Research Journal of Biological Sciences 3 (1): 132-135, 2008
ISSN: 1815-8846


# The Effect of Butter Intake on Coagulating Factors in Healthy Males

A. Nemati, H. Alimohammadi and A. Naghizadeh Baghi
Department of Basic Sciences, Faculty of Medicine, Ardebil University of Medical Sciences, Ardebil, Iran

**Abstract:** Food of high fat intake may increase the risk of blood clotting, heart attackes, coagulating factors and cardiovascular disease. The purpose of this study was to determine the effect of saturated fat (butter) intake on serum cholesterol, triglgycerides and coagulating factors including Protherombin Time (PT), Partial Thromboplastin Test (PTT), Bleeding Time (BT), factorVII and fibrinogen. In 2006 with randomized clinical trial, 23 healthy males aged 18-28 years old were selected for study. After taking of 24 recall h, subjects consumed daily 30 g butter intake for 28 days and blood sample was taken for measuring of factors at the weekend. Data were analyzed by Iranian food processor and repeated-measures analysis of variance with SPSS version 13. The results showed that butter intake increased significantly coagulating factor VII at the end of the 2nd and 4th week ($p<0.05$). Bleeding time decreased significantly at 4th week ($p<0.05$). Serum fibrinogen decreased significantly at the end of 2nd and 4th week ($p<0.05$ ). Changes of PT and PTT were diverge at the end of 2nd and 4th week, which decreased significantly at the end of 2nd week and increased significantly at the end of 4th week ($p<0.05$). There was no significant changes of serum cholesterol and triglycerides after butter intake. This study showed that high saturated fat diet intake can affect some clotting factors in healthy individuals.

**Key words:** Butter, coagulating factors, healthy person, male, Iran

## INTRODUCTION

Factor VII is the first enzyme in the extrinsic pathway of blood coagulation (Fair, 1983). Dietary studies in human and animal models have established a connection between plasma concentrations of triglyceride-rich lipoproteins and factor VII coagulant activity, as measured by one-stage bioassays. For instance, addition of fat to the diet causes a rapid increase in factor VII coagulant activity (VIIa), which has been interpreted to reflect an increased conversion of the zymogene to VIIa (Miller *et al*., 1986; Mitropoulos *et al*., 1987; Marckman and Sandstrom, 1990; Miller *et al*., 1991; Connelly *et al*., 1993; Bladberg *et al*., 1994). Intake of specific nutrients is related to cardiovascular disease. Prospective studies have shown that an increased intake of saturated fat or a decreased intake of dietary fiber is associated with the development of coronary heart disease (Khaw and Banrat, 1987; Kromhout *et al*., 1982; Kushi *et al*., 1985). Factor VII, a vitamin K-dependent coagulation factor, is one of those indicators highly influenced by nutrition. Factor VII Clotting activity (FVII: C) and total factor VII were found to be positively associated with intake of dietary fat in a cross-sectional study (Miller *et al*., 1995). Results from several experiments showed an increase of FVII: C in subjects when they consumed a high fat diet, whereas a decrease was noted when subjects consumed a low fat diet (Miller *et al*., 1986; Marckman *et al*., 1990). The effects of a high fat diet on total factor VII are less clear (Mennen *et al*., 1996). A variety of environmental factors are known to influence levels of factor VII and fibrinogen and therefore support their role in the development of coronary thrombosis. Factor VII is known to correlate with total cholesterol level and there is a relationship between dietary variability of fat intake and factor VII, which is likely to play an important role in the risk of coronary heart disease (Kelleher, 1992). Several reports have suggested that dietary fat intake or hypertriglyceridaemia are associated with elevated levels of FVII (Sanders *et al*., 1996). Several clinical studies have suggested that Factor VII Clotting (FVIIC) activity in middle-aged persons is directly associated with the risk for cardiovascular disease (Meade *et al*., 1986; Heinrich *et al*., 1994). Dietary intervention studies have shown that various plasma components related to the thrombosis process may be affected by the fatty acid composition of the diet (Mitropoulos *et al*., 1994). Others study showed that diet enriched in saturated fatty acids raises plasma levels of Factor VII and induces activation of Factor VIIC during the postprandial period (Mennen *et al*., 1996;

**Corresponding Author:** Ali Nemati, Department of Basic Sciences, Faculty of Medicine, Ardebil University of Medical Sciences, Ardebil, Iran

Sanders, 1996; Marckmann *et al*., 1998). Accordingly, we examined effects of butter intake (saturated fat) on coagulating factors, serum cholesterol and triglycerides in healthy person.

## MATERIALS AND METHODS

In 2006 with randomized clinical trial study 23 nonsmoking healthy male volunteers were selected from the student population of Ardebil University of Medical Sciences, Iran. None of them had a history of atherosclerotic disease and all were apparently healthy as judged by their responses to a standardized medical questionnaire. None of the subjects had hypertension or were taking medication of any kind. The protocol and the aim of the study were fully explained to the subjects and the written consent was taken. Mean age and body mass index were 25±4.1 years old (range: 18-28 y) and 24.8±3.2 (kg $m^{-2}$) (range: 20.7-29.1), respectively. Blood samples were taking before starting butter intake and end of 2nd and 4th week. Their calorie and nutrients intake were taken by 24 h recall 3 days in week before of starting study and in duration of butter intake every week. After taking 24 h recall three days and clarification of calorie and nutrients intake, individuals took 30 g butter daily for four weeks. Meals with 105 g fat intake plus 30 g butter were given that was 48% of total energy from fat. The nutrient composition of the meals was calculated from food tables and the processor of Iranian food information. Venous blood samples were collected into evacuated tubes with minimal compression necessary to display the vein. Blood samples were analyzed in a laboratory at the Ardebli University of Medical Sciences for measuring of serum cholesterol and triglycerides and coagulating factors including Prothrombin Time (PT), Partial Thromboplastin Test (PTT), Bleeding Time (BT), factor VII and fibrinogen. Factor VII, fibrinogen, cholesterol, triglycerides, PT and PTT were measured by commercial diagnostic kits; TECO (Germany) and Mahsa Yaran, Pars Azomon (Iran) and Difco (France), respectively. BT was analyzed by routine laboratory technