Palm Oil Effects on Postprandial Lipid and Prothrombotic Response

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INTRODUCTION

Postprandial lipid metabolism refers to the series of metabolic processes which occur following the ingestion of a meal containing fat (Roche, 2000). The responses of plasma lipoproteins during absorption of dietary fats have gathered increasing interest due to the fact that man by eating regular meals, spends most of the time in the postprandial phase (Thomsen *et al.,* 1999). Depending on the size and composition of a meal, the postprandial response can last up to 8 hr. Therefore, most humans are in an almost constant postprandial state.

POSTPRANDIAL LIPEMIA

Dietary fat is principally composed of triacylglycerol (TAG). Therefore, following digestion of a meal, there is a significant increase in the plasma TAG concentration. Recent prospective epidemiological studies show that plasma TAG, especially the non-fasting level is an important factor in the pathogenesis of coronary heart disease (CHD) (Roche, 2000). A positive correlation between plasma TAG levels and CHD risk has been found in women, diabetics, the Japanese and those with elevated low density lipoprotein (LDL) or decreased high density lipoprotein (HDL)-cholesterol(C) levels. An Israeli study suggests that elevated plasma TAG levels are an independent risk factor for mortality among CHD patients (Vogel *et al.,* 1997). Elevation of postprandial TAG rich plasma lipoproteins and suppression of HDL-C concentrations are considered potentially atherogenic (Patsch, 1994).

Several clinical studies have shown that elevated levels of TAG rich lipoprotein and its remnants during the postprandial phase of lipid metabolism are related to the presence and progress of coronary atherosclerosis (Cohn, 1994; Roche and Gibney, 1995). Atherosclerosis and thrombosis are the two key pathophysiological processes which lead to the development of CHD. Roche *et al.* (2000) suggest the following mechanisms in which postprandial TAG metabolism affects the athero-thrombotic potential and thereby the pathogenesis and progress of CHD:

i. The chylomicron remnants, like LDL cholesterol mediates cholesterol influx into the arterial wall intima;
ii. Excessive enrichment of HDL-C with TAG during elevated postprandial lipemia which are catabolized, leading to low concentrations of HDL-C;
iii. Postprandial hypertriacylglycerolemia stimulates the formation of small dense LDL particles which are highly atherogenic and increase the risk of CHD; and
iv. A prothrombotic state is produced by elevated postprandial lipemia because a high concentration of TAG rich lipoprotein in the circulation activates coagulation factor VII (FVII).

There is a strong inverse correlation between HDL-C and the peak postprandial concentration of TAG after a meal of fat. The negative correlation between HDL-C concentration and CHD stems from the

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highly positive correlation between postprandial TAG concentration and CHD. A correlation has also been recorded between the magnitude of postprandial triacylglycerolemia after a fatty meal and fasting apo B in healthy subjects. Both these observations suggest that for many individuals, increased levels of apo B point to postprandial lipid abnormalities (Betterbridge, 1999).

The inverse relationship between the chylomicron cholesterol and HDL-C concentrations is probably a result of the cholesteryl ester transfer protein mediated transfer of cholesteryl esters from HDL to TAG rich lipoproteins. The reverse transfer of TAG from TAG rich lipoproteins to HDL may explain the postprandial increase in HDL-TAG concentrations observed in some of the studies. One mechanism by which chylomicron remnants and other triglyceride rich lipoproteins may lead to atherosclerosis is through the induction of endothelial dysfunction. Several studies have demonstrated that all the traditional coronary risk factors are associated with endothelial dysfunction, independent of the presence of CHD (Vogel *et al.,* 1997).

IMPLICATIONS FOR PALM OIL

Palm oil (PO) is a major edible oil in the world and its nutritional and health attributes have been well documented (Chandrasekharan *et al.,* 2000). Nevertheless, there are some aspects of its metabolism that need further elucidation, including its postprandial response which continues to generate much interest. This paper highlights the effects of PO on the postprandial lipid responses as observed in some recent well conducted studies on human volunteers. Since there are indications that dietary fat intake is a major determinant of factor VII activity (FVIIc), this aspect is also discussed from the perspective of PO. Some essential background information is provided for a better appreciation of postprandial lipemia and hemostasis especially for the benefit of those not familiar with these subjects.

DIGESTION, ABSORPTION, TRANSPORT AND METABOLISM OF LIPIDS

Following a meal, chylomicrons which are TAG rich lipoproteins synthesized in the intestinal enterocyte, transport dietary fat (TAG) from the intestine throughout the circulation to adipose tissue where it is off loaded. Chylomicron core TAGs are rapidly hydrolyzed to free fatty acids by the action of lipoprotein lipase, an enzyme bound to the capillary endothelium of muscle, adipose and other tissues. This is a rate limiting enzyme that determines the magnitude of postprandial lipemia. The resultant delipidated chylomicron rich in cholesterol and now termed 'chylomicron remnant' is removed from the circulation by the liver and catabolized (*Figure 1*). Plasma total TAG levels increase shortly after the first meal of the day because of release of chylomicrons from the gut and VLDL from the liver and return to the baseline concentration several hours after the last meal. This is a normal physiological process, during which there is rise and fall in plasma TAG concentration in the postprandial state.

An excessive postprandial TAG response to a meal high in fat can be due to over production of TAG rich lipoproteins to inadequate lipolysis or to abnormalities in the metabolism of remnant lipoproteins. In the latter instance, the remnant lipoproteins will accumulate in the circulation. In this situation, chylomicrons remain in the circulation longer and interact with both LDL and HDL.

Chylomicrons give their TAGs to the LDLs which become smaller and denser, and more atherogenic (Patsch, 1994). The HDLs also become over enriched with TAGs. The resultant HDLs are more susceptible to catabolism, whereby the liver removes the cardioprotective HDL fraction from the circulation. Research has shown that these chylomicron remnants are a component of the atherosclerotic plaque, therefore excessive chylomicron remnant concentrations promote the process of atherogenesis (Slyper, 1992). Previous studies have shown that

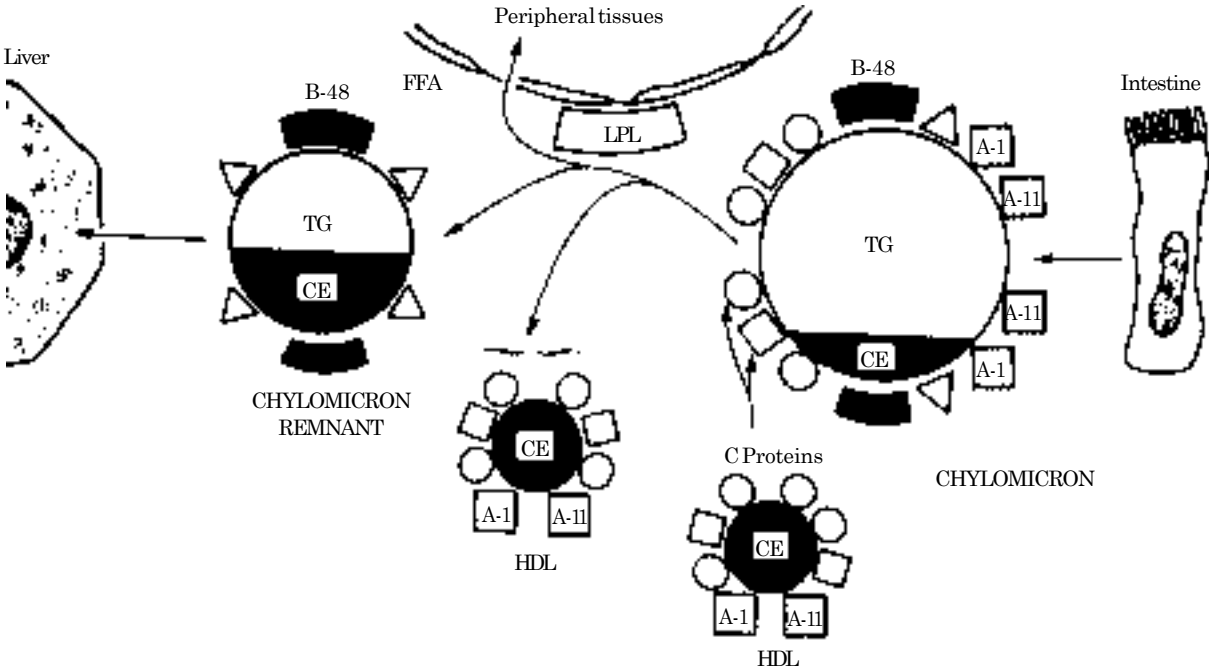

Figure 1. Metabolism of chylomicrons. TG = triglyceride; CE = cholesteryl ester.

delayed clearance of the TAG circulating in the blood, the intensity of postprandial lipaemia and the presence of remnant particles play an important role in the pathogenesis and progression of atherosclerosis (Jensen *et al*., 1999).

