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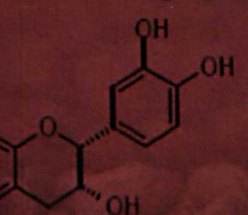
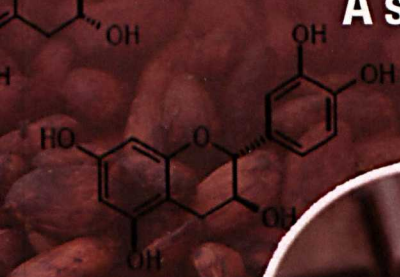
Malaysian Cocoa or Chocolates

A story of antioxidants and more...





PROFESOR DR. AMIN ISMAIL

Malaysian Cocoa or Chocolates

A story of antioxidants and more...

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Bac. Food Science & Technology (UPM), PhD (Food Chemistry & Biochemistry) (UPM), FNSM

14 AUGUST 2015

Dewan Kuliah Utama
Fakulti Perubatan dan Sains Kesihatan
Universiti Putra Malaysia

Universiti Putra Malaysia Press
Serdang • 2015
http://www.penerbit.upm.edu.my

Cetakan Pertama 2015

Penerbit UPM adalah anggota Persatuan Penerbit Buku Malaysia (MABOPA)
No. Ahli: 9802

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ABSTRACT

For centuries, cocoa has been recognized as a rich source of dietary antioxidants, especially polyphenols. It is known not only for its good flavour but also for its health benefits. Cocoa has drawn increased attention because of its antioxidant properties and marked effects in the prevention of various oxidative stress-associated diseases. In the last few years, research and development on polyphenols and extracts from cocoa and cocoa-derived products, such as cocoa powder, cocoa liquor and chocolates, has become a major area of health and medical related research. The recommended human diet contains a significant amount of polyphenols, as they are assumed to be 'antioxidants' that scavenge excessive harmful free radicals arising from normal metabolic processes. *In vitro* as well as *in vivo* data indicate that polyphenols present in Malaysian cocoa may have antioxidant capacity, anti-diabetes and anti-inflammatory properties and also promote an anti-obesity phenotype. Over the last 2-3 years, there have been exciting new developments which have shone more light on the *in vivo* mechanisms behind the health benefits of Malaysian cocoa. Our studies showed that cocoa polyphenols not only function as antioxidants but also as non-antioxidants. Several molecular targets (e.g., nuclear factor Kappa B (NF-kB), activated protein-1 (AP-1) peroxisome proliferator-activated receptors (PPARs) and liver X receptors (LXRs)) have been recently identified and may partly explain the potential benefits of cocoa in relation to combating obesity-associated diseases. Cocoa polyphenols have been reported to regulate lipid metabolism by inducing metabolic gene expression and activating transcription factors that regulate the expression of numerous genes, many of which play an important role in energy metabolism. Further studies have been performed to investigate the protective effects of cocoa polyphenols against metabolic diseases

which include acting as an antioxidant or suppressing transcription factors that antagonize lipid accumulation. Recent evidence suggests that polyphenols also have indirect antioxidant effects through the induction of endogenous protective enzymes. Evidence of potential benefits through polyphenolic-mediated regulation of cellular processes such as inflammation is also increasing, and these signalling effects may occur at concentrations which are much lower than those required for effective radical scavenging. Thus, polyphenol-rich cocoa products may potentially diminish obesity-mediated metabolic diseases by multiple mechanisms, thereby attenuating chronic inflammation. Our findings from *in-vitro* and *in-vivo* studies on the health benefits of Malaysian cocoa-derived products, suggest that the intake of cocoa polyphenols could lead to reduced disease risk. Moreover, the consumption of a balanced diet that includes a variety of polyphenol-rich food sources is important for the promotion of health.

INTRODUCTION

The chronology of the history of cocoa begins in 2,000 B.C. This date is attributed by historians to the oldest drinking cups and plates ever discovered in Latin America in a small village in the Ulúa valley in Honduras, where cocoa played a central role. In 200 -900 AD, cocoa was one of the main products in Mayan agriculture and religion (Barry Callebaut, 2008). The word cacao is derived from the Olmec and the subsequent Mayan languages (Kakaw), and the name chocolate is derived from Olmec/Mayan etymology. In 1773, the cocoa tree was named *Theobroma cacao*, which can be attributed to the mythical background of the tree, and literally means "Food of Gods" (Barry Callebaut, 2008). The medicinal uses of cocoa have been traced to Mexican sources, and more than 150 uses of cocoa in medicines have been documented (Dillinger et al., 2000). Later, in 1630, in Europe, cocoa was used as a medicine rather than as a delicious foodstuff. The use of chocolate to stimulate the normal functions of the spleen and other digestive system functions had been recognized. Additionally, during the 18th century, chocolate was regularly mixed into medications for many diseases, including the common cold, cough and high blood pressure (Barry Callebaut, 2008). The first evidence of the health benefits of cocoa and its products comes from the Kuna Indians, a native population living on the coast of Panama. The Kunas consumed adequate amounts of cocoa daily, usually evenly mixed with salt. Physical and clinical investigations found that the Kunas indeed had lower blood pressure and no age-dependent decreases in kidney functions. Furthermore, mortality due to cardiovascular diseases was markedly lower in this native population, as compared to other citizens.

Cocoa is a food with many uses. Cocoa generally refers to cocoa powder, which is made from roasted cocoa beans. This is not to be confused with *Theobroma cacao*, which literally refers to the

cocoa tree. Good quality cocoa beans are produced through two vital steps, namely primary and secondary processing. The primary steps are fermentation and drying, whilst secondary processing involves cleaning and cracking, roasting, grinding, pressing (optional) and tempering.

There are different types of cocoa and cocoa-derived products available in the market. Cocoa powder and cocoa liquor are used as ingredients in chocolate manufacturing, along with cocoa butter and milk. Dark and milk chocolates are made from a mixture of cocoa liquor and sugar, but the latter involves the addition of cocoa butter. White chocolate, however, is not 'real' chocolate because it is made from a mixture of cocoa butter, milk and sugar. Dark chocolate is bitter and less sweet compared to milk and white chocolate. Dark chocolate is considered one of the major contributors of antioxidants to the American diet, after fruits and vegetables. Cocoa beans and their derived-products (Figure1) have been used as the major ingredient in chocolate and cocoa powder for a long period of time.

Malaysia was ranked the world's fifth largest producer of cocoa beans in 2012. Today, Malaysia is one of the main producers of cocoa-based products in the world and the biggest in Asia. The utilization and exploitation of cocoa extract and/or polyphenol substances (fine chemicals) from Malaysian beans can contribute to the nation's economic development. It will benefit the Malaysian cocoa industry to exploit and diversify the use of cocoa extract, which is a rich source of polyphenols. The standardized polyphenol-rich extract and its fine chemicals can be exploited for the development of functional foods, nutraceuticals and pharmaceuticals. In Malaysia, the development of the cocoa industry has begun and a variety of cocoa products are now available in the local market. With the growing interest in health foods, products that incorporate cocoa polyphenol extract have an

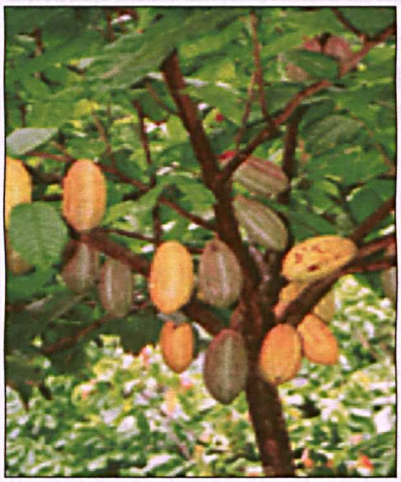
added value due to the potential health benefits. Our local cocoa industry, especially the grinding sector, has grown steadily over the years and should continue at grow at a faster rate to advance this agro-industry sector. Due to a shortage in the production of cocoa beans in Malaysia, our country imports approximately 44,000 tons annually from Indonesia (most of the beans are under-fermented and inexpensive). The manufacturers usually blend these beans with those from West Africa and Ghana (expensive well-fermented beans) to meet their requirements. Through partial polyphenol extraction, which can reduce excessive astringent and improve the bitter taste, valuable polyphenol substances can be produced as by-products which can be utilized for human benefit. Our study can help improve the competitiveness of cocoa beans from Asian regions, especially Malaysian beans, in global markets.

In the year 2000, our research group reported that Malaysian cocoa beans and their derived products had significant antioxidant capacity compared to other cocoa beans (Azizah et al., 2007). Thus the Malaysian cocoa beans and their derived products could help decrease chronic disease risk factors (Abbe et al., 2009; Abbe et al., 2008a; Azizah et al. 2007; Ruzaidi et al. 2005; Amin et al. 2004b; Amin et al. 2004c).

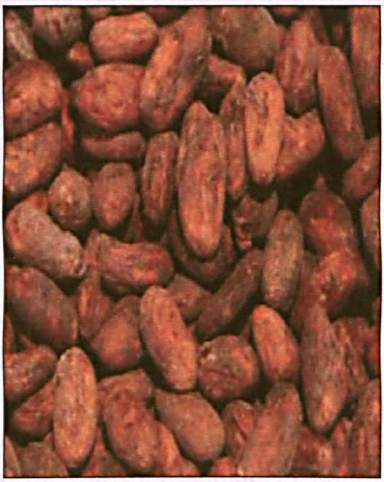
Cocoa beans are reported to have a high content of antioxidant polyphenols, which comprise 12-18% of the dry weight of whole beans, compared to other foods. Besides polyphenols, proteins play an important role in its flavour quality (Amin et al., 2002a, b).

Polyphenols or phenolics are one of the non-nutrient groups found in plants, and they are characterized by the presence of one or more hydroxyl groups on aromatic rings. They are found widely in the plant kingdom and are the secondary metabolites of plants. They are involved in the defence against UV and pathogens. More than 8,000 phenolic compounds have been reported as being

antioxidants (Bravo, 2000). Nutritionally, polyphenol-rich foods can strongly inhibit iron absorption. Due to the chelating properties of these compounds, they can bind more or less strongly to iron in the intestinal lumen and influence iron absorption. Polyphenol compounds were not considered necessary from a nutritional point of view during the early years due to their mutagenic and genotoxic activities. However, data from epidemiological studies suggest that high dietary intake of polyphenols is associated with decreased risk of a range of diseases, including cardiovascular diseases, certain cancers and neurodegenerative diseases. Epidemiological studies also demonstrate that regular dietary intake of cocoa polyphenols reduces the risk of coronary heart disease and stroke and is inversely associated with the risk of cardiovascular diseases (Hooper et al., 2012).



Fruits of *Theobroma cacao*



Dried cocoa beans (raw cocoa)

Cocoa powder

Cocoa liquor/mass

Chocolates

Figure 1 Fruits of the *Theobroma cocoa* tree and their derived products.

Polyphenols in Cocoa and Cocoa-derived Products

Food generally contains complex mixtures of polyphenols and numerous factors may affect the content of polyphenols in plants and plant products. Our studies have reported that Malaysian fruits,

vegetables, legumes and their by-products are rich in polyphenols (Chew et al., 2011; Emmy Hainida et al., 2008 & 2009; Khoo & Amin, 2008; Prasad et al., 2010; Marina et al., 2009; Sun et al., 2013; Tan et al., 2010a, b; Zabidah et al., 2014; Azrina et al., 2010; Fouad et al., 2011; Sadeq et al., 2012; Kong et al., 2010a,b & 2011). Flavonoids are one of the polyphenol groups in foods which have attracted great interest since the 1990s. Cocoa is a rich source of dietary flavanol (a sub-class of flavonoids). Epicatechin and catechin are the major dietary flavanols in cocoa beans (Ali et al., 2014a; Abbe & Amin, 2010; Azizah et al., 2007) (Figure 2). Some chocolates (especially dark chocolates) remain good sources of polyphenols, especially flavonol (Figure 3). Researchers are very much interested in cocoa polyphenols due to their potent antioxidant properties as well as their credible effects in the prevention of various free radicals associated diseases.

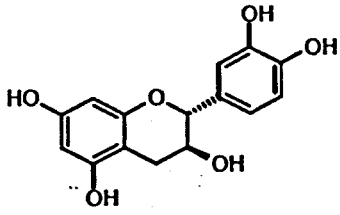


Figure 2(a) Catechin

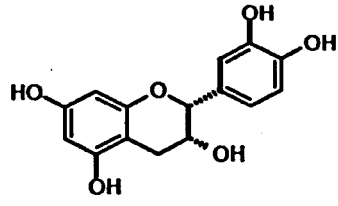


Figure 2(b) Epichatechin

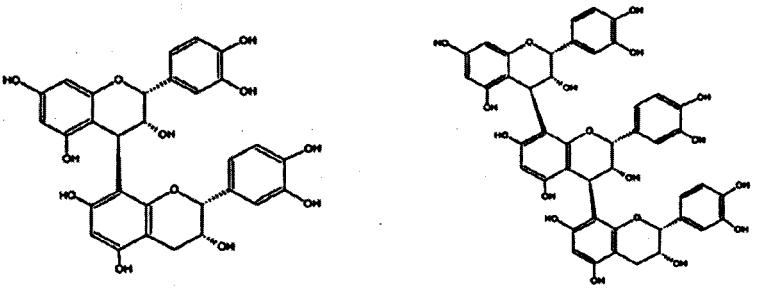


Figure 2(c) Procyanidins dimer and trimer in cocoa

Figure 2 Major polyphenol compounds (catechin, epicatechin and procyanidins) in cocoa. (Source: Ali et al., 2014a; Abbe & Amin, 2010; Azizah et al., 2007)

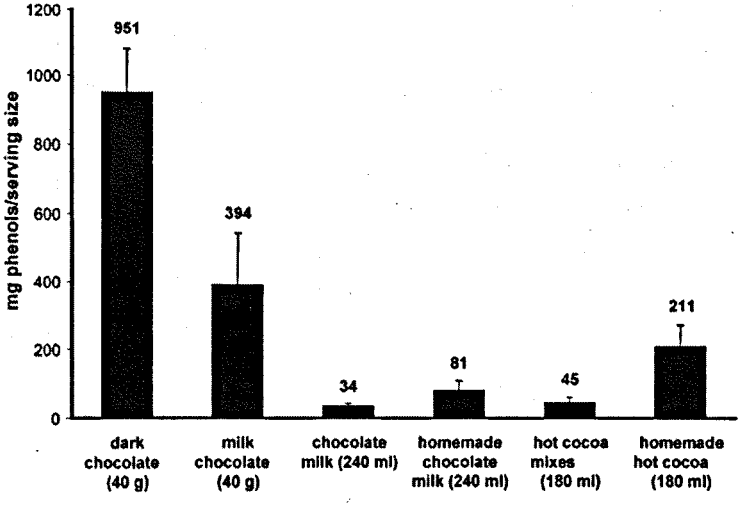


Figure 3: Polyphenols content in chocolate products

(Source: Visioli et al., 2009)

The total intake of polyphenol-rich food in humans is about 1g/day with some large inter individual variability (Nobutomo et al. 2010). A recent study by Buijsse et al. (2010) among German adults suggested that 7.5 g/day intake of chocolate (24% of intake from dark chocolate) is associated with lower systolic and diastolic blood pressure and a 10% lower 8 years risk of stroke. In the Dutch population cocoa products contribute up to 20% of the total flavonoids intake in adults, while in children the percentage is even higher. However, the mean daily intake of polyphenols in the Spanish diet was estimated at between 2590 and 3016 mg/ person/day. It is important to realize that the biological actions and health benefits of cocoa polyphenols depend mainly on their bioavailability, metabolism and amount consumed. However, previous studies of various classes of polyphenols have shown that bioavailability varies widely from one polyphenol to another, so the most abundant polyphenols in our diet are not necessarily those leading to the highest levels of active metabolites in target tissues. The impacts of food compositions on the bioavailability of polyphenols have not been clearly investigated. The bioavailability of all phenolics is still largely unexplored, which demands further investigation, especially with regards to its functions. For example, independent of the doses of chocolate and cocoa ingested, only 0.5% of catechin was recovered in free unbound form from human plasma and urine. However, scientists hypothesize that some individuals could have better absorption and tissue distribution than others, possibly because of particular polymorphisms. This could be the mechanism that explains the high variability in the levels of flavonoid absorption that have been published (Borchers et al., 2000). Currently there is experimental evidence that cocoa polyphenols can act as dietary signals for direct interaction with DNA and gene expression (Manach et al., 2005).There has,

however, been relatively little study of the molecular mechanisms underlying the protective effects of cocoa polyphenols on energy metabolism and relevant gene expression profiles. Thus, the possible mechanisms involved in the cellular uptake of cocoa polyphenols, as well as, its cellular concentrations and distribution, have to be extensively clarified.

The identification of the polyphenols in cocoa products (cocoa beans, cocoa powder, chocolate and cocoa liquor) is the first step in the utilization of these compounds in the preparation of nutraceuticals and functional foods. In our studies (Ali et al., 2014a; Abbe & Amin, 2010), polyphenols from cocoa were extracted from defatted cocoa products (Figure 4).

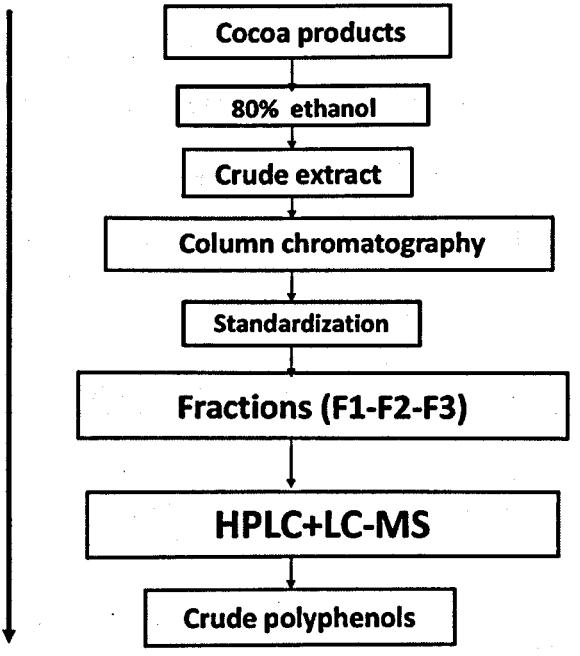


Figure 4 Isolation steps of crude polyphenols from cocoa products
(Source: Abbe & Amin, 2010)

Polyphenol compounds in each fraction were detected by using high-performance liquid chromatography (HPLC) (Agilent 1100, Palo Alto, USA) equipped with a quaternary pump, auto injector, degasser and DAD. A reversed-phase C18 column (Alltech, Licosphere, United States) (250 mm × 4 mm, 5 μm I.D) was used for the separation of bioactive compounds and gradient elution of (A) water - trifluoroacetic acid (99.9: 0.1, v/v) and (B) acetonitrile - trifluoroacetic acid (99.9: 0.1, v/v) (Nobutomo et al., 2010). A linear tendency elution of 0 - 10% (A) for 5 min, 10 - 25% (A) for 25 min and 25 - 100% (A) for 5 min, with a flow rate of 0.8 mL/ min, was applied to the analysis along with UV spectra recorded from 280 – 360 nm. The amount of catechin, epicatechin, gallic acid, protocatechuic acid and chlorogenic acid (mg/g fraction) were quantitatively assessed based on external standards (100 - 1000 μg/ml). The eluent was well analyzed by ESI - MS - MS using an electron spray ionization tandem mass spectrometer (Finnigan LCQ Advantage MAX ion-trap mass spectrometer) operating in a negative mode. Cocoa contains five compounds, namely, catechin, epicatechin, gallic acid, protocatechuic acid and chlorogenic acid (Table 1).

Table 1 Flavonoids and phenolic acids in cocoa powder

(Source: Ali et al., 2014a)

Peaks	Compounds	RT(min)	Concentrations mg/g CP
1	Gallic acid	5.9	0.84±0.45
2	Protocatechuic acid	10.1	18.8±2.40
3	Chlorogenic acid	12.8	1.18±0.33
4	Epicatechin	13.5	1.39±0.14
5	Catechin	11.03	1.32±0.47
	Phenolic acid amount	114 mg/g	
	Flavonoid amount	94.95 mg/g	
	Yield extract[a]	23.75 g/100 g	

The data are given as mean ± SD (n =3)

[a] Yield (percent) [solvent extracts wt (g)/sample wt (g)] × 100

The cocoa polyphenols were then analyzed by HPLC/UV-ESI-MS/MS through molecular ion and mass (Figure 5). At the same time, the HPLC-MS/MS results were further confirmed using our standard library information. Through our standard library information search (e.g. Peak retention times, UV spectrum, [M-H] (m^2), molecular mass and ESI-MS/MS data), the five phenolic compounds that had been investigated using the HPLC-UV were further confirmed in HPLC-MS-MS.

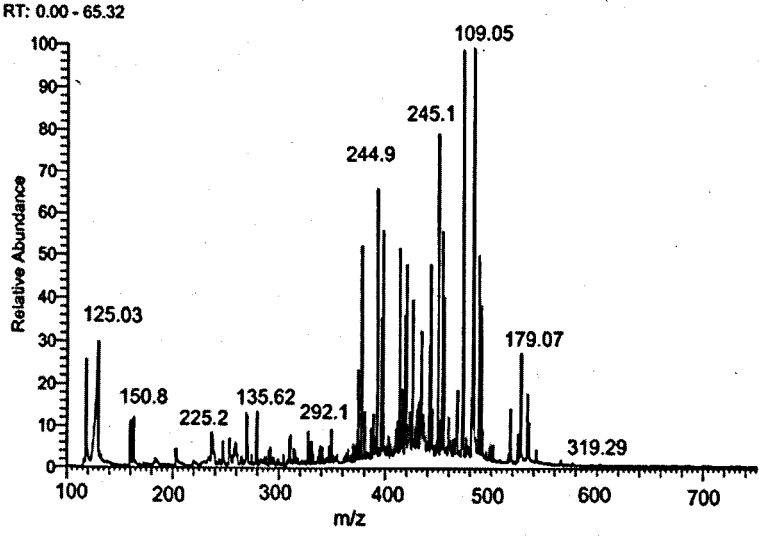


Figure 5 Polyphenol compounds in cocoa by LC-MS/MS with ESI.
(Source: Ali et al., 2014a)

Antioxidant Capacity and Health Benefits of Cocoa Polyphenols

It has been reported that the health properties of cocoa products can be attributed to their antioxidant capacity, and the antioxidant capacity itself is related to the presence of cocoa polyphenols. Over the last decade numerous studies have shown the health effects and phytotherapy of polyphenols from cocoa *in vitro* and *in vivo* (Abbe & Amin, 2013; Abbe & Amin, 2008b; Ali et al., 2014b). Most of the experimental and epidemiological outcomes led to the hypothesis that such health benefits might be linked, at least in part, to flavonoids, a large subgroup of the heterogeneous group of polyphenols. Moreover, most of the outcomes of the studies on cocoa polyphenols were related to the health effects of polyphenolics towards the antioxidant status, endothelial function, blood pressure, insulin resistance, inflammatory process and platelet function (Figure 6). Strictly speaking, the previous studies emphasized on the preventive role of polyphenolics, which means that it is the effects before the development of disease or dysfunction. However, some studies have also investigated the therapeutic role of polyphenolics, meaning its effects after the onset of disorders. In our works, both protection and pharmacological activities were assessed, including, cell culture, experimental animals and human studies. Recently, we have shifted from classical research onto molecular, cellular and functional genomics analysis using sophisticated techniques to unveil the molecular mechanism by which polyphenols prevent or ameliorate metabolic diseases with special emphasis on obesity and related diseases, such as, diabetes, osteoporosis, vascular and inflammation disorders.

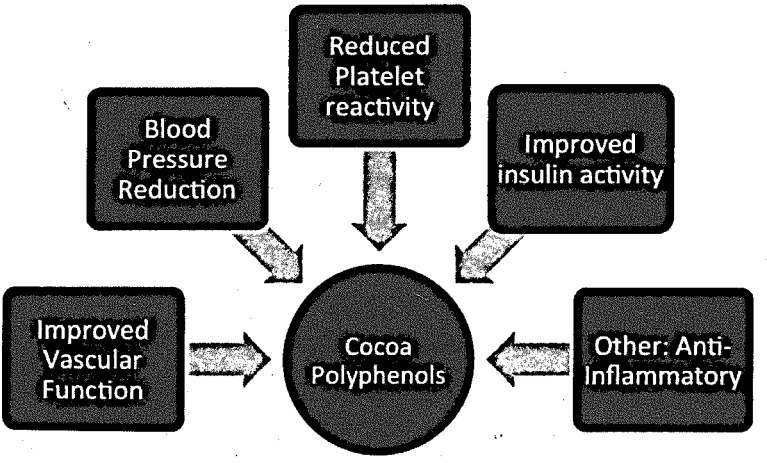


Figure 6 Potential Health benefits of cocoa polyphenols (Source: Ali et al., 2014b; Abbe & Amin, 2008b; Abbe & Amin, 2013)

The medicinal properties of polyphenols against many health problems have been widely studied. Existing information on the benefits of polyphenols is mainly focussed on its preventive benefits, but how about its therapeutic benefits if abnormalities have already occurred in the cardiovascular system? Currently, there is limited data on the therapeutic benefits of cocoa supplement ingestion to know how well it benefits those with existing diseases. Our studies were mainly focused on the beneficial effects of polyphenol-rich cocoa extracts on a number of chronic non-communicable diseases, in *vitro* and *in vivo,* including one human intervention trial, as follows:-

- Cocoa polyphenols and antioxidant capacity
- Cocoa polyphenols and diabetes mellitus.
- Cocoa polyphenols and inflammatory mediators.

- Cocoa polyphenols and cancer
- Cocoa polyphenols and osteoporosis
- Cocoa polyphenols and cardiovascular disorders
- Cocoa polyphenols and obesity

The interrelationship between the above mentioned diseases and the health effects of cocoa polyphenols are discussed further in the following sections.

Cocoa Polyphenols and Antioxidant Capacity

Antioxidants can be defined as any substances which when present at low concentrations compared with those of an oxidisable substrate significantly delays or prevents the oxidation of that substrate. The common dietary antioxidants include β-carotene, vitamin E, vitamin C and selenium. Apart from these components, polyphenols are also reported to have antioxidant properties, which can be found naturally in fruits, vegetables (Amin & Tan, 2002; Amin & Cheah, 2003; Amin et al., 2004a; Amin & Lee, 2005; Amin et al., 2006; Amin & Mukrizah, 2006; Lee at al., 2007; Tiong et al., 2010; Khoo et al., 2011), legumes (Hasnah et al., 2009) and beverages such as tea, cocoa and dark chocolates (Zabidah et al., 2011; Ruzaidi et al., 2008a, b; Azizah et al., 2007; Abbe & Amin, 2007).

A study was conducted to investigate the antioxidant capacity and total phenolic and (-) epicatechin contents of cocoa beans from different countries, namely, Malaysia, Ghana, Cote d'Ivoire and Sulawesi. Several methods are available to assess antioxidant capacity/activity, based on chemical and biological principles (Amin et al., 2013). In our efforts antioxidant capacity was assayed using four different assays, namely, β-carotene bleaching, scavenging activity, ferric reducing/antioxidant potential (FRAP) and trolox

equivalent antioxidant capacity (TEAC) methods. To estimate the content of total phenolics, an assay using Folin-Ciocalteu reagent was used. Further, high-performance liquid chromatography (HPLC) was used to determine the (-) epicatechin content. The antioxidant capacity/activity of the cocoa bean based on β-carotene bleaching method followed the order of Cote d'Ivoire > Malaysia > Ghana > Sulawesi. The Ghanaian beans exhibited the highest scavenging activity, followed by Cote d'Ivoirian, Malaysian and Sulawesian. Malaysian beans showed significant highest value ($p < 0.05$) in phenolic content followed by the Sulawesian, Ghanaian and Cote d'Ivoirian. Sulawesian beans exhibited significant highest ($p < 0.05$) amount of epicatechin content among the studied beans (Figure 7). The results indicated that different assays revealed different antioxidant values. Moreover, the cocoa beans extracts from the four different countries of origin showed different antioxidant capacities. A positive and high correlation was found between total phenolics and antioxidant potential (FRAP) (Azizah et al., 2007). Antioxidant capacity of cocoa beans could be contributed by phenolic substances, through its reducing potential. Moreover, (-) epicatechin content showed a positive and high correlation with antioxidant capacity, thus, indicating that, (-) epicatechin could be one of the phenolic substances that contributes towards antioxidant capacity. The results indicated that the antioxidant capacity and total phenolic and (-) epicatechin content of Malaysian beans were comparable to that of the Ghanaian and Cote d'Ivoirian beans (Azizah et al., 2007).

