified at both 8- and 12-week time intervals (Fig. 2C-D). RCA itself and branching vessels (cardiac arteries and vein) revealed unhealthy shrinkage characteristics together with rough surface of vessels. Moreover, the signs of capillaries dropout were also presented extensively. On the contrary, RCA in curcumin-supplied group: DMC became regenerated and repaired, presenting healthy and firm calibers (Fig. 2E-F).

Comparative arterioles and capillaries among C, DM, and DMC at 8-week time interval

According to C group at 8-week experiment, cardiovascular arrangement showed typical arteries, which splited off from right coronary artery. Then, the arteries broke up into many arterioles which continued dividing into a dense capillary meshwork (Fig. 3A). Concerning the DM group, the explosions of diabetic

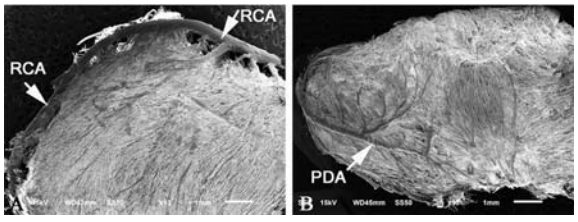

Fig. 1 Survey SEM micrographs of heart vascular cast of control group at 12-week experiment at low magnification, showing whole blood vessels. Bar = 1 mm. A) Anterior view presented right coronary artery (RCA) which branched off into artery, arterioles, and finally capillary meshwork. B) Posterior view illustrated posterior descending artery (PDA) that branched off from RCA.

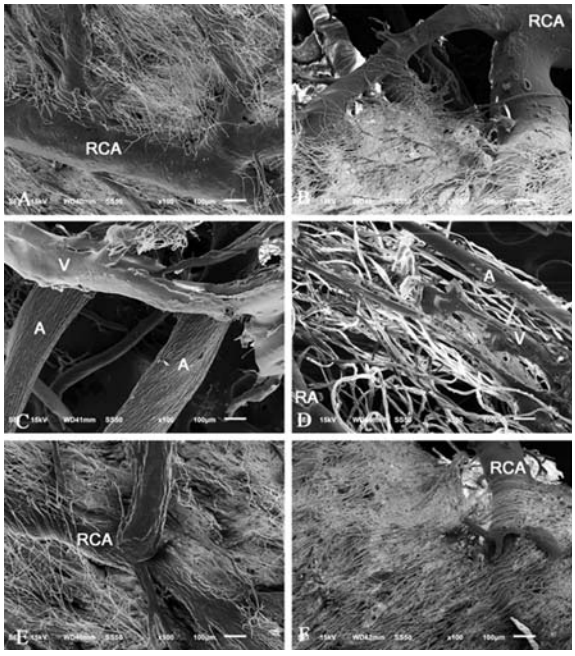

Fig. 2 SEM pictures of heart vascular cast of large arteries at 8 and 12 weeks. Bar = 100 μm. A, B) Control group, healthy typical right coronary arteries (RCA) and its branching arrangements at 8- and 12-week, respectively. C, D) DM group, destroyed arteries (A) and veins demonstrated signs of unhealthy shrinkage together with capillaries dropout at 8- and 12-week, respectively. E, F) DMC group, shrinkage of RCA was also observed at 8 weeks E) whereas recovery and restoration were illustrated at 12 weeks F), respectively.

cardiovascular complication were displayed in different patterns, including shrinkage of arteries, capillary dropout, constriction and tortuousity of small cardiac vein (Fig. 3B). Moreover, many venules revealed tortuosity and irregular caliber in shape together with spots of microaneurysm (Fig. 3C). Interestingly, arteries and capillary networks of DMC group were recovered and restored to the typical patterns, especially at the levels of arteriole and capillaries network (Fig. 3D).