It is known that the quantity of dietary fat increases postprandial lipemia in a dose dependent manner and that the production and clearance of lipoproteins and lipoprotein derived remnants are affected by the composition of the diets.

THE COAGULATION POTENTIAL, FACTOR VII AND BLOOD LIPIDS

Blood coagulates by the transformation of soluble fibrinogen into insoluble fibrin (*Figure 2*). More than a dozen circulating proteins interact in a cascading series of limited proteolytic reactions to form the clot. Factor VII (a clotting factor zymogen) undergoes limited proteolysis and becomes an active protease (FVIIa or activated form of FVII). Blood coagulation is a risk factor for atherogenesis and thombogenesis and the best measure of the coagulable potential is the coagulant activity of factor VII (FVIIc is a functional assay of factor VII activity).

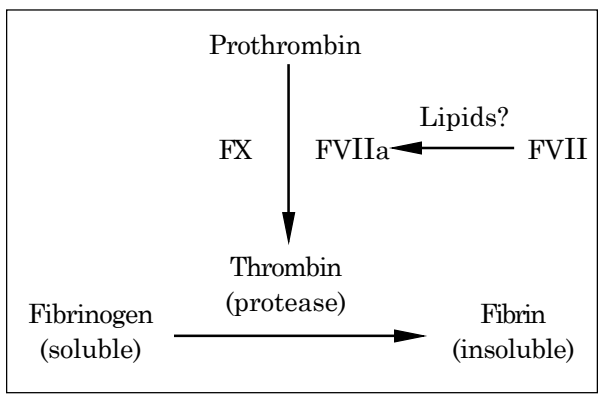

Figure 2. The clotting process.

Elevated FVIIc is believed to indicate a hypercoagulable state predisposing to coronary thrombosis in subjects with extensive atherosclerosis.

The literature relating to the effect of dietary fat composition on postprandial FVIIc is confusing and the relevant studies need to be considered in terms of their study design (Roche and Gibney, 1997). Nevertheless, the crucial role of lipids in blood coagulation has been appreciated for many years. They participate in several steps in the coagulation cascade, increasing the rate with which thrombin is formed. FVII is activated during postprandial triacylglycerolemia and fasting FVIIc is the single most

important factor affecting postprandial FVIIc irrespective of plasma lipid concentration and meal fat composition (Roche and Gibney, 1997).

Elevated FVIIc levels have been identified in hyperlipidemic subjects (Marckmann *et al.,* 1990). There is a positive correlation between FVIIc and serum lipids (especially TAG) and dietary fat intake. FVIIc is positively related to plasma TAG concentration. An acute elevation of FVIIc is observed after consumption of a high fat meal. Lipid mediated activation of FVII to FVIIa may lead to a higher level of FVIIc, caused by an increase in the concentration of FVIIa. Postprandial TAG rich lipoprotein enhances postprandial FVIIc. A positive relationship between FVIIc and CHD mortality has been demonstrated. Patients with CHD have high levels of FVIIc. The possible mechanisms involved could be that the plasma TAG concentration affects the concentration and catabolism of FVII and converts the inactive FVII (zymogen) to FVIIa. Altering the saturated:monounsaturated fatty acid (SFA:MUFA) ratio of an acute test meal does not influence the magnitude of postprandial FVIIc.

The study of the interactions between dietary lipids and hemostasis is a complex and difficult process. Hemostatic factors are difficult to measure. Measurements are usually made in venous blood, hence tell us little about the *in vivo* situation and thrombotic tendency in the arteries. Further, many different methods are used, making comparisons between studies difficult.