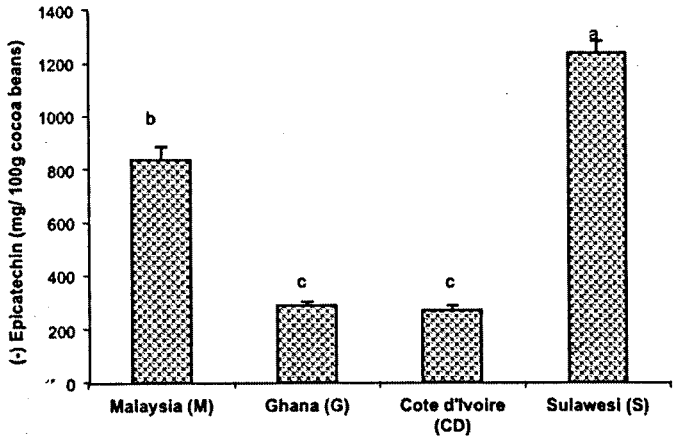


Figure 7 (-) Epicatechin content of cocoa beans extract.
(Source: Azizah et al., 2007)

Furthermore, Cheng et al. (2009) showed that Malaysian dark chocolates exhibited the highest phenolic and flavonoid contents, followed by, milk and white chocolates. Flavonols were the major flavonoids detected in dark chocolates. Theobromine was detected in dark and milk chocolates but not in white chocolates. A very high correlation ($r = 0.93$) between total phenolic and flavonoid contents indicates that the major phenolic compound in dark chocolates is from the flavonoid classes. As far as nutrition and health promotion are concerned, dark chocolates would be recommended over milk and white chocolates owing to their higher amount of antioxidant phenolic compounds. Abbe and Amin (2010) found that the presence of methylxanthines could reduce antioxidant capacity of flavonoids in cocoa powder.

Although cocoa polyphenols do not appear to have any significant *in vivo* antioxidant capacity, some of our data demonstrated that they can protect cells from oxidative stress *in vitro*, at physiologically relevant concentrations. Our studies

indicate that polyphenols extracted from cocoa powder may induce the activity of endogenous antioxidant enzymes *in vivo* and thus possess an indirect antioxidant effect.

Cocoa, a naturally occurring plant containing various functional compounds, has been used to determine the cytotoxicity and antioxidant efficacy in 3T3 fibroblast cells (Ranneh et al., 2014). In our study, ABTS and ORAC assays were deployed as a comprehensive analysis for evaluating the antioxidant capacity of the cocoa polyphenol extracts (CP) *in vitro* (Figs. 8 & 9). Pretreatment of cells with 250, 500, 1000 mg/ml of CPE completely prevented any toxicity of 3T3 cells and enhanced antioxidant capacity. The CP had significant ($P < 0.05$) potential antioxidant activities compared with the Trolox equivalent. The high correlation between antioxidant capacity and phenolic contents indicated that phenolic compounds from cocoa were a major contributor of antioxidant activity ($0.967 \leq r \leq 1.00$). These results show that treatment of 3T3 cells in culture with CPE confers the cells significant protection against oxidation.

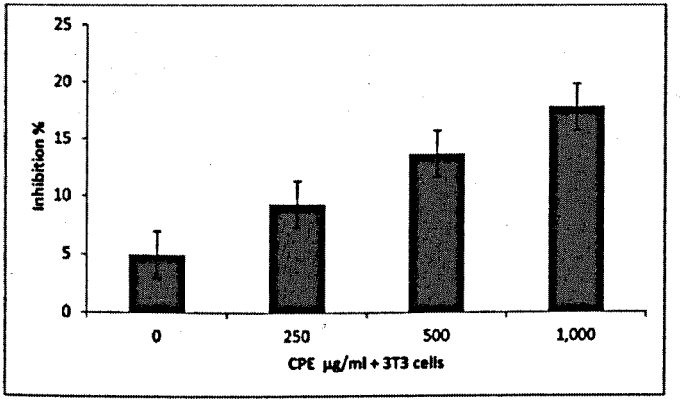


Figure 8 Antioxidant capacity of 3T3 cells treated with CPE (250, 500 and 1000 µg/ml) compared with Trolox using ABTS. The positive control contained 3T3 cells with Trolox while the negative control contained 3T3 cells with ABTS alone.

(Source: Ranneh et al., 2014)

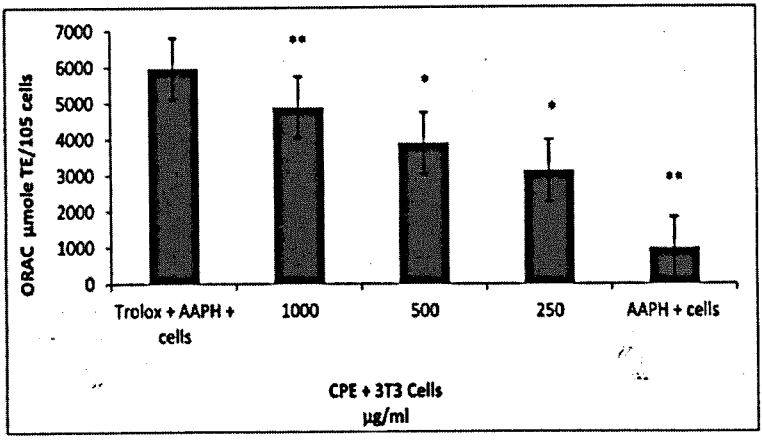


Figure 9 Total Antioxidant ability of 3T3 cells treated with CPE (250, 500 and 1000 µg/ml) compared with Trolox

(Source: Ranneh et al., 2014)

The positive control contained 3T3 cells with Trolox while the negative control contained 3T3 cells with AAPH alone. Results are expressed as means ±SD (n=3). Differences between means were significantly different at $p < 0.05$. Tukey's test: *P<0.05 ,**P< 0.01 versus AAPH. TE: Trolox equivalent per gram of extract.

Cocoa Polyphenols and Diabetes Mellitus

Findings from a systematic review and meta-analysis of randomized trials show the potential health benefits of cocoa and chocolate on flow-mediated dilation (FMD), insulin and insulin resistance (Hooper et al., 2012). An observational study by Jacques et al. (2013), among members of the Framingham Heart Study Offspring cohort, reported that higher dietary flavonol intake is associated with lower incidence of Type 2 diabetes. Although promising effects of cocoa polyphenols on biomarkers of non-communicable disease risk have emerged, limited studies have been done on the possible mechanisms behind the actions of cocoa polyphenols (Hollman et al., 2011)

Cocoa polyphenols induce the activity of endogenous antioxidant enzymes and thereby exert an indirect antioxidant effect. Our work investigated the role of polyphenols in activating the antioxidant enzymes and suppression of lipid peroxidation markers in rats (Abbe et al., 2008a). The effects of cocoa extract containing polyphenols, prepared from cocoa powder, on the liver enzymes' antioxidant parameters of obese-diabetic (Ob-db) rats were assessed. The Ob-db rats were developed using a high-fat diet (49% fat, 32% carbohydrates and 19% protein from total energy, kcal) for 3 months, followed by a low dose (35 mg/kg body weight) streptozotocin (STZ) injection. The rats were given cocoa polyphenols-rich extract (600 mg/kg body weight/day) for 4 weeks. The oxidative stress biomarkers (8-isoprostane) were significantly ($p < 0.05$) reduced after cocoa supplementation (Figure 10). Further, superoxide dismutase activity was enhanced in the Ob-db rats compared to that in the non-supplemented rats (Figure 11). The results showed that cocoa supplementation had an effect on the prevention of lipid peroxidation and in enhancing the antioxidant defense system.

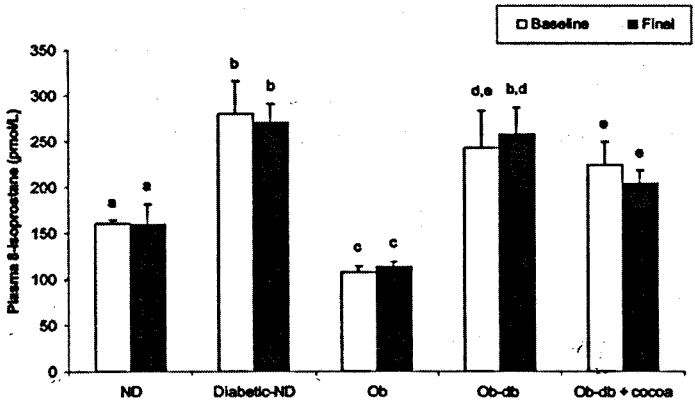


Figure 10 Plasma 8- isoprostane of experimental rats

Baseline, week-13; after high-fat diet for 12 weeks followed by low-dose of STZ injection; Final, week-17. ND,normal diet; Diabetic-ND, normal diet + low-dose STZ injection; Ob, obese; Ob-db, obese-diabetic; Ob-db + cocoa, Ob-db + 600 mg cocoa/kg body weight.

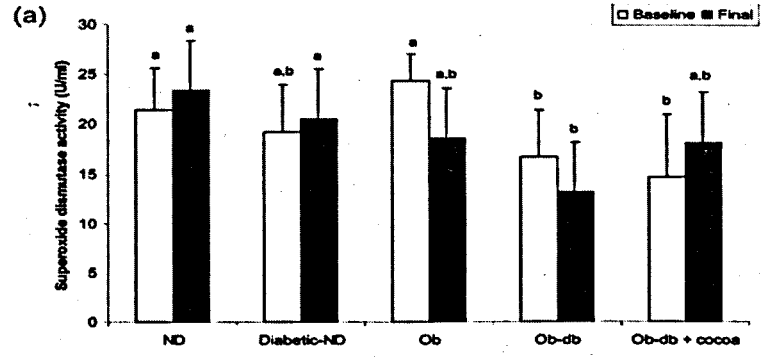


Figure 11 Superoxide dismutase activity of experimental rats.

(Source: Abbe et al., 2008a)

More than 80% of diabetic patients are overweight or obese. This group of obesity-related metabolic diseases is also known as the metabolic syndrome. Insulin resistance is a pre-diabetic state characterized by diminished tissue sensitivity to endogenous insulin, leading to chronic elevation of blood glucose levels. There are *in-vitro* and *in-vivo* methods to evaluate the antidiabetic properties of cocoa. The effects of cocoa extract containing polyphenols, prepared from cocoa powder, on the oral glucose tolerance test (OGTT), blood glucose and insulin levels of Ob-db rats were assessed. Cocoa extract (600 mg/kg body weight/day) was supplemented to the rats for 4 weeks. The results indicated that there were no significant differences in fasting plasma glucose and insulin levels after 4 weeks of cocoa extract administration (Table 2). OGTT revealed that cocoa supplementation in Ob-db rats significantly ($p < 0.05$) reduced plasma glucose at 60 and 90 min compared to that in the non-supplemented Ob-db rats (Figure 12). The results showed that cocoa supplementation had an effect on postprandial glucose control but not in the long term. Improved insulin sensitivity *in vitro* study using BRIN-BD11cell lines has also been reported (Ruzaidi et al., 2005). Our studies also found that other useful substances in cocoa include polyphenols, cocoa peptides and amino acids, which have anti diabetic properties (Sarmadi et al., 2012; Sarmadi et al., 2011; Sarmadi & Amin, 2010).

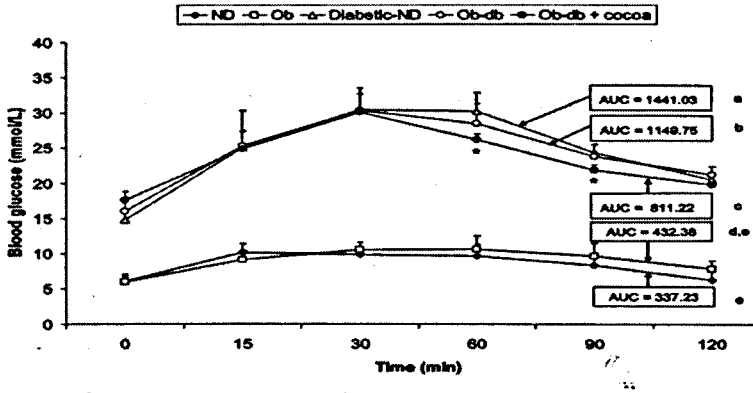


Figure 12 Oral glucose tolerance test (OGTT) results of the rats.

(Source: Abbe et al., 2008a)

ND, normal diet; Diabetic-ND, normal diet + low-dose STZ injection; Ob, obese; Ob-db, obese-diabetic; Ob-db + cocoa, Ob-db + 600 mgcocoa/kg body weight.

Table 2 Glucometabolism Parameters of the Experimental Rats

(Source: Abbe et al., 2008a)

	glucose level (mmol/L)		insulin level (pmol/L)	
rats	baseline*	final**	baseline	final
ND	7.06 ± 0.78 a	7.68 ± 0.50 a	209.01 ± 60.3 a	242.65 ± 42.56 a
Diabetic-ND	14.93 ± 3.76 b	20.33 ± 3.39 b	281.87 ± 49.53 b	179.18 ± 60.17 c
Ob	8.16 ± 0.83 a	7.08 ± 0.49 a	375.46 ± 60.65 c,d	316.12 ± 70.12 d
Ob-db	18.41 ± 1.63 c	15.72 ± 3.07 c	129.45 ± 29.24 e	112.18 ± 40.82 e
Ob-db + cocoa	18.78 ± 1.19 c	16.21 ± 4.18 c	132.95 ± 50.60 e	123.29 ± 57.19 e

Cocoa Polyphenols and Inflammatory Mediators

Reactive oxygen species (ROS) are produced as a normal product of cellular metabolism of oxygen in all aerobic organisms. Many studies have indicated the deleterious effect of ROS in deteriorating health. In addition, a wide range of diseases associated with inflammation are correlated with a high production of ROS. For centuries, cocoa has been a rich source of dietary polyphenols. It has been known not only for its good taste but also for its health effects. The consumption of polyphenols-rich foods like cocoa or its derived products has traditionally been used to reduce inflammation-related diseases. The effect of cocoa polyphenols extract (CP) on RAW 264.7 macrophage cells sensitized by lipopolysaccharide (LPS) as *in vitro* inflammatory model was tested in our study (Ranneh et al., 2014). The treatment of LPS-stimulated cells with CP at concentrations of up to 1000 μg/ml did not affect the viability of the cells compared with the untreated LPS-stimulated cells. The anti-inflammatory activity of CP was assessed by measuring its ability to inhibit the pro-inflammatory enzyme 5-lipoxygenase (5-LOX) and the pro-inflammatory mediators prostaglandin E_2 (PGE_2), reactive oxygen species (ROS), nitric oxide (NO) and tumor necrosis factor-alpha (TNF-α). The results show that CP significantly inhibits 5-LOX activity ($p<0.01$) (Figure13). Additionaly, CP dose-dependently suppressed the production of PGE_2, ROS, NO and TNF-α in the RAW 264.7 cells (Figure 14). Collectively, our results provide interesting insights on the beneficial effects of CP in the prevention and maintenance of the inflammation mediated reactive oxygen species *in vitro*.

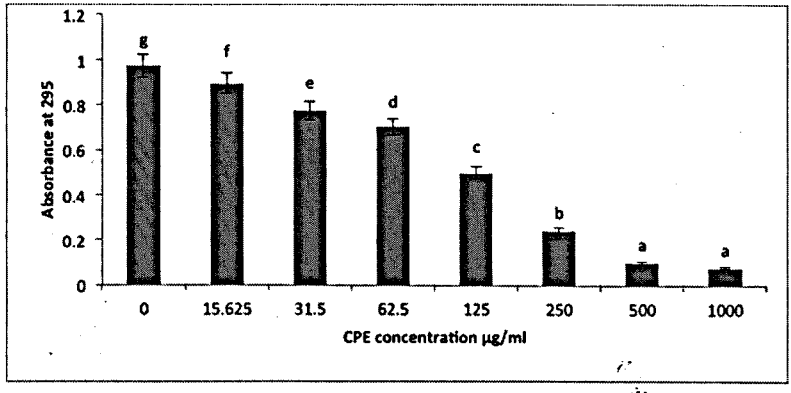


Figure 13 Inhibition of 5-LOX by cocoa polyphenols extract

(Source: Ranneh et al., 2014)

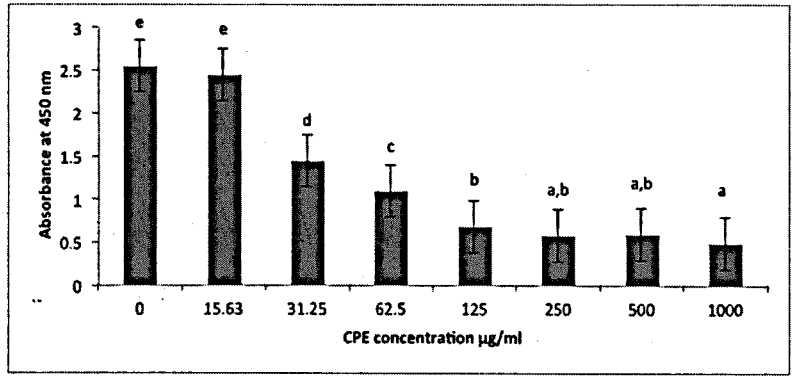


Figure 14 Effects of CPE on the LPS-stimulated production of inflammatory mediators in RAW 264.7 cells

(Source: Ranneh et al., 2014)

Cocoa Polyphenols and Cancer

The effect of cocoa polyphenols extract (CP) on tumour marker enzymes, which are, alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT), glutathione-*S*-transferase (GST) and glutathione reductase (GR) activities, in the plasma and/or liver of hepatocarcinogenesis rats, which were induced with diethylnitrosamine (DEN) and 2-acetylaminofluorene (AAF), was determined. The findings showed that CP could lower the activity of tumour marker enzymes in rats during hepatocarcinogenesis (Amin et al., 2004b). Based on the results obtained, polyphenol compounds present in the cocoa liquor, extracted using ethanol, showed potential in decreasing the severity of hepatocarcinogenesis.

Colorectal cancer (CRC) is the third most common malignancy in males and the second most common cancer occurring worldwide. Chronic colonic inflammation is a known risk factor for CRC. Cocoa contains many polyphenolic compounds that have beneficial effects in humans. Pandurangan et al. (2015) assessed the antioxidant properties of cocoa on CRC, the mouse model of azoxymethane (AOM)/dextran sulfate sodium (DSS)-induced colitis-associated cancer, focusing on the activation of Nrf2 signaling. Mice were treated with AOM/DSS and randomized to receive either a control diet or a 5 and 10% cocoa diet during the study period. On day 62 of the experiment, the entire colon was processed for biochemical and histopathological examination (Figure15). Increased levels of malondialdehyde (MDA) were observed in the AOM/DSS-induced mice. However, subsequent administration of cocoa decreased the MDA. Enzymatic and non-enzymatic antioxidants, such as, superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase, were decreased in the AOM/DSS mice. Cocoa treatment increases the activities/levels of enzymatic and non-enzymatic antioxidants. Inflammatory mediators, such as, inducible nitric oxide synthase

(iNOS) and cyclooxygenase (COX)-2, were elevated during AOM/DSS-induction, and treatment with 5 and 10% cocoa effectively decreased the expression of iNOS and COX-2. The NF-E2-related factor 2 and its downstream targets, such as NQO1 and UDP-GT, were increased by the cocoa treatment. The results of our study suggest that cocoa may merit further clinical investigation as a chemo preventive agent that helps prevent colorectal cancer.

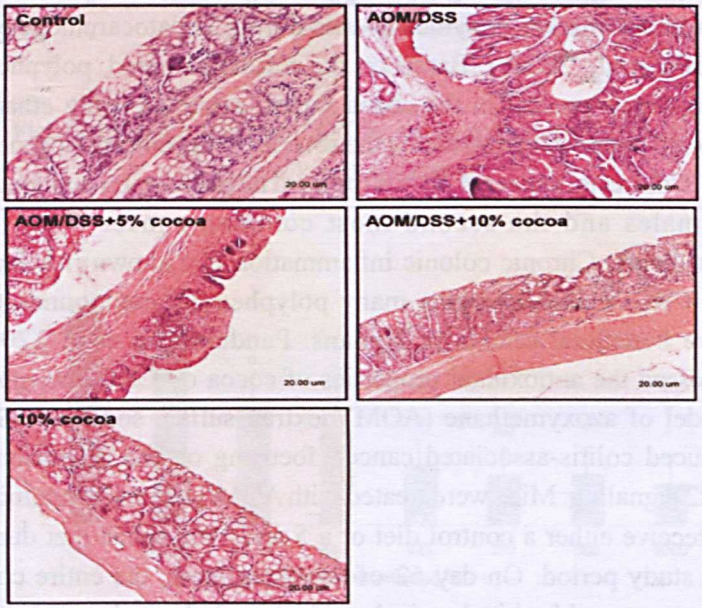


Figure 15 Histopathology of colonic lesions

(Source: Pandurangan et al., 2015)

(Control): normal colonic specimen depicting intact crypt architecture. (AOM/DSS) group of mice with tubular growth pattern and severe cellular polymorphism resembling human tubular adenoma with high grade intra-epithelial neoplasia. (AOM/DSS 1 5% cocoa) group showed an almost complex reduction in tumor size. (AOM/DSS 1 10% cocoa) the hyperplastic colonic mucosa exhibits reduced branching and budding in crypts. (10% cocoa) showed similar pattern in the control.

Cocoa Polyphenols and Osteoporosis

Osteoporosis is a skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, resulting in increased fragility and subsequently, enhanced fracture risk. Postmenopausal osteoporosis is the most widespread cause of bone loss relating to age, in which the ovarian hormone deficiency is a major risk factor. To delay or avoid functional impairments, it is crucial to focus on early prevention of osteoporosis. Hormone therapy is the most common approach in the management of osteoporosis. However, estrogen is reported to be related to occurrences of breast cancer and vascular thrombosis. Fruits and vegetables can have significant long-term health benefits since they contain of a variety of phytochemicals, or naturally occurring bioactive non-nutrients, besides vitamins and minerals. Certain phenolic compounds can also be applied as anti-inflammatory and bone-sparing agents. In line with this, various studies have been conducted in the search for new antiosteoporotic agents from natural sources, such as, dried plums, blueberries, oranges, green tea and onions. Our studies reported that tempeh may also provide readily available polyphenols and calcium for the studied population of women at risk of low bone mass (Hasnah et al., 2010).

Among the various sources of polyphenols, cocoa has been the focus of research attention, mostly due to its high polyphenol content. A vast number of studies have indicated its health benefits. However, no research was found that studied the effect of cocoa on bone. In our study, it was hypothesized that cocoa polyphenols may be effectively involved in bone metabolism and prevention of bone loss. Meanwhile, cocoa is also rich in minerals like magnesium, zinc, potassium and copper and therefore, it was assumed that cocoa minerals may also positively contribute to bone health. In our study female Sprague–Dawley rats were fed with 6% (C6%)

or 12% (C12%) cocoa diet (w/w) after ovariectomy for 95 days, and compared with ovariectomized and sham-operated controls. Based on our results, bone mineral density (BMD) and bone mineral content (BMC) of the femur of the C12% rats were significantly ($p<0.05$) lower than that of all the other groups (Table 3). Cocoa at lower concentrations did not exert any adverse effects on BMD while cocoa diet was seen to have significantly elevated vertebra BMD and BMC. Based on these results it is presumed that the effects of cocoa on BMD are moderate and site-specific (Sarmadi, 2015). It is evident that certain inflammatory cytokines like IL-1, TNF and IL-6. play key roles in pathogenesis of osteoporosis. Elevated levels of serum inflammatory cytokines (TNF-α, IL-1β, and IL-6) were reported in postmenopausal women. Likewise, in our study, ovariectomy significantly enhanced serum levels of IL-1, TNF and IL-6. However, cocoa dose-dependently attenuated the levels of these inflammatory biomarkers. In addition, mRNA levels of IL-6, IL-1 and TNF were higher in the OVX group as compared with the sham and cocoa groups. Expression of IL-1, TNF and IL-6 was down-regulated by the cocoa diet. Cocoa can attenuate such inflammatory conditions by down-regulating IL-1, IL-6 and TNF-α genes as well as by decreasing the serum levels of these markers (Sarmadi, 2015). Cocoa had no effect on whole body BMD and it increased bone density in the 4th lumbar vertebrae. Additionally, cocoa had no effects at low dose levels and adverse effects at high dose levels on bone density of the femur in the ovariectomized rats. Both concentrations of cocoa reduced inflammatory biomarkers. We thus assume that cocoa has potential to modulate bone metabolism through its anti-inflammatory properties.

Table 3 Effects of cocoa on the whole body, femur, vertebra BMD and BMC

(Source: Sarmadi, 2015)

	Sham	OVX	C6%	C12%
Whole body				
BMD (g/cm^2)	0.172±0.005^a	0.154±0.005^b	0.147±0.005^b	0.152±0.005^b
BMC (g)	11.5±0.387	10.6±0.387	10.43±0.387	10.49±0.387
Femur				
BMD (g/cm^2)	0.278±0.05^c	0.255±0.03^a	0.26±0.04^a	0.24±0.01^b
BMC (g)	0.6±0.016^c	0.5±0.016^a	0.503±0.017^a	0.44±0.016^b
L4				
BMD (g/cm^2)	0.39±0.04^c	0.19±0.08^b	0.23±0.071^a	0.23±0.082^a
BMC (g)	0.2±0.088^c	0.10±0.09^b	0.153±0.08^a	0.156±0.012^a

Values are mean±se (n=4-5). OVX: Ovariecomized group, C6%: OVX fed 6% of cocoa (w/w), C12%: OVX fed 6% of cocoa (w/w). Within a row values with different letters are significantly different (p<0.05)

Cocoa Polyphenols and Cardiovascular

Population studies have shown that plant polyphenol is inversely correlated with mortality from cardiovascular disease and numerous dietary flavonoids have been shown to beneficially impact atherosclerosis, including lipoprotein oxidation, blood platelet aggregation and vascular reactivity. Based on our review articles, there are many studies that reported that cocoa flavonoids had shown a similar degree in being protective against CVD due to antioxidant, anti-platelet and anti-inflammatory effects, as well as increasing HDL-c, lowering blood pressure and improving endothelial functions (Abbe & Amin, 2008b; Abbe & Amin, 2013; Kurlandsky et al., 2006; Visioli et al., 2011).

Male New Zealand White rabbits were fed with a specially designed cholesterol-rich diet for 12 weeks to study the effects of CP on plasma lipids concentrations, atherosclerotic plaque formation and other biomarkers and parameters. Rats were not used as the animal model because of their resistance or lower sensitivity to the atherogenic effects of a cholesterol-rich diet. The phenolic content of CP was about 70 mg of ECE/g extract as assayed by Folin-Ciocalteu method. Based on our previous findings, CP is rich in polyphenol content (Ruzaidi et al. 2005; Amin et al. 2004a; Amin et al. 2004b). The dosage used in this study was based on an aforementioned study which stated that about 2610 mg of total polyphenol showed significant increase in the lag phase of LDL to be oxidized *ex vivo* (Baba et al. 2000). Our findings showed that the administration of CP did not only stabilize the plaque, but also reduced the area of aorta occupied with atherosclerotic lesions (Figure 16- 20). Furthermore, the present study showed that, administration of CP to hypercholesterolemic rabbits reduced approximately 50% of total area of atherosclerotic lesions compared to that in the untreated hypercholesterolemic rabbits (CP group). The development of atherosclerotic lesion is dependent on the accumulation of fatty streaks. Fatty streaks are developed by the scavenging process of oxidized lipid molecules (e.g. LDL-c) by macrophages (monocytes). The results indicated that polyphenol-rich extract prepared from Malaysian cocoa has potential to prevent the risk of atherosclerosis (Faizul, 2007).

We also conducted a study to determine the effects of Malaysian cocoa, in beverage form, on biochemical parameters among healthy subjects in UPM. A randomized and cross-over design study involving 37 living and healthy subjects was carried out over 9 weeks. Our results showed that plasma total cholesterol of subjects in the treatment group decreased ($p<0.05$) whereas their antioxidant

enzymes increased significantly ($p<0.05$) at the end of the study (Suryati, 2010). The consumption of 18 g of cocoa beverage daily for 9 weeks had improved several biomarkers associated with cardiovascular diseases. Thus, Malaysian cocoa may possibly help in preventing the promotion of oxidative stress.

Figure 16 Intimal Surfaces of the Aorta from Control Rabbit (CN group) showing Sudan IV Stainable Lipid Deposits. There was no Atherosclerotic Lesions as shown by these staining.

(Source: Faizul, 2007)

Figure 17 Intimal Surfaces of the Aorta from Hypercholesterolemic Rabbit (CP group) showing Lipid Deposit Stain with Sudan IV. Atherosclerotic Lesions were indicated by Concentrated Brick Red Colors.

(Source: Faizul, 2007)

Figure 18 Intimal Surfaces of the Aorta from Hypercholesterolemic Rabbit Treated with Cocoa Extract (300 mg CE group) showing Lipid Deposit Stained with Sudan IV. Atherosclerotic Lesions were indicated by Concentrated Brick Red Colors.

Figure 19 Intimal Surfaces of the Aorta from Hypercholesterolemic Rabbit Treated with Cocoa Extract (600 mg CE group) showing Lipid Deposit Stain with Sudan IV. Atherosclerotic Lesions were indicated by Concentrated Brick Red Colors.

(Source: Faizul, 2007)

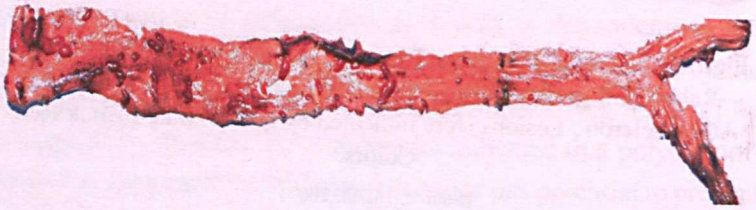


Figure 20 Intimal Surfaces of the Aorta from Hypercholesterolemic Rabbit Treated with Cocoa Extract (800 mg CE group) showing Lipid Deposit Stain with Sudan IV. Atherosclerotic Lesions were indicated by Concentrated Brick Red Colors.

(Source: Faizul, 2007)

Cocoa polyphenols and Obesity

Cocoa, the fruit of the *Theobroma cacao* plant, is traditionally used in folk medicine as a pharmaceutical for blood pressure reduction and cardiovascular disease prevention. The nuclear receptor peroxisome proliferator-activated receptor gamma (PPAR-γ) is widely known to improve insulin sensitivity and is therefore being used as a major drug target for the treatment of type 2 diabetes mellitus. A study was done to investigate the anti-diabetic/anti-obesity effects of cocoa polyphenol-rich extract (CP) (Farhana et al., 2015). The rats received either normal diet, high-fat diet or high-fat diet with additional cocoa polyphenols for 8 weeks. At the end of the treatment, body weight, plasma glucose and insulin were measured. Additionally, mRNA and protein levels of PPARγ in skeletal muscle and white adipose tissue were also measured. Compared to the high-fat diet group, increases in body weight, plasma glucose and insulin were significantly suppressed for the CP-treated groups. Compared to the high-fat diet group, the PPARγ mRNA level was significantly higher in both the skeletal muscle and the white adipose tissue for the CP groups (Figure 21 & 22). Protein expression of PPARγ in the CP groups was also significantly higher as compared to the high-fat diet group. The anti-diabetic mechanism of CP along with the metformin hypoglycemic drug partially attributed to the increased expression of PPARγ in the skeletal muscle and adipose tissues. These results suggest that CP could be a useful phytomedicine agent for alleviating insulin resistance.

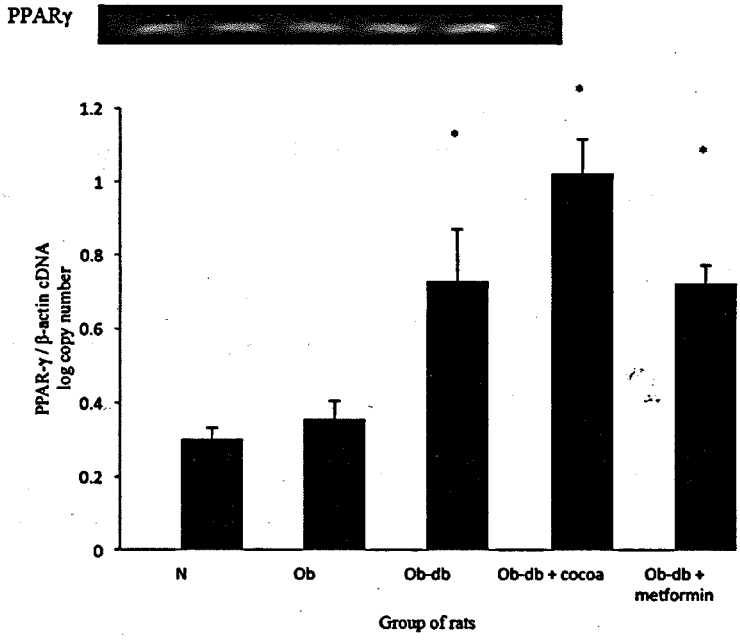


Figure 21 mRNA levels PPAR-γ in the adipose tissue of different groups of rats

(Source: Farhana et al., 2015)

The mean values of cDNA copies were corrected with respect to the reference gene (β-actin). The presence of a single RT-PCR product was verified by 2% gel electrophoresis for its specificity. * $P< 0.05$ vs normal (N).

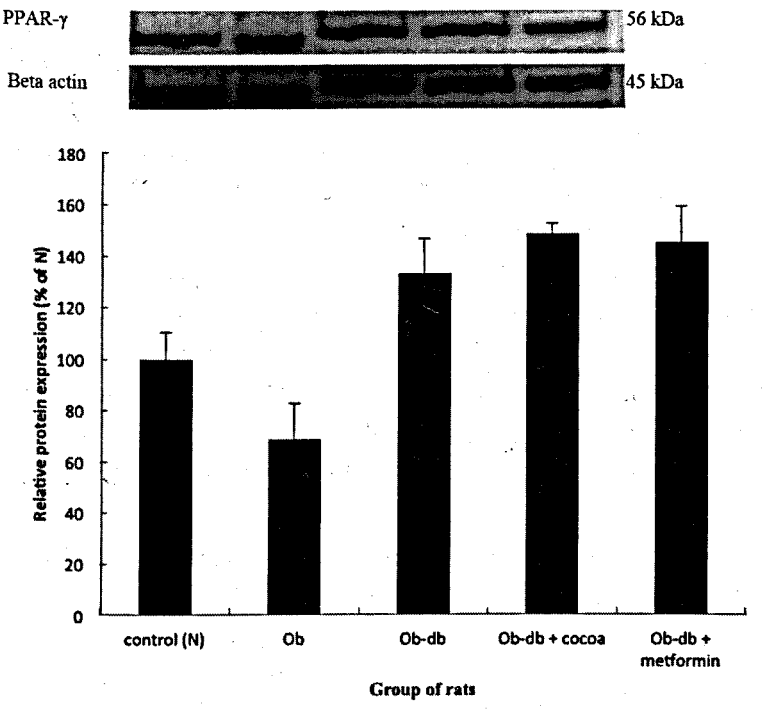


Figure 22. Expression of PPAR-γ protein in rat adipose tissue

(Source: Farhana et al., 2015)

The protein extracts were subjected to immunoblotting by the PPAR-γ antibody, and levels were normalized γ-actin. Levels in the control were arbitrarily assigned a value of 100.0. All values are significantly different at the level of $P< 0.05$. Protein contents were determined using the bicinchoninic acid method with BSA as a standard. * $P< 0.05$ vs normal (N).

Development of obesity diseases due to dietary factors, particularly a high fat intake, is of increasing global concern. This study was conducted to investigate the pharmacological activities of cocoa polyphenols (CP) on visceral obesity in diet-induced obese rats and the possible mechanisms involved. Sprague–Dawley (SD) rats were fed a low-fat (LF) or high-fat (HF) diet for 10 weeks. Thereafter, the HFD rats (n=10/group) were treated with a dose of 600 mg/kg b.w/day CP (HFD+CPs) for 4 weeks. Lipid contents and morphological changes in the liver and mesenteric white adipose tissue were analyzed. The gene encoding AMPK-activated protein kinase and protein expression of phosphorylated (AMPK α/β) were measured using real time-PCR and western blotting. The mRNA expression level of lipogenic key enzymes (Acaca, Fasn, Mcat and Scd-1) and lipolysis key enzymes (CPT1, Acox1) were investigated. In addition, upstream transcription factors (PPARα, PPARγ, C/EBPα and SREBP-1c) were also examined.

Our findings showed that CP treatment improved visceral adiposity, adipocytes hypertrophy and liver steatosis induced by chronic HFD feeding in rats (Ali et al., 2015). AMPKα/β phosphorylation in the liver and adipose tissue of HFD+CP-treated rats was activated compared with the HFD-fed rats. The expression of lipogenesis related-genes were found to have decreased while expression level of oxidation -related genes was increased compared with that in the HFD-fed rats (Figures 23- 25). The results partially unraveled the ameliorative effect of CP treatment on obesity biomarkers by inhibiting lipogenesis and promoting lipolysis through activation of the AMPK pathway (Ali et al., 2015).

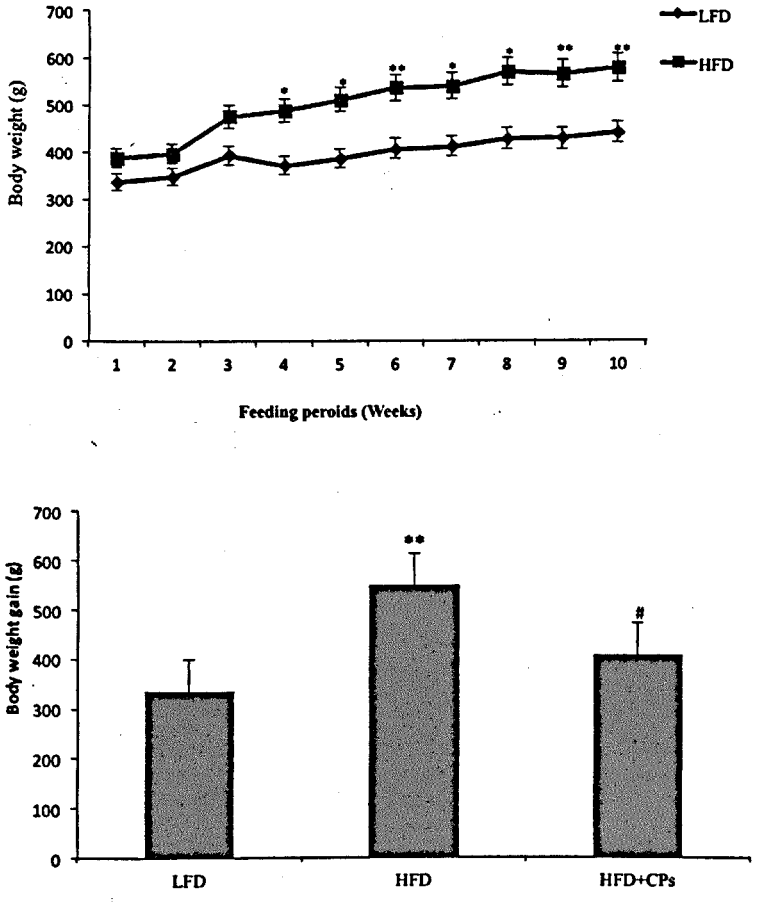
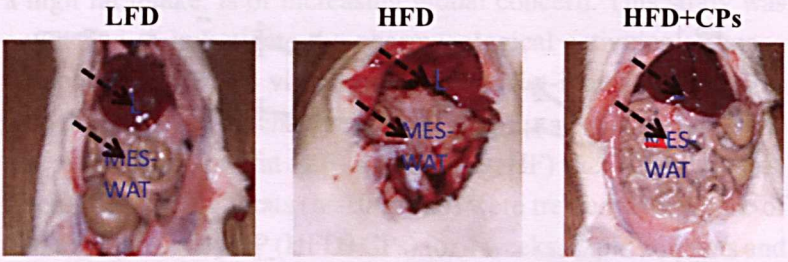


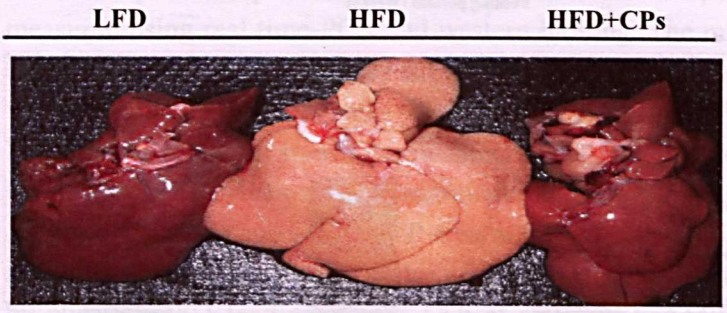
Figure 23 Effects of CP treatment on body weight of HFD-induced obese rats

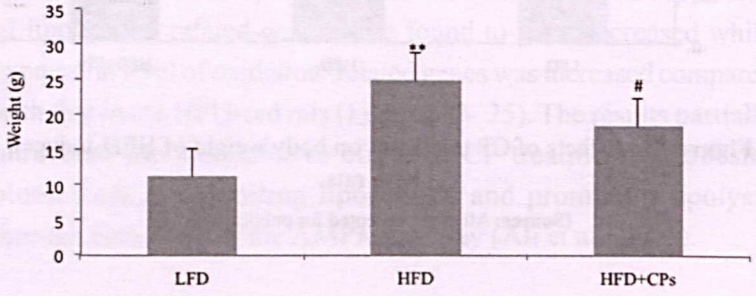
(Source: Ali et al., accepted for publication)