Comparative arterioles and capillaries among C, DM, and DMC at 12-week time interval

Regarding control group at 12-week experiment, RCA branched into many straight noticeable arteries. The artery gave many small branches of arterioles which further distributed widely to form dense capillaries meshwork (Fig. 4A). In addition to DM group, the cardiovascular complications were demonstrated in various patterns, including arterial constrictions and stenosis, arterial blind endings, capillary dropout and shrinkage (Fig. 4B). Additionally, the remarkable abnormality of vessels obviously recognized such as microaneurysm dilatation of arterial branch of RCA, arterial tortuosity, coiled & twisting arteries (Fig. 4C). After curcumin supplementation, well organized architectures of artery arterioles and capillary meshwork have recovered and got restoration in DMC group (Fig. 4D).

Comparison of cardiovascular diameters among C, DM, and DMC at 8- and 12-week time interval

To compare the cardiovascular diameters among C, DM, and DMC at 8- and 12-week experiments, the heart vessels were categorized into five types, defining as RCA, medium arteries (MA), small arteries (SA), arterioles, and capillaries network.

At 8 weeks experiment, pathology and small diameter of vessels in DM were recognized in all five

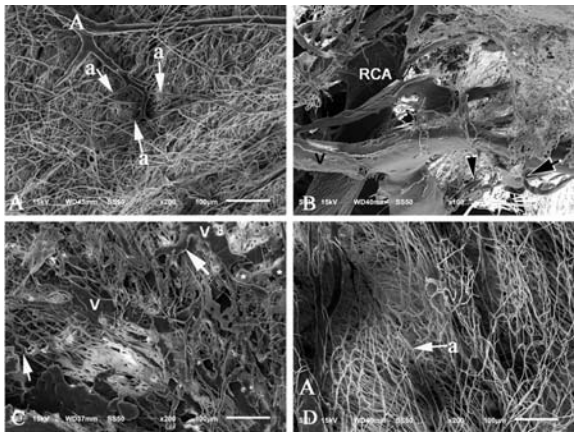

Fig. 3 SEM micrograph of heart vascular casts of 8-week experiment. Bar = 100 μm. A) Control group, healthy typical cardiac arteries (A) provided smaller branching arterioles (a), which branched further into numerous capillaries, forming dense capillaries meshwork. B) DM group, cardiac vein (V) revealed shrinkage and rough surfaces. Black arrowheads indicated constrictions and tortuousity. Deformation of blood vessels from right coronary artery (RCA) and capillaries dropout were also observed. C) DM group, the (V) and venules (white arrows) became tortuosity and presented irregular caliber in shape. Capillaries networks were gradually decreased in numbers. Micro-aneurysms (*) were observed as spherical or oval shapes. D) DMC group, the recovery and redevelopment of artery (A), arterioles (a) and capillaries network were evidently verified.

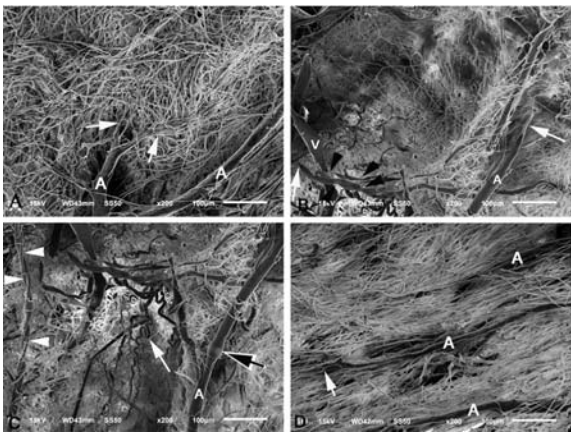

Fig. 4 SEM micrographs of heart vascular cast of 12-week experiment. Bar = 100 μm. A) Control group, typical arteries (A) passed by and gave off branches to be arterioles (white arrow) lying in a dense capillary meshwork. B) DM group, vascular lesions were confirmed by presentation of arterial constrictions and stenosis (black arrowheads) and blind endings (white arrow), and destroyed capillaries. C) DM group, medium arterial branch of RCA validated microaneurysm dilatation (black arrow). Remarkable tortuous small arteries showed abnormalities as coiling (white arrows) and twisting (white arrowheads) patterns. D) DMC group, typical organization of artery (A), arterioles (white arrows) and capillary network have evidently recovered and restored.

types of vessel: RCA, MA, SA, arterioles, and capillaries. Diameters of DM vessels explored reduced sizes, compared to the ones of C group. SA, arterioles, and capillary revealed remarkable decrease in sizes more than ones of RCA and MA. Interestingly, the signs of vessel recovery and restoration were also presented by the increase of diameters of all types of vessels in DMC experiment. The diameters of all vessels were measured and compared in Table 1 and Fig. 5, 6.