Highlights of some recent studies on the effect of dietary fat quality on postprandial lipemia and hemostasis are summarized below. The composition of the diets used are shown in *Table 1.*

TABLE 1. COMPOSITION OF TEST DIETS

Researcher	Energy (MJ)	Fat (g)	En (%)
Pedersen *et al.*	7.1	81	43
Jensen *et al.*	5.2	51	65
Larsen *et al.*	5.8	70	42
Sanders *et al.*	5.1	50	37
Ong *et al.*	3.2	50	58

Postprandial Lipid/Lipoprotein Response in Men after Meals Containing Rapeseed Oil, Sunflower Oil or PO

The investigation by Pedersen *et al.* (1999) was conducted on 11 healthy adult males in Denmark. On six occasions, each subject consumed consecutive meals containing 70 g of rapeseed oil, sunflower oil or PO. One fasting and 15 postprandial blood samples were taken over 9 hr. Postprandial lipid, lipoprotein and non-esterified fatty acid concentrations were determined. There were no statistically significant differences in lipoprotein and apolipoprotein responses after rapeseed, sunflower and POs (*Figure 3*). The

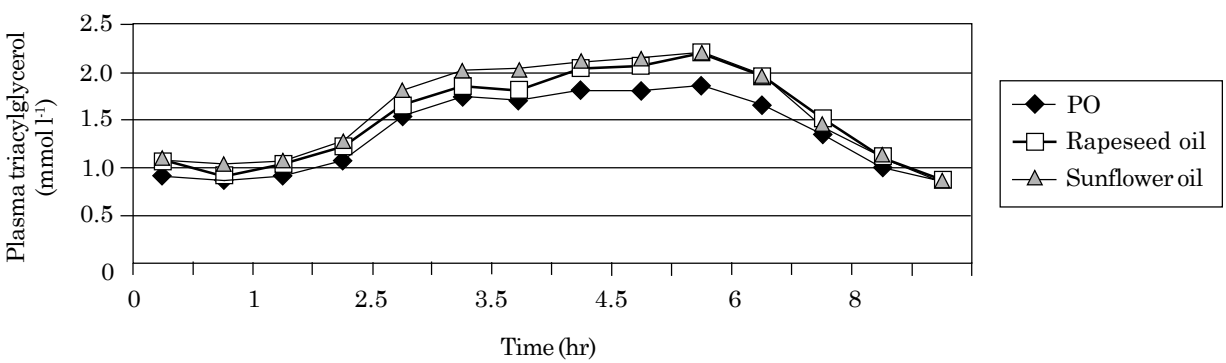

Figure 3. Total plasma triacylglycerol concentrations after consumption of two consecutive meals containing 15 and 55 g of test oil respectively.

Source: adapted from Pederson *et al.* (1999).

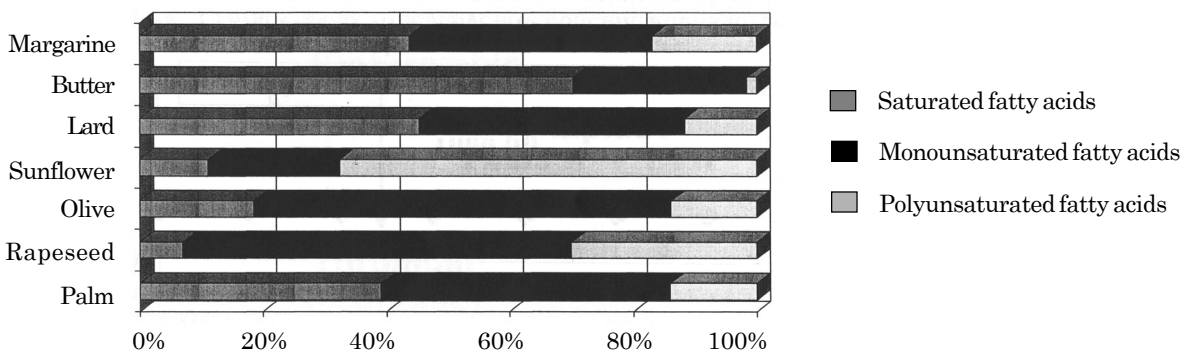

Figure 4. Fatty acid composition of test oils/fats.

fatty acid composition of the meal did not significantly affect the lipid and lipoprotein responses (*Figure 4*).

Postprandial Lipid/Lipoprotein Response in Women after Meals Containing PO, Lard (LD) or Puff-pastry Margarine (PPM)

In this study by Jensen *et al.* (1999), the acute postprandial effects of three normal edible fats used for spreads and cooking, differing only in the content of fatty acids on plasma total TAG and chylomicron (CM)-TAG were compared in eight normal weight women in Denmark. The test meals provided an average of 51 g of fat per meal. The concentrations of plasma total TAG and CM-TAG were determined before the meal and monitored over 8 hr. The fatty acid composition of the postprandial CM lipids was also studied to determine if discrimination in the absorption or a specific clearing was taking place (*Tables 2* and *3*).