A) Visceral adipose tissue



B) Liver





C) Epididymal adipose tissue

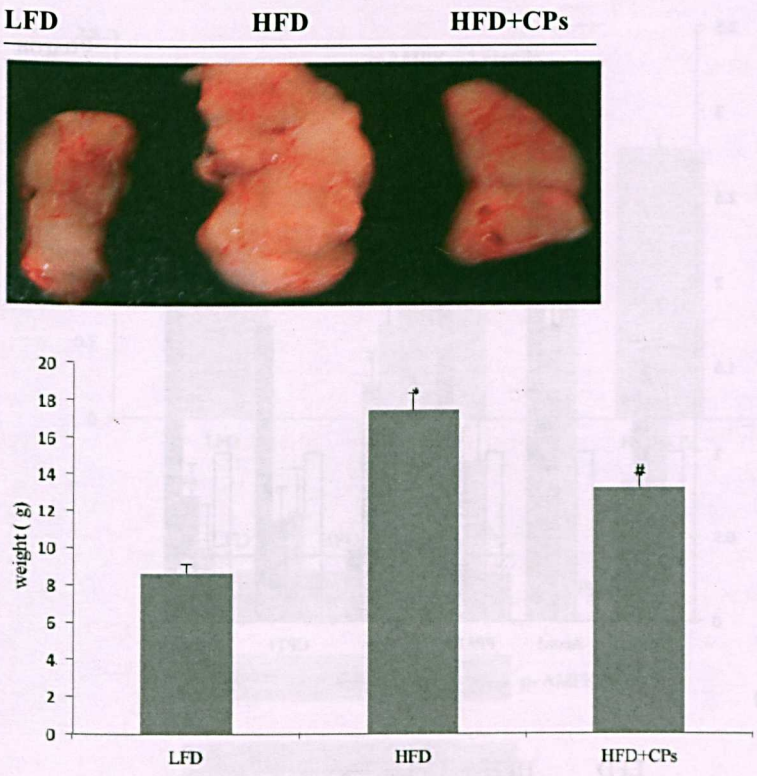
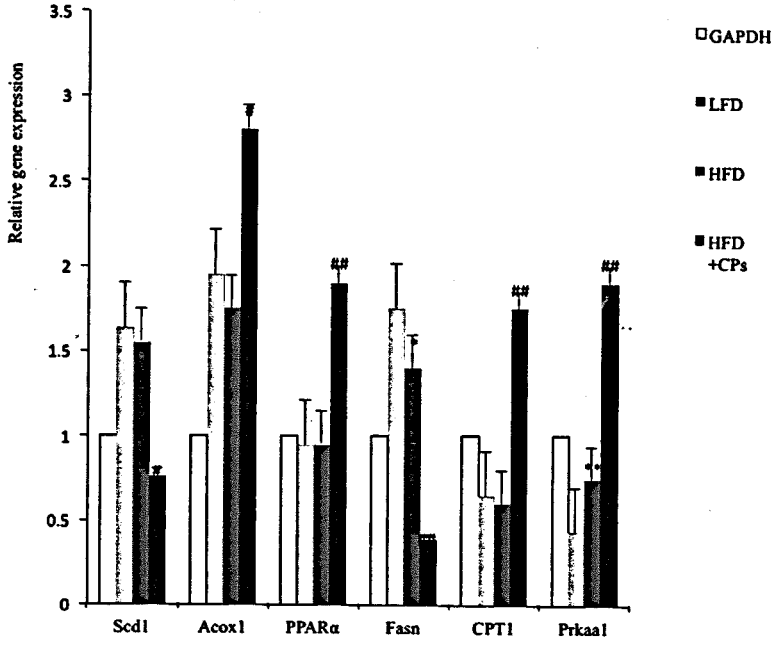


Figure 24 Effect of CP treatment on adipose tissues and liver mass in HFD-induced obese rats

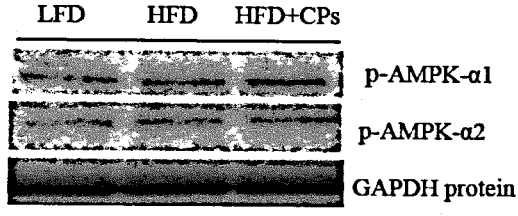
(Source: Ali et al., accepted for publication)

(A) Whole visceral adipose tissue; (B) Liver; and (C) Epididymal adipose tissue were obtained from rats after fasting overnight at the end of the study and weighed and photographed. L, liver; MES-WAT, mesenteric white adipose tissue.

(A)


Relative gene expression
3.5
3
2.5
2
1.5
1
0.5
0
Scd1
Acox1
PPARα
Fasn
CPT1
Prkaa1
GAPDH
LFD
HFD
HFD +CPs

(B)


LFD
HFD
HFD+CPs
p-AMPK-α1
p-AMPK-α2
GAPDH protein

(C)

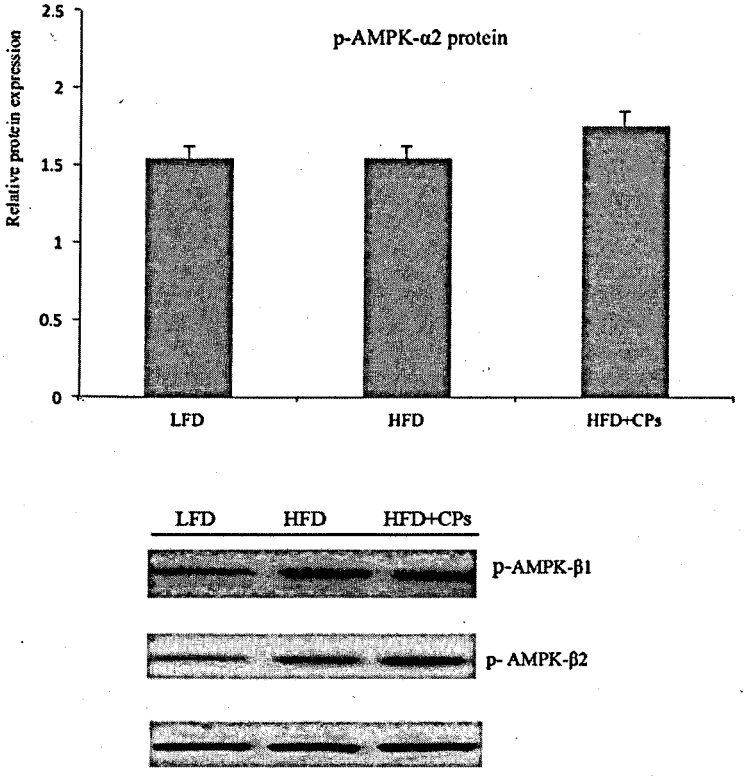


Figure 25 Effect of CP on mRNA expression of lipid metabolism-related genes in liver and AMPK protein expression

(Source: Ali et al., accepted for publication)

(A) The values of gene levels were normalized to the value of GADPH, which was set to 1. (B) Liver tissue was homogenized and the lysates were subjected to western blot analysis for AMPK-β1/2. (C) The intensity of each band was quantified using western bolt densitometry measurement.

Molecular Mechanisms Underlying the Health Benefits of Cocoa Polyphenols

Cocoa polyphenols (CP) have been shown to exhibit hypolipidemic actions, suggesting that CP holds great promise for correction of lipid abnormalities. Indeed, recent research demonstrates the beneficial effect of CP on obesity and its mediation of blood pressure, insulin resistance and vascular and inflammation related diseases. Although still debatable, there is a range of potential mechanisms through which CP might exert its benefits on obesity health. This work investigated the hepatic genetic expression patterns in high-fat diet (HFD)-induced obese rats using the microarray system. Rats were fed either a low fat or HFD for 12 weeks. After diet intervention, HFD rats (n=10/group) were treated with 600 mg/kg bw/day CP (HFD+CP) for 4 weeks. As compared to the HFD group those receiving CP treatment showed significant decrease in lipids in the liver and in body weight as well as visceral fat accumulation. DNA microarray analysis resulted in a differential expression of 862 genes out of the 12,282 genes expressed in the liver. The differential expression patterns of selected genes were confirmed with real-time-PCR. Metabolic pathway analysis via bioinformatics tools showed that in the CP group the genes in lipid lipolysis, primarily in fatty acid oxidation, were up-regulated whereas the genes in lipid synthesis pathways were down-regulated (Figure 26). Our data provides new insights into the possible mechanisms behind the actions of CP on the management of obesity markers in rats fed a HFD (Figure 27).

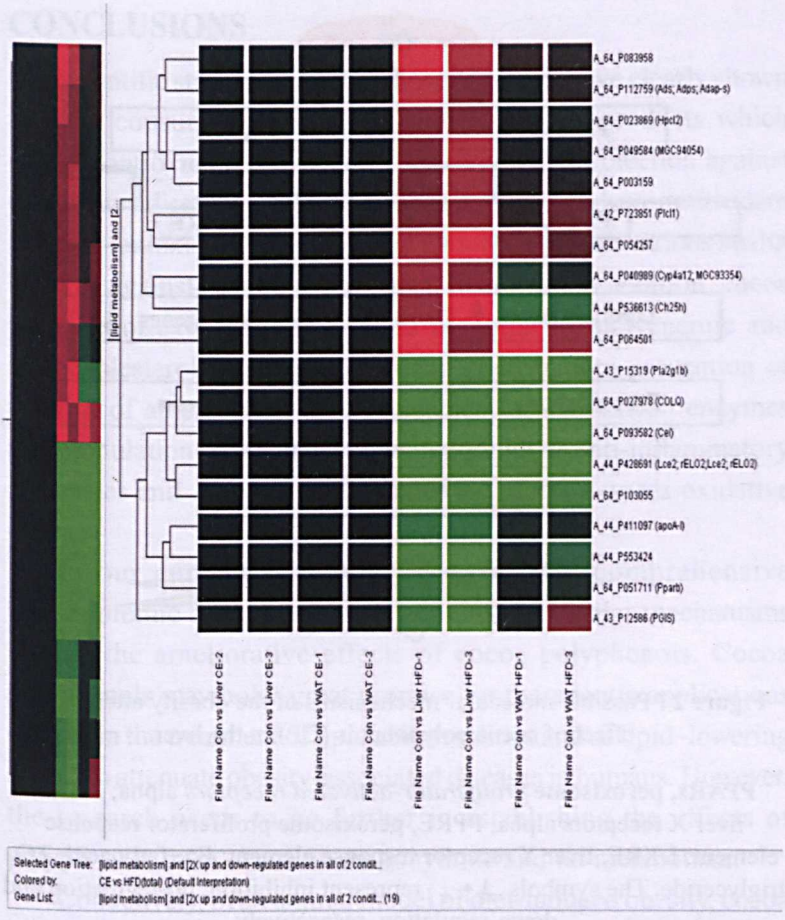


Figure 26 Hierarchical clustering of HFD and HFD + CP treated rat groups based on microarray gene expression profiling

(Source: Ali et al., 2015)

Heat maps were obtained using the Cluster-Tree view program within the GeneSpring GX (Agilent) platform. Red = upregulation, green = downregulation and black = unchanged. The 862 differentially expressed genes according to their relative expression levels and ontology.

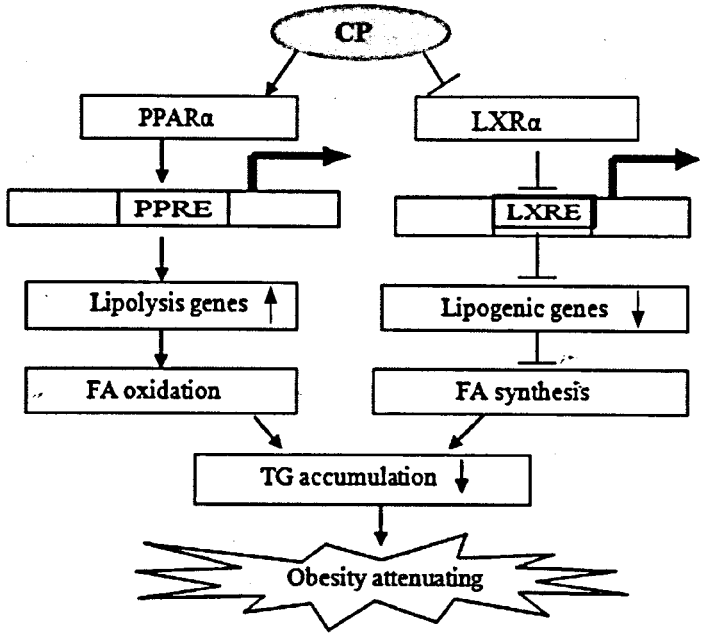


Figure 27 Possible molecular mechanisms of the obesity attenuating effect of cocoa polyphenols (CP) in the liver

PPARs, peroxisome *proliferator-activated receptors* alpha; LXRs, liver X receptors alpha; PPRE, peroxisome proliferator response element; LXRE, liver X receptor response element; FA, fatty acid; TG, triglyceride. The symbols ⊥↑ ↓ represent inhibition, up-regulation and down-regulation, respectively.

(Source: Ali et al., 2015)

CONCLUSIONS

Our scientific studies, as well as those of others, have clearly shown that the consumption of cocoa and its derived products which contain antioxidant polyphenols could provide protection against diet-related diseases. Malaysian cocoa polyphenols have antioxidant and non-antioxidant properties that endow them with various health benefits against several pathological disorders. In addition, cocoa polyphenol extracts may possess potential hypoglycaemic and hypocholesterolaemic properties and contribute to prevention of the risk of atherosclerosis, enhancement of antioxidant enzymes and modulation of bone metabolism through its anti-inflammatory properties and exert anti-inflammation effects towards oxidative stress.

In our current research, we have used comprehensive transcriptomic analysis to understand the molecular mechanisms behind the ameliorative effects of cocoa polyphenols. Cocoa polyphenols may hold great promise for therapeutic applications such as in the treatment of lipid abnormalities and as lipid–lowering agents to attenuate obesity-associated diseases in humans. However, the research needs to go further in establishing the effects of polyphenols from cocoa on carbohydrate and fat metabolism.

Collectively, in an animal model of diet-induced obesity, cocoa polyphenol administration improved some metabolic parameters and decreased both adiposity and body weight gain. Through microarray and qPCR analysis, genome-wide profiling of mRNA expression in the liver and visceral adipose tissue showed that cocoa polyphenol treatment increased the expression of genes involved in fatty acid oxidation while decreasing the expression of lipogenic genes. However, further research is needed on the regulation of such nuclear receptors by cocoa polyphenols to determine which specific polyphenols (flavonols or phenolic acids) are involved.

Consumption of cocoa and cocoa-derived products in the form of chocolate (milk or dark) or as an ingredient in foods may significantly contribute to human intake of dietary polyphenols and health. It must however be noted that high sugar content and the presence of other compounds may hinder the healthful effects of cocoa. Moderate intake of cocoa products (dark chocolate) is highly recommended owing to its high antioxidant polyphenols and low sugar content. Furthermore, our studies did not show conclusive proof of the most effective dose of cocoa consumption that promotes beneficial effects towards our health.

It should be noted that limitations in nutrition research are unavoidable due to the challenges of time, confounding factors and the high cost of arrays, which can prevent large-scale studies. In the research described in this lecture series, an important mechanism that is still not fully understood is whether cocoa polyphenols only have a local effect in the tissues which are tested or whether they also affect other tissues. Another key question is whether the impacts of the cocoa polyphenol treatment on lipid metabolism are particularly mediated solely by the activation of transcription regulatory factors or also include other biological factors. In addition to these challenges, determining the definite mechanism in living organisms is highly complicated. The complex process *in vivo* involves many variations due to different genetic backgrounds between animal models and/or hormonal feedback due to diet supplementation. These physiological factors could undeniably influence the genome-wide expression of metabolic genes involved in lipid metabolism. Therefore, an analysis of a wide array of genes in the genome under different conditions and a single polyphenol has to be conducted in the future.