The comparative diameter sizes of all vessels among C, DM, and DMC groups at 12 weeks experiments also demonstrated the phenomenon of reduced diameter sizes, as same as at 8 weeks experiments. However, the more severity of decreased-diameter sizes of all types of vessels were seriously observed in DM group, compared to C and DMC ones. Additionally, the diabetic-diameters of MA, SA, arterioles, and capillaries of 12-week experiment were critically decreased and much more severe compared to the ones of 8-week experiment as shown in Table 2 and Fig. 7, 8.

Discussion

Cardiovascular disease is pronounced to be one of the diabetes complications. Specifically, vascular supply of heart is very complicated and so much important to the human body. The damages of large and small blood vessels throughout the heart certainly cause the onset morbidity and mortality. Moreover, many serious symptoms and disease are the consequence of diabetes complication, including atherosclerosis, cardiovascular dysfunction, and cardiomyopathy[1,7,8].

Several studies have reported that curcumin is an active therapeutic agent against diabetic vascular disease, presented by lots of information. Molecular evidences showed that curcumin prevented diabetic cardiomyopathy by modulation Protein Kinase C-Mitogen activated protein kinases (PKC-MAPK) signaling pathway[15]. Curcumin inhibited myocardial infarction in cat model by prevention the ischemia-induced biochemical changes, concerning the content levels of malonaldehyde (MDA) and lactate

Table 1. The average diameters of right coronary arteries (RCAs), medium arteries (MA), small arteries (SA), arterioles and capillaries in control, diabetes (DM) and diabetes treated with curcumin (DMC) at 8 weeks experiment

Groups	Diameters of blood vessels (μm), mean ± SE				
	RCAs	MA	SA	Arterioles	Capillaries
Control	232.25±10.40	62.85±3.93	37.45±3.67	16.53±0.81	5.65±0.15
DM	226.75±9.18	22.88±2.70	19.28±1.90	5.57±0.28	2.30±0.28
DMC	228.25±11.40	56.50±1.71	28.33±4.55	11.12±0.66	4.23±0.32

SE = Standard error of mean

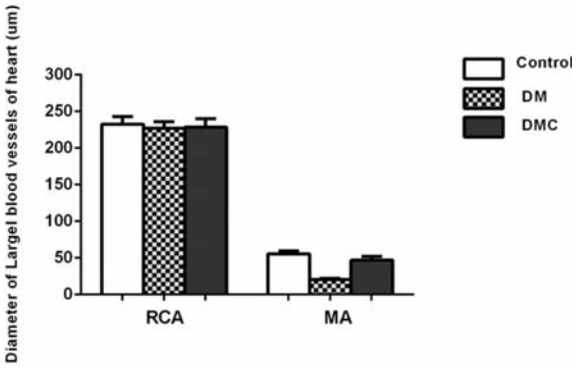

Fig. 5 The average diameters of right coronary arteries (RCA) and medium arteries (MA) in control (C), diabetes (DM), and diabetes treated with curcumin (DMC) rats at 8 weeks. Values are mean ± SE.

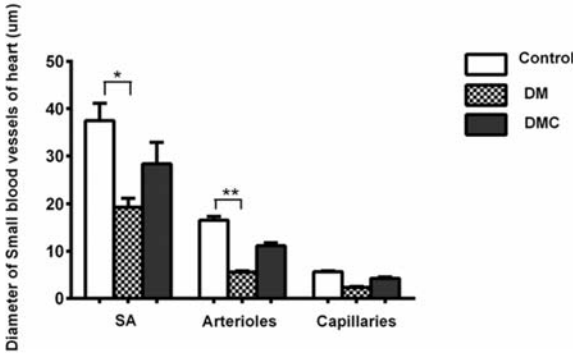

Fig. 6 The average diameters of small arteries (SA), arterioles and capillaries in control (C), diabetes (DM), and diabetes treated with curcumin (DMC) rats at 8 weeks. Values are mean ± SE, * $p<0.05$; ** $p<0.01$.

Table 2. The average diameters of right coronary arteries (RCAs), medium arteries (MA), small arteries (SA), arterioles and capillaries in control, diabetes (DM) and diabetes treated with curcumin (DMC) at 12 weeks experiment

Groups	Diameters of blood vessels (μm), mean ± SE				
	RCAs	MA	SA	Arterioles	Capillaries
Control	263.75±13.75	60.60±1.56	45.10±1.40	16.30±0.89	5.64±0.15
DM	101.86±3.70	21.86±0.74	16.55±0.46	4.20±0.32	1.85±0.11
DMC	266.00±22.27	54.95±3.40	43.53±2.54	14.90±1.45	5.06±0.22

SE = Standard error of mean

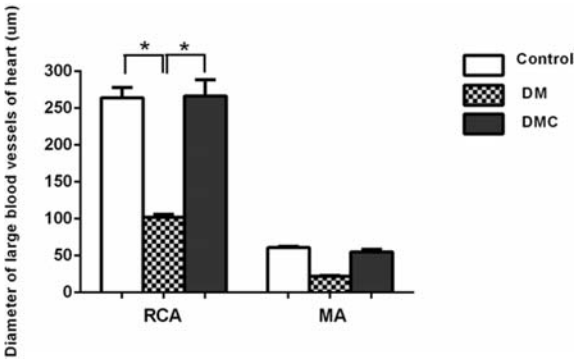

Fig. 7 The average diameters of right coronary arteries (RCA) and medium arteries (MA) in control (C), diabetes (DM), and diabetes treated with curcumin (DMC) rats at 12 weeks. Values are mean ± SE, * p<0.05.

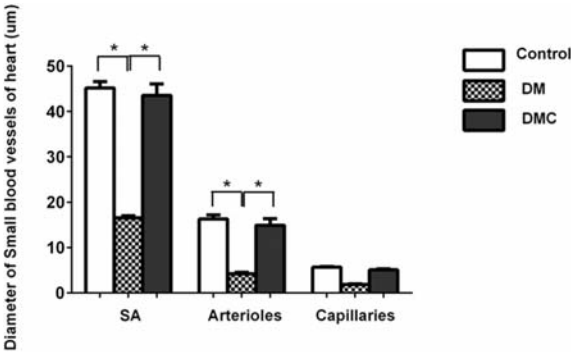

Fig. 8 The average diameters of small arteries (SA), arterioles and capillaries in control (C), diabetes (DM), and diabetes treated with curcumin (DMC) rats at 12 weeks. Values are mean ± SE, * p<0.05.

dehydrogenase (LDH). In the isoproterenol (ISO)-induced myocardial infarction, the level of lysosomal hydrolase was decreased after curcumin treatment. As a result, curcumin restored the normal level and activity of this enzyme in order to protect myocardial infarction[13].

Regarding atherosclerosis, curcumin also showed the prevention of pathological changes of vascular smooth muscle cells by inhibition of cell proliferation, prohibition of cell cycle, and induction of apoptosis[9,13]. It is suggested that curcumin could reduce the peroxide-associated injury, which was the cause of arterial diseases and liver pathology. Correspondingly, our results have shown the well-defined restoration and repair of heart vessels, including coronary artery, medium and small arteries, arterioles, and capillary network, after curcumin supplementation. Therefore, curcumin might have the concurrent action to boost up the structure and functions of heart vessels within the appropriate time intervals. Interestingly, the effect of curcumin demonstrated the recognized decrease in serum cholesterol, serum lipid peroxides, and increase in high-density lipoproteins cholesterol. These results were affiliated with inhibition of lipid peroxidation in the liver, kidney, lung, and brain in animal models.

The characterizations of atherosclerosis are associated with the oxidation of low-density lipoproteins (LDL) and oxidative damages, which further destruct the blood vessel walls and subcellular membrane. However, the effect of curcumin was shown to inhibit oxidation of LDL at both initiation and propagation stages of LDL oxidation[9,13,16]. Moreover, curcumin extract might have the protective action against lipoperoxidation of subcellular membranes in a dosage-dependant approach. In addition, curcumin has potential to decrease liver triglyceride, plasma triacylglycerols in LDL fractions, and cholesterol concentrations. It is suggested that curcumin has possibility on lipid-decreasing manners, association with fatty acid metabolism.

Regarding cardiovascular complications in diabetes, the endothelial dysfunction is a key maker,

due to the alteration of biological action of nitric oxide (NO). Pathology of blood vessels in diabetes were characterized by increased vascular tone, platelet accumulation, microvascular endothelial cells dysfunction, inflammation, and oxidative stress, which were mostly related with the level of NO. Focusing on diabetic-models, curcumin ameliorated diabetes-provoked vascular dysfunction, presenting by inhibition the activities of cyclooxygenase-2, Nuclear Factor Kappa, and protein kinase C[17]. Additionally, curcumin improved overstressed vascular contractility, shown by decreasing tumor necrosis factor alpha and aortic reactive oxygen species together with upregulation of heme oxygenase-1 (HO-1) in diabetic rat[18]. At present, HO system is strongly interested as anti-diabetic modulator because of its essential cellular protection and detoxification activities, performing in stimulation of insulin release and control glucose metabolism. Curcumin possesses anti-diabetic effect by increasing HO-1 expression and also help to maintain equilibrium of lipid profile in diabetic model by decreasing total cholesterol, triglycerides, LDL whereas increasing HDL levels. In addition, malondialdehyde, which is lipid peroxide, was simultaneously decreased in diabetic-pancreas, liver, and aorta in the experiments[19,20].

According to vascular complication, curcumin as well improved neovascularization, improvement of antioxidant enzymes and vascular reactivity of aorta, controlling microcirculation and edema in micro-angiopathy and retinopathy, and obstructed macrophage foam cell formation in human diabetic atherosclerosis[9,13,21,22].

Our previous reports have continuously established that curcumin repaired and redeveloped microvascular architectures in many STZ-induced diabetes, including in kidney, pancreas, liver, and choroid vessels in eyes[12,23-25]. In term of protein-related expression, the effect of curcumin on the balance of production and release of vascular endothelial growth factor was also the important factor for amelioration of diabetes-associated complications in different tissues. According to literature reviews as described, numerous potential effects of curcumin as therapeutic agent on diabetic complications have been pronounced in both experimental models and clinical trials. Scientific attentions firmly focus on the properties of curcumin in many aspects, including anti-hyperglycemia, anti-hyperlipidemia, anti-tumor, immunomodulation, anti-bacterial, anti-inflammatory and antioxidant properties[10,26,27].

Normal structure and function of heart vessels are so important for human body. In this study, significant destruction of heart blood vessels of both large vessels (RCA, medium and small arteries) and small vessels (arterioles and capillary network) were demonstrated in terms of qualification and quantitation data. However, curcumin supplementation in diabetic group reflected the recovery and redevelopment for all categories of heart blood vessels. Significant healthy architecture of vessels returned. In concomitant, most of damaged signs of vessels were disappeared such as constriction, shrinkage, blind ending, twisting, microaneurysm, capillary dropout, capillary discontinuity and breakage. Moreover, the diameter sizes of all types of heart vessels in curcumin-treated group prominently revealed the better situations closely to control group, especially in arterioles and capillary levels.

Conclusion

To explore the effect of curcumin on microvasculature improvement of heart in diabetic rat, curcumin might be potential agent that has a beneficial effect on restoration and redevelopment of heart vessels for both morphological characteristics and diameter sizes. All types of heart vessels, including RCA, medium and small arteries, arterioles and capillary network explored typical recovery patterns. These results indicated that curcumin had ability to improve vascular diabetic complication of heart.

What is already known on this topic ?

In diabetes mellitus, the complications of microvascualr and macrovascular characteristic have been known in many organs, including heart vessels. The malfunctions of these vascular complications are mainly focus on metabolic alteration, artherosclerosis and ischemic heart disease because of seriously significant for morbidity and mortality. Many therapeutic modalities have been explored in order to encounter with diabetic vascular complication, especially at heart cardiovascular system.

What this study adds ?

This study emphasized on the effect of curcumin in diabetic animal model on heart cardiovascular improvement, particularly at coronary blood vessels and related microvascular networks. Regarding corrosion vascular corrosion cast/scanning electron microscopy technique, we observed the recovery of heart cardiovascular after curcumin

supplementation, emphasizing on morphological improvement of blood vessels and the comparative changes of diameter sizes of both groups of large and small blood vessels. The results implied the benefit of curcumin regarding on the alternative treatment in diabetic condition.

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Potential conflicts of interest

None.

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ผลของ curcumin ต่อการฟื้นฟูและซ่อมแซมหลอดเลือดหัวใจของหนูที่เป็นเบาหวาน

วิภาวี อนุพันธ์พิศิษฐ์, หัทยา เพชรพิบูลย์ไทย, วิภาพรรณ ขิมมากทอง

วัตถุประสงค์: เพื่อศึกษาผลของสาร curcumin ต่อการฟื้นฟูและซ่อมแซมโครงสร้างหลอดเลือดหัวใจในหนูทดลองที่ถูกเหนี่ยวนำให้เป็นเบาหวานโดยสาร streptozotocin (STZ)

วัสดุและวิธีการ: หนูถูกเหนี่ยวนำให้เป็นเบาหวานโดยสาร STZ (60 mg/kg BW) หนูเพศผู้ถูกแบ่งออกเป็น 3 กลุ่ม ได้แก่หนูกลุ่มควบคุม กลุ่มเบาหวาน และกลุ่มเบาหวานที่ได้รับสาร curcumin (200 mk/kg BW) เป็นระยะเวลา 8 และ 12 สัปดาห์ ได้ศึกษาลักษณะโครงสร้างของหลอดเลือดหัวใจของหนูทั้ง 3 กลุ่มโดยวิธี vascular corrosion cast ร่วมกับกล้องจุลทรรศน์อิเล็กตรอนชนิดส่องกราด

ผลการศึกษา: หนูกลุ่มเบาหวานมีความผิดปกติ มีการทำลายโครงสร้างหลอดเลือดหัวใจที่ระยะเวลา 8 และ 12 สัปดาห์ ศึกษาหลอดเลือดห้าระดับได้แก่ right coronary arteries (RCA), medium arteries (MA), small arteries (SA), arterioles, capillaries และ vein venules ที่เกี่ยวข้องกัน หลอดเลือด RCA และ arteries ในกลุ่มเบาหวานมีความเสียหาย มีลักษณะเหี่ยวแฟบ หลอดเลือดฝอยเสียหาย (capillary drop-out) รวมถึง cardiac vein ที่หดเล็กลง และ venules ที่คดงอที่ระยะเวลา 12 สัปดาห์ หลอดเลือดมีความเสียหายเพิ่มมากขึ้น arteries มีลักษณะขดงอและตีบ หลอดเลือดมีปลายตัด การโป่งพอง และการขดบิดเป็นเกลียว หลอดเลือดระดับต่าง ๆ ที่มีภาวะเบาหวานมีขนาดหดเล็กลง มีขนาดเส้นผ่าศูนย์กลางเล็กลงมากเมื่อเทียบกับกลุ่มควบคุม แต่ในหนูที่เป็นเบาหวานและได้รับการรักษาด้วยสาร curcumin พบว่าโครงสร้างหลอดเลือดหัวใจทั้งห้าระดับมีการซ่อมแซมและฟื้นฟูสภาพเข้าสู่สภาวะปกติและใกล้เคียงกลุ่มควบคุม รวมทั้งหลอดเลือดมีขนาดเส้นผ่าศูนย์กลางเพิ่มขึ้นโดยเฉพาะที่ระดับ arteries, arterioles และ capillaries

สรุป: สาร curcumin ช่วยการรักษา ฟื้นฟูและซ่อมแซมสภาพหลอดเลือดหัวใจที่เสียหายเสื่อมสภาพจากสภาวะเบาหวาน ส่งผลดีต่อการลดภาวะแทรกซ้อนของหลอดเลือดหัวใจ คุณสมบัติของสาร curcumin จึงน่าจะเป็นประโยชน์ในการพัฒนาด้านการรักษาโรคเบาหวานต่อไป