There was no significant difference in the postprandial responses between the three test meals (*Figure 5*). The different content of fatty acids provided by PO, LD or PPM had no effect on the postprandial lipid responses. These results indicate that test meals containing PO, LD or PPM produce similar postprandial responses of plasma total TAG and CM-TAG in normal women although the differences in the fatty acid composition of the fats were distinct.

Effects of Rapeseed/Olive/Sunflower/PO/Butter on the Coagulation Potential

Larsen *et al.* (1999) investigated whether saturated, monounsaturated or polyunsaturated fats differed in postprandial activation of FVII in 18 healthy young men in Den-

TABLE 2. MAJOR FATTY ACIDS IN PO AND CHYLOMICRONS ISOLATED EVERY SECOND HOUR IN THE POSTPRANDIAL PERIOD (n=8)

Time (hr)	PO	0	2	4	6	8
fatty acid	Mean values (%)					
16:0	43.5	25.2	36.6	35.7	36.0	33.0
16:1 n-7	0.2	2.0	0.6	0.6	0.5	0.8
18:0	4.6	11.3	6.3	6.5	6.1	7.2
18:1 *trans*	0.2	0.8	0.3	0.3	0.3	0.5
18:1 *cis*	38.9	26.7	36.8	37.1	37.4	32.4
18:2n-6	10.3	16.7	13.2	11.6	13.5	15.8
18:3n-6	0.7	0.5	0.5	0.4	0.3	0.5

Source: adapted from Jansen (1999).

TABLE 3. FASTING AND POSTPRANDIAL PEAK MEAN CONCENTRATIONS OF PLASMA FREE FATTY ACIDS AFTER INTAKE OF MEALS ENRICHED WITH RAPESEED OIL, OLIVE OIL, SUNFLOWER OIL, PO OR BUTTER (41.5 en%) OR ISOENERGETIC LOW FAT MEALS (6.3 en%)

	Free fatty acids (mmol l^{-1})	
	Fasting	**Time 3.5 hr**
Rapeseed oil	0.55	0.18
Olive oil	0.50	0.17
Sunflower oil	0.55	0.20
PO	0.49	0.19
Butter	0.51	0.24
Low fat meals	0.51	0.02

Source: adapted from Jansen (1999).

Dietary Sunflower/PO and Factor VII Activity

Sanders *et al.* (1999) compared the effects of oleic acid rich sunflower oil and PO on postprandial TAG concentration as well as FVIIc in 52 adults in England with moderately elevated TAG levels. A high palmitate meal (PO), despite leading to the same degree of postprandial lipemia as a high oleate meal (sunflower oil) did not lead to any postprandial change in FVIIc. The concentration of FVIIa increased after the high palmitate meal but this increase was only half that seen after a high oleate meal (*Table 4*).

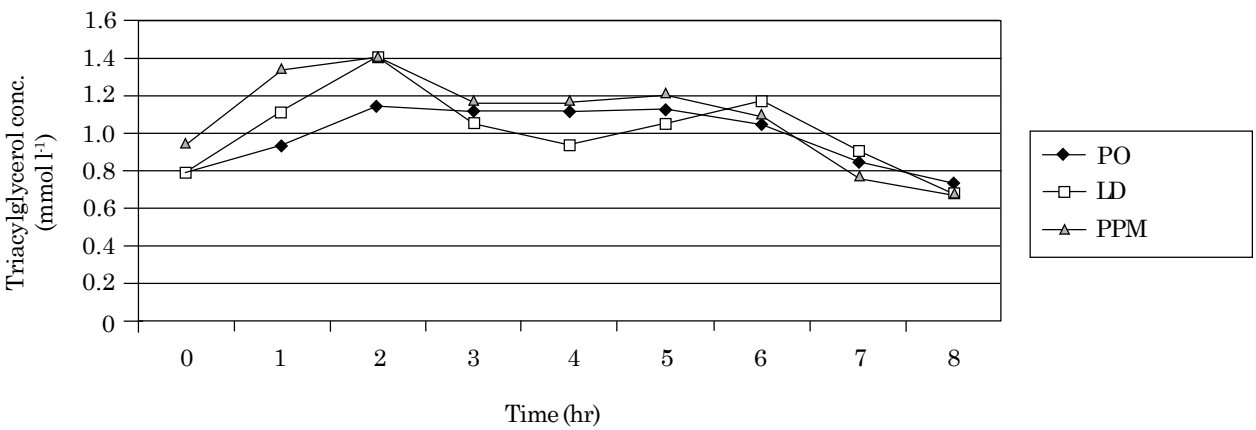

Figure 5. Plasma triacylglycerol/responses (0-8 hr) to test meals containing PO/LD/PPM in normal weight women.