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BIOGRAPHY

Prof. Dr. Amin bin Ismail was born in Kubang Pasu, Kedah on 11 April 1969. Dr. Amin started his career as a tutor in July 2000 in the Department of Nutrition and Dietetics (formerly known as the Department of Nutrition and Health Sciences), Faculty of Medicine and Health Sciences, Universiti Putra Malaysia. Subsequently, in December 2000, he was appointed as a lecturer in the department. Dr. Amin was promoted to senior lecturer in 2004 and Associate Professor in May 2006, in the same department. In December 2010, he was appointed to the rank of full professor in the field of "Food Chemistry and Biochemistry". From 2005 – 2006, he served as the head of the Food Quality Laboratory, Centre of Strategic Studies and Food Innovation in UPM. He was then selected to lead the Laboratory of Halal Science Research (formerly known as the Laboratory of Analysis and Authentication), Halal Research Products Institute, Universiti Putra Malaysia, and was also the Programme Coordinator for the Bachelor of Science (Nutrition and Community Health) programme in the Department of Nutrition and Dietetics from 2009 - 2012. He is currently the Deputy Dean (Graduate Student Affairs & Industry and Community Relations) at the Faculty of Medicine and Health Sciences and has held this position since 2012.

Dr. Amin has 15 years of teaching experience and more than 19 years of research experience. His abilities and full commitment to administrative duties are well known within his department, faculty, UPM, Ministry of Health Malaysia (MOH) and other professional bodies. At the university, national and international levels, he has been appointed as chairman, coordinator, adviser, secretary, facilitator and member of several committees, student programs, research mentoring programmes and conferences. He has been appointed to the Programme Advisory Panel for the Master's in

Nutrition programme at UKM and is actively involved as a member of the MQA Panel for assessing undergraduate programmes related to nutrition and food science at various universities in Malaysia.

Dr. Amin is currently a Fellow of the Nutrition Society of Malaysia and was an Assistant Honorary Secretary of the Nutrition Society of Malaysia (2001 – 2006). He is also a member of the International Society for Nutraceuticals and Functional Foods.

Dr. Amin's research focus areas include the health benefits of antioxidant polyphenols from Malaysian cocoa products, the utilization of food processing by-products and antioxidant and nutritional analysis. In the past, he has received several research grants (more than RM 1 Million) from different ministries and UPM for projects related to antioxidants and polyphenols derived from fruits and cocoa, as well as the utilization of food processing by-products for functional foods. He has also collaborated with several research institutes and industries – the Malaysia Cocoa Board (MCB), the Forestry Research Institute of Malaysia (FRIM), the Malaysian Agricultural Research Development Institute (MARDI), Golden Hope Fruits and Beverages Industry Sdn. Bhd, Kotra Pharma (M) Sdn. Bhd, and the International Atomic Energy Agency (IAEA). Dr. Amin has received several research awards at the faculty, UPM, national and international levels. He was also awarded the Young Scholar Award in 2005 and received a Fellowship award from the United Nations University in 2001.

Dr. Amin has graduated 10 PhD and 15 MSc students. The majority of them have published in Q1 & Q2 journals and have won various national and international awards. To date, Dr. Amin has more than 150 articles in peer-reviewed journals, book chapters, proceedings and research/consultancy reports. He has had two patents issued and several pending patents. Since 2000, he has presented more than 100 papers at national and international

conferences. Dr. Amin's publications have been cited more than 2,331 times, and as of May 2015 his h-index is 24 (based on SCOPUS).

Dr. Amin was appointed as an Editorial Board member for "Food Chemistry" (a Q1 journal, published by Elsevier) from 2007 till 2013. Currently, he is an Associate Editor for "Food Chemistry." Known for his expertise in polyphenols and antioxidant research, Dr. Amin has reviewed more than 200 manuscripts being considered for publication in peer-reviewed journals (more than 60 manuscripts for ISI journals) from 2004 - 2014. He has been appointed as an external examiner by both local and foreign universities (University of New South Wales, University of Newcastle, University of Mysore and University of Madras) for MS and PhD thesis adjudication and academic promotion. Since 2012, he has been appointed as a Visiting Researcher at the Guangxi Academy of Agricultural Sciences, Nanning, China.

ACKNOWLEDGEMENTS

First and foremost, thank you to Allah Al-Mighty for the blessings on all my professional work as an academician.

The realization of this inaugural lecture would not have been possible without the support and contribution of many individuals who provided their kind help in one way or the other.

My appreciation to Prof. Dato' Dr. Mohd Fauzi Hj. Ramlan, the Vice Chancellor; Prof. Dr. Abdul Jalil Nordin, the Dean; and Associate Prof. Dr Norhaizan Mohd Esa, the Department Head, for their support.

My heartfelt gratitude and appreciation goes to all my former graduate students (Dr. Faisal Ali, Dr. Bahareh, Dr. Aida Hamimi, Dr. Chang Sui Kiat, Dr. Fouad Hassan, Dr. Sadeq Hassan, Dr. Tan Seok Tyug, Dr. Hasnah Haron, Dr. Muhammad Ibrahim, Dr. Nurulhidayah, Faizul Helmi, Emmy Hainida, Ruzaidi, Azizah, Kong Kin Weng, Khoo Hock Eng, Chew Lye Yee, Abbe Maleyki, Suryati, Naeem, Hanaffi, Alia, Aina, Nur Azira, Nadia and Zabidah) and my current students for their contributions to my academic and research activities.

I express my deep gratitude and heartfelt thanks to my Ph.D. supervisor, Prof. Dr. Jinap Selamat, for her incessant guidance and coaching in research when I was her student. I am thankful to my international colleagues, Prof. Dr. Feereidon Shahidi from Canada, Prof. Dr. Chin Kun Wang from Taiwan and Prof. Dr. Manohar Garg from Australia, for their continuous support since our first meeting in 2000.

My special gratitude goes to Prof. Dr. Norlijah Othman (former Dean), all colleagues, academic and non-academic staff, at the Department of Nutrition and Dietetics, for their support and cooperation. I bow and doff my cap to all of you. Special thanks

goes to Prof. Dr. Maznah Ismail, the former department head, for her continuous support and motivation when I first joined the department in 2000. I would not have been a member of UPM if it had not been for her decision.

My heartfelt appreciation for the love, continuous support, encouragement and great patience of my wife Fatimah Omar and the love and endurance of my children Amir Farhan, Amir Safuan, Alya Izzati and Amir Haziq. I am also grateful to my mother, Che Rokiah Md Isa, my late father, Ismail Dee, my sisters, brothers and in-laws for their love, unconditional support and doa.

I also take this opportunity to thank all my colleagues/ collaborators at the Faculty of Medicine and Health Sciences and other faculties and institutes for their continuous support and knowledge sharing. Special thanks goes to my former lecturers at the Faculty of Food Science and Technology (Prof. Dr. Jinap, Prof. Dr. Hasanah, Prof. Dr. Jamilah, Prof. Azizah, Prof. Nazamid, Assoc. Prof. Dr. Kharidah, Prof. Russly, Prof. Dato' Mohd. Yazid) for their guidance and encouragement when I was enrolled with the faculty in 1989 as an undergraduate student.

I would also like to thank the CoSComm, UPM Press and the special committee headed by Dr. Nurul Husna Shafie who worked very hard to ensure the success of this inaugural event – Thank you

Amin Ismail

LIST OF INAUGURAL LECTURES

1. Prof. Dr. Sulaiman M. Yassin
   The Challenge to Communication Research in Extension
   22 July 1989

2. Prof. Ir. Abang Abdullah Abang Ali
   Indigenous Materials and Technology for Low Cost Housing
   30 August 1990

3. Prof. Dr. Abdul Rahman Abdul Razak
   Plant Parasitic Nematodes, Lesser Known Pests of Agricultural Crops
   30 January 1993

4. Prof. Dr. Mohamed Suleiman
   Numerical Solution of Ordinary Differential Equations: A Historical Perspective
   11 December 1993

5. Prof. Dr. Mohd. Ariff Hussein
   Changing Roles of Agricultural Economics
   5 March 1994

6. Prof. Dr. Mohd. Ismail Ahmad
   Marketing Management: Prospects and Challenges for Agriculture
   6 April 1994

7. Prof. Dr. Mohamed Mahyuddin Mohd. Dahan
   The Changing Demand for Livestock Products
   20 April 1994

8. Prof. Dr. Ruth Kiew
   Plant Taxonomy, Biodiversity and Conservation
   11 May 1994

9. Prof. Ir. Dr. Mohd. Zohadie Bardaie
   Engineering Technological Developments Propelling Agriculture into the 21st Century
   28 May 1994

10. Prof. Dr. Shamsuddin Jusop
    Rock, Mineral and Soil
    18 June 1994

11. Prof. Dr. Abdul Salam Abdullah
    Natural Toxicants Affecting Animal Health and Production
    29 June 1994

12. Prof. Dr. Mohd. Yusof Hussein
    Pest Control: A Challenge in Applied Ecology
    9 July 1994

13. Prof. Dr. Kapt. Mohd. Ibrahim Haji Mohamed
    Managing Challenges in Fisheries Development through Science and Technology
    23 July 1994

14. Prof. Dr. Hj. Amat Juhari Moain
    Sejarah Keagungan Bahasa Melayu
    6 August 1994

15. Prof. Dr. Law Ah Theem
    Oil Pollution in the Malaysian Seas
    24 September 1994

16. Prof. Dr. Md. Nordin Hj. Lajis
    Fine Chemicals from Biological Resources: The Wealth from Nature
    21 January 1995

17. Prof. Dr. Sheikh Omar Abdul Rahman
    Health, Disease and Death in Creatures Great and Small
    25 February 1995

18. Prof. Dr. Mohamed Shariff Mohamed Din
Fish Health: An Odyssey through the Asia - Pacific Region
25 March 1995

19. Prof. Dr. Tengku Azmi Tengku Ibrahim
Chromosome Distribution and Production Performance of Water Buffaloes
6 May 1995

20. Prof. Dr. Abdul Hamid Mahmood
Bahasa Melayu sebagai Bahasa Ilmu-Cabaran dan Harapan
10 June 1995

21. Prof. Dr. Rahim Md. Sail
Extension Education for Industrialising Malaysia: Trends, Priorities and Emerging Issues
22 July 1995

22. Prof. Dr. Nik Muhammad Nik Abd. Majid
The Diminishing Tropical Rain Forest: Causes, Symptoms and Cure
19 August 1995

23. Prof. Dr. Ang Kok Jee
The Evolution of an Environmentally Friendly Hatchery Technology for Udang Galah, the King of Freshwater Prawns and a Glimpse into the Future of Aquaculture in the 21st Century
14 October 1995

24. Prof. Dr. Sharifuddin Haji Abdul Hamid
Management of Highly Weathered Acid Soils for Sustainable Crop Production
28 October 1995

25. Prof. Dr. Yu Swee Yean
Fish Processing and Preservation: Recent Advances and Future Directions
9 December 1995

26. Prof. Dr. Rosli Mohamad
Pesticide Usage: Concern and Options
10 February 1996

27. Prof. Dr. Mohamed Ismail Abdul Karim
Microbial Fermentation and Utilization of Agricultural Bioresources and Wastes in Malaysia
2 March 1996

28. Prof. Dr. Wan Sulaiman Wan Harun
Soil Physics: From Glass Beads to Precision Agriculture
16 March 1996

29. Prof. Dr. Abdul Aziz Abdul Rahman
Sustained Growth and Sustainable Development: Is there a Trade-Off 1 or Malaysia
13 April 1996

30. Prof. Dr. Chew Tek Ann
Sharecropping in Perfectly Competitive Markets: A Contradiction in Terms
27 April 1996

31. Prof. Dr. Mohd. Yusuf Sulaiman
Back to the Future with the Sun
18 May 1996

32. Prof. Dr. Abu Bakar Salleh
Enzyme Technology: The Basis for Biotechnological Development
8 June 1996

33. Prof. Dr. Kamel Ariffin Mohd. Atan
The Fascinating Numbers
29 June 1996

34. Prof. Dr. Ho Yin Wan
Fungi: Friends or Foes
27 July 1996

35. Prof. Dr. Tan Soon Guan
Genetic Diversity of Some Southeast Asian Animals: Of Buffaloes and Goats and Fishes Too
10 August 1996

36. Prof. Dr. Nazaruddin Mohd. Jali
Will Rural Sociology Remain Relevant in the 21st Century?
21 September 1996

37. Prof. Dr. Abdul Rani Bahaman
Leptospirosis-A Model for Epidemiology, Diagnosis and Control of Infectious Diseases
16 November 1996

38. Prof. Dr. Marziah Mahmood
Plant Biotechnology - Strategies for Commercialization
21 December 1996

39. Prof. Dr. Ishak Hj. Omar
Market Relationships in the Malaysian Fish Trade: Theory and Application
22 March 1997

40. Prof. Dr. Suhaila Mohamad
Food and Its Healing Power
12 April 1997

41. Prof. Dr. Malay Raj Mukerjee
A Distributed Collaborative Environment for Distance Learning Applications
17 June 1998

42. Prof. Dr. Wong Kai Choo
Advancing the Fruit Industry in Malaysia: A Need to Shift Research Emphasis
15 May 1999

43. Prof. Dr. Aini Ideris
Avian Respiratory and Immunosuppressive Diseases- A Fatal Attraction
10 July 1999

44. Prof. Dr. Sariah Meon
Biological Control of Plant Pathogens: Harnessing the Richness of Microbial Diversity
14 August 1999

45. Prof. Dr. Azizah Hashim
The Endomycorrhiza: A Futile Investment?
23 October 1999

46. Prof. Dr. Noraini Abdul Samad
Molecular Plant Virology: The Way Forward
2 February 2000

47. Prof. Dr. Muhamad Awang
Do We Have Enough Clean Air to Breathe?
7 April 2000

48. Prof. Dr. Lee Chnoong Kheng
Green Environment, Clean Power
24 June 2000

49. Prof. Dr. Mohd. Ghazali Mohayidin
Managing Change in the Agriculture Sector: The Need for Innovative Educational Initiatives
12 January 2002

50. Prof. Dr. Fatimah Mohd. Arshad
Analisis Pemasaran Pertanian di Malaysia: Keperluan Agenda Pembaharuan
26 January 2002

51. Prof. Dr. Nik Mustapha R. Abdullah
Fisheries Co-Management: An Institutional Innovation Towards Sustainable Fisheries Industry
28 February 2002