Source: adapted from Jansen *et al.* (1999).

mark, consuming meals enriched with 70 g of either rapeseed oil, olive oil, sunflower oil, PO or butter. Fasting and a series of non-fasting blood samples were collected. The five different fat qualities caused similar postprandial increases in the plasma TAG, FVIIa and FVIIc levels. These findings indicate that high fat meals may be prothrombotic, irrespective of their fatty acid composition. The postprandial FVIIa level was not associated with the plasma TAG or free fatty acid responses (*Table 4*).

Impairment of Endothelial Function by Monounsaturated Fat

Recently, it has become increasingly clear that endothelial cells play important roles in the maintenance of the homeostatic balance *in vivo* and in the modulation of vascular function in health and disease. Ong *et al.* (1999) have reported that the consumption of a meal high in monounsaturated fat was associated with acute impairment of endothelial function (as measured by flow

TABLE 4. POSTPRANDIAL CHANGES IN BLOOD FVIIa, FVIIc AND PLASMA TRIGLYCERIDES CONCENTRATIONS IN SUBJECTS CONSUMING TEST MEALS WITH DIFFERENT OILS/FATS

Oil/fat	FVIIc	FVIIa	Triglyceride
	(% change from fasting values)		
Time (hr)	8	6	4.5
In normo triglyceredemic subjects[a]			
Rapeseed	2.4	73	95
Olive	2.4	66	112
Sunflower	3.8	60	107
PO	2.5	71	118
Butter	5.0	72	106
Low fat	-3.7	8	5
In moderately hypertriglyceredemic subjects[b]			
Sunflower 3 hr	8.4	55	89
6 hr	8.8	48	23
PO 3 hr	0.7	25	70
6 hr	0.3	18	16

Sources: adapted from [a]Larsen *et al.* (1999) and [b]Sanders *et al.* (1999).

TABLE 5. ENDOTHELIAL FUNCTION AND FLOW MEDIATED VASOACTIVITY (% changes from fasting values)

Low fat high carbohydrate diet	+1.30	Diet with high monounsaturated fat (sunflower oil 50 g)	-1.60

Source: adapted from Ong *et al.* (1999).

mediated reactivity of the brachial artery) when compared with a carbohydrate rich meal (*Table 5*). Their findings suggest an adverse effect of oleic and linoleic acids on the endothelial function. Oleic acid rich oils have been touted as heart healthy based on the benefits of the Mediterranean diet. However, these recommendations need be reviewed in the light of recent findings.

DISCUSSION

Conventional definitions of normolipidemia and hyperlipidemia are based on 12 hr fasting values. A 12 hr fast is, however, an arbitrary convention that provides little information about the metabolism of lipoproteins during most of the day. It is in this context that postprandial lipidemia continues to be of interest in terms of its genetic and dietary determinants and its relationship to atherosclerosis and coronary heart disease.

The different fatty acid compositions of normal dietary fats and oils discussed in this paper show no influence on the measured postprandial lipid and lipoprotein responses. There was no significant effect on the postprandial responses with the level of saturated, monounsaturated or polyunsaturated fatty acid within population cohorts.

Postprandial FVIIa level is not associated with plasma TAG or free fatty acid responses. A low fat diet with relatively high content of saturated fats lowers the FVII level in healthy individuals and so probably reduces the risk of atherosclerosis and throm-

bosis without lowering the serum lipids (Marckman *et al.,* 1990). It is pertinent in this context to note that a recent study in the US found that men with the highest level of saturated fatty acids had the lowest incidence of ischaemic stroke (Gillman *et al.,* 1997).

These findings once again reaffirm that fats and oils with different fatty acid compositions do not differ in their acute effects on plasma TAG and FVII levels. The present observations lend further testimony to the merits of PO in that it is comparable to the other oils in terms of its postprandial lipid response and effects on prothrombotic activity. In developing countries, vegetable oils are replacing animal fats because of the cost and health concerns and PO has become one of the major edible oils in the world (Chandrasekharan, 1999). It is reassuring to know that the consumption of PO as a source of dietary fat does not pose any additional risks for coronary artery disease when consumed in realistic amounts as part of a healthy diet.

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