52. Prof. Dr. Gulam Rusul Rahmat Ali
Food Safety: Perspectives and Challenges
23 March 2002

53. Prof. Dr. Zaharah A. Rahman
Nutrient Management Strategies for Sustainable Crop Production in Acid Soils: The Role of Research Using Isotopes
13 April 2002

54. Prof. Dr. Maisom Abdullah
Productivity Driven Growth: Problems & Possibilities
27 April 2002

55. Prof. Dr. Wan Omar Abdullah
Immunodiagnosis and Vaccination for Brugian Filariasis: Direct Rewards from Research Investments
6 June 2002

56. Prof. Dr. Syed Tajuddin Syed Hassan
Agro-ento Bioinformation: Towards the Edge of Reality
22 June 2002

57. Prof. Dr. Dahlan Ismail
Sustainability of Tropical Animal-Agricultural Production Systems: Integration of Dynamic Complex Systems
27 June 2002

58. Prof. Dr. Ahmad Zubaidi Baharumshah
The Economics of Exchange Rates in the East Asian Countries
26 October 2002

59. Prof. Dr. Shaik Md. Noor Alam S.M. Hussain
Contractual Justice in Asean: A Comparative View of Coercion
31 October 2002

60. Prof. Dr. Wan Md. Zin Wan Yunus
Chemical Modification of Polymers: Current and Future Routes for Synthesizing New Polymeric Compounds
9 November 2002

61. Prof. Dr. Annuar Md. Nassir
Is the KLSE Efficient? Efficient Market Hypothesis vs Behavioural Finance
23 November 2002

62. Prof. Ir. Dr. Radin Umar Radin Sohadi
Road Safety Interventions in Malaysia: How Effective Are They?
21 February 2003

63. Prof. Dr. Shamsher Mohamad
The New Shares Market: Regulatory Intervention, Forecast Errors and Challenges
26 April 2003

64. Prof. Dr. Han Chun Kwong
Blueprint for Transformation or Business as Usual? A Structurational Perspective of the Knowledge-Based Economy in Malaysia
31 May 2003

65. Prof. Dr. Mawardi Rahmani
Chemical Diversity of Malaysian Flora: Potential Source of Rich Therapeutic Chemicals
26 July 2003

66. Prof. Dr. Fatimah Md. Yusoff
An Ecological Approach: A Viable Option for Aquaculture Industry in Malaysia
9 August 2003

67. Prof. Dr. Mohamed Ali Rajion
The Essential Fatty Acids-Revisited
23 August 2003

68. Prof. Dr. Azhar Md. Zain
Psychotheraphy for Rural Malays - Does it Work?
13 September 2003

69. Prof. Dr. Mohd. Zamri Saad
Respiratory Tract Infection: Establishment and Control
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70. Prof. Dr. Jinap Selamat
Cocoa-Wonders for Chocolate Lovers
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71. Prof. Dr. Abdul Halim Shaari
High Temperature Superconductivity: Puzzle & Promises
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72. Prof. Dr. Yaakob Che Man
Oils and Fats Analysis - Recent Advances and Future Prospects
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73. Prof. Dr. Kaida Khalid
Microwave Aquametry: A Growing Technology
24 April 2004

74. Prof. Dr. Hasanah Mohd. Ghazali
Tapping the Power of Enzymes-Greening the Food Industry
11 May 2004

75. Prof. Dr. Yusof Ibrahim
The Spider Mite Saga: Quest for Biorational Management Strategies
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76. Prof. Datin Dr. Sharifah Md. Nor
The Education of At-Risk Children: The Challenges Ahead
26 June 2004

77. Prof. Dr. Ir. Wan Ishak Wan Ismail
Agricultural Robot: A New Technology Development for Agro-Based Industry
14 August 2004

78. Prof. Dr. Ahmad Said Sajap
Insect Diseases: Resources for Biopesticide Development
28 August 2004

79. Prof. Dr. Aminah Ahmad
The Interface of Work and Family Roles: A Quest for Balanced Lives
11 March 2005

80. Prof. Dr. Abdul Razak Alimon
Challenges in Feeding Livestock: From Wastes to Feed
23 April 2005

81. Prof. Dr. Haji Azimi Hj. Hamzah
Helping Malaysian Youth Move Forward: Unleashing the Prime Enablers
29 April 2005

82. Prof. Dr. Rasedee Abdullah
In Search of An Early Indicator of Kidney Disease
27 May 2005

83. Prof. Dr. Zulkifli Hj. Shamsuddin
Smart Partnership: Plant-Rhizobacteria Associations
17 June 2005

84. Prof. Dr. Mohd Khanif Yusop
From the Soil to the Table
1 July 2005

85. Prof. Dr. Annuar Kassim
Materials Science and Technology: Past, Present and the Future
8 July 2005

86. Prof. Dr. Othman Mohamed
Enhancing Career Development Counselling and the Beauty of Career Games
12 August 2005

87. Prof. Ir. Dr. Mohd Amin Mohd Soom
Engineering Agricultural Water Management Towards Precision Framing
26 August 2005

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Bioremediation-A Hope Yet for the Environment?
9 September 2005

89. Prof. Dr. Abdul Hamid Abdul Rashid
The Wonder of Our Neuromotor System and the Technological Challenges They Pose
23 December 2005

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Rumen Microbes and Some of Their Biotechnological Applications
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Haemorrhagic Septicaemia in Cattle and Buffaloes: Are We Ready for Freedom?
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Activating Teachers' Knowledge and Lifelong Journey in Their Professional Development
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Development and Innovation in the Fracture Management of Animals
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Strategic Feeding for a Sustainable Ruminant Farming
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Green Organic Chemistry: Enzyme at Work
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Towards Large Scale Unconstrained Optimization
20 April 2007

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Trade and Sustainable Development: Lessons from Malaysia's Experience
22 June 2007

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Econometric Modelling for Agricultural Policy Analysis and Forecasting: Between Theory and Reality
13 July 2007

100. Prof. Dr. Zainal Abidin Mohamed
Managing Change - The Fads and The Realities: A Look at Process Reengineering, Knowledge Management and Blue Ocean Strategy
9 November 2007

101. Prof. Ir. Dr. Mohamed Daud
Expert Systems for Environmental Impacts and Ecotourism Assessments
23 November 2007

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Pathogens and Residues; How Safe is Our Meat?
30 November 2007

103. Prof. Dr. Jayum A. Jawan
Hubungan Sesama Manusia
7 December 2007

104. Prof. Dr. Zakariah Abdul Rashid
Planning for Equal Income Distribution in Malaysia: A General Equilibrium Approach
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Newcastle Disease virus: A Journey from Poultry to Cancer
11 January 2008

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Palm Oil: Still the Best Choice
1 February 2008

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Probing the Microscopic Worlds by Lonizing Radiation
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108. Prof. Dr. Mohd Ali Hassan
Waste-to-Wealth Through Biotechnology: For Profit, People and Planet
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Metrology at Nanoscale: Thermal Wave Probe Made It Simple
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The Future of Pesticides Technology in Agriculture: Maximum Target Kill with Minimum Collateral Damage
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Probiotics: Your Friendly Gut Bacteria
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Sustainable Supply of Wood and Fibre: Does Malaysia have Enough?
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Connecting the Bee Dots
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Gender & Career: Realities and Challenges
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Biochemistry of Xenobiotics: Towards a Healthy Lifestyle and Safe Environment
1 August 2008

116. Prof. Dr. Mohd Yunus Abdullah
Penjagaan Kesihatan Primer di Malaysia: Cabaran Prospek dan Implikasi dalam Latihan dan Penyelidikan Perubatan serta Sains Kesihatan di Universiti Putra Malaysia
8 August 2008

117. Prof. Dr. Musa Abu Hassan
Memanfaatkan Teknologi Maklumat & Komunikasi ICT untuk Semua
15 August 2008

118. Prof. Dr. Md. Salleh Hj. Hassan
Role of Media in Development: Strategies, Issues & Challenges
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Gender in Everyday Life
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120 Prof. Dr. Mohd Shahwahid Haji Othman
Mainstreaming Environment: Incorporating Economic Valuation and Market-Based Instruments in Decision Making
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Big Questions Small Worlds: Following Diverse Vistas
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Responding to Changing Lifestyles: Engineering the Convenience Foods
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Aesthetics in the Environment an Exploration of Environmental: Perception Through Landscape Preference
9 January 2009

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Leadership Theories, Research & Practices: Farming Future Leadership Thinking
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Waste Management, What is the Choice: Land Disposal or Biofuel?
23 January 2009

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Freshwater Fish: The Overlooked Alternative
30 January 2009

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The Chemistry of Nanomaterial and Nanobiomaterial
6 February 2009

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Crop Breeding: Exploiting Genes for Food and Feed
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3 April 2009

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Volunteerism: Expanding the Frontiers of Youth Development
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8 May 2009

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10 July 2009

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137 Prof. Dr. Raja Noor Zaliha Raja Abd. Rahman
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138 Prof. Ir. Dr. Barkawi Sahari
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Family Purchase Decision Making: Current Issues & Future Challenges
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4 June 2010

145. Prof. Dr. Raha Hj. Abdul Rahim
Designer Genes: Fashioning Mission Purposed Microbes
18 June 2010

146. Prof. Dr. Hj. Hamidon Hj. Basri
A Stroke of Hope, A New Beginning
2 July 2010

147. Prof. Dr. Hj. Kamaruzaman Jusoff
Going Hyperspectral: The "Unseen" Captured?
16 July 2010

148. Prof. Dr. Mohd Sapuan Salit
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30 July 2010

149. Prof. Dr. Shattri Mansor
Google the Earth: What's Next?
15 October 2010

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Haute Couture: Molecules & Biocatalysts
29 October 2010

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Poultry Vaccines: An Innovation for Food Safety and Security
12 November 2010

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Fern of Malaysian Rain Forest
3 December 2010

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Preparing Malaysian Youths for The World of Work: Roles of Technical and Vocational Education and Training (TVET)
14 January 2011

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Are there "Magic Bullets" for Cancer Therapy?
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155. Prof. Dr. Mohd Azmi Mohd Lila
Biopharmaceuticals: Protection, Cure and the Real Winner
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Genetic Manipulation in Farmed Fish: Enhancing Aquaculture Production
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Energy Crisis 2050? Global Scenario and Way Forward for Malaysia
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Managing Plant Under Stress: A Challenge for Food Security
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Does Genetic Polymorphisms Affect Health?
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Wonders of Glass: Synthesis, Elasticity and Application
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Fruits: Nutritious, Colourful, Yet Fragile Gifts of Nature
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Climate Change: Crop Performance and Potential
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165. Prof. Dr. Fauziah Othman
My Small World: In Biomedical Research
23 December 2011

166. Prof. Dr. Japar Sidik Bujang
The Marine Angiosperms, Seagrass
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167. Prof. Dr. Zailina Hashim
Air Quality and Children's Environmental Health: Is Our Future Generation at Risk?
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168. Prof. Dr. Zainal Abidin Mohamed
Where is the Beef? Vantage Point form the Livestock Supply Chain
27 April 2012

169. Prof. Dr. Jothi Malar Panandam
Genetic Characterisation of Animal Genetic Resources for Sustaninable Utilisation and Development
30 November 2012

170. Prof. Dr. Fatimah Abu Bakar
The Good The Bad & Ugly of Food Safety: From Molecules to Microbes
7 December 2012

171. Prof. Dr. Abdul Jalil Nordin
My Colourful Sketches from Scratch: Molecular Imaging
5 April 2013

172. Prof. Dr. Norlijah Othman
Lower Respiratory Infections in Children: New Pathogens, Old Pathogens and The Way Forward
19 April 2013

173. Prof. Dr. Jayakaran Mukundan
Steroid-like Prescriptions English Language Teaching Can Ill-afford
26 April 2013

174. Prof. Dr. Azmi Zakaria
Photothermals Affect Our Lives
7 June 2013

175. Prof. Dr. Rahinah Ibrahim
Design Informatics
21 June 2013

176. Prof. Dr. Gwendoline Ee Cheng
Natural Products from Malaysian Rainforests
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177. Prof. Dr. Noor Akma Ibrahim
The Many Facets of Statistical Modeling
22 November 2013

178. Prof. Dr. Paridah Md. Tahir
Bonding with Natural Fibres
6 December 2013

179. Prof. Dr. Abd. Wahid Haron
Livestock Breeding: The Past, The Present and The Future
9 December 2013

180. Prof. Dr. Aziz Arshad
Exploring Biodiversity & Fisheries Biology: A Fundamental Knowledge for Sustainabale Fish Production
24 January 2014

181. Prof. Dr. Mohd Mansor Ismail
Competitiveness of Beekeeping Industry in Malaysia
21 March 2014

182. Prof. Dato' Dr. Tai Shzee Yew
Food and Wealth from the Seas: Health Check for the Marine Fisheries of Malaysia
25 April 2014

183. Prof. Datin Dr. Rosenani Abu Bakar
Waste to Health: Organic Waste Management for Sustainable Soil Management and Crop Production
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Poultry Viruses: From Threat to Therapy
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185. Prof. Dr. Mohamad Pauzi Zakaria
Tracing the Untraceable: Fingerprinting Pollutants through Environmental Forensics
13 June 2014

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Space System Trade-offs: Towards Spacecraft Synergisms
15 August 2014

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Tranformasi Kesihatan Wanita ke Arah Kesejahteraan Komuniti
7 November 2014

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Fat and Oils for a Healthier Future: Makro, Micro and Nanoscales
21 November 2014

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Lignocellulosic Biofuel: A Way Forward
28 November 2014

190. Prof. Dr. Robiah Yunus
Biobased Lubricants: Harnessing the Richness of Agriculture Resources
30 January 2015

190. Prof. Dr. Khozirah Shaari
Discovering Future Cures from Phytochemistry to Metabolomics
13 February 2015

191. Prof. Dr. Tengku Aizan Tengku Abdul Hamid
Population Ageing in Malaysia: A Mosaic of Issues, Challenges and Prospects
13 March 2015

192. Prof. Datin Dr. Faridah Hanum Ibrahim
Forest Biodiversity: Importance of Species Composition Studies
27 March 2015

192. Prof. Dr. Mohd Salleh Kamarudin
Feeding & Nutritional Requirements of Young Fish
10 April 2015

193. Prof. Dato' Dr. Mohammad Shatar Sabran
Money Boy: Masalah Sosial Era Generasi Y
8 Mei 2015

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Developing Students' Mathematical Thinking: How Far Have We Come?
5 June 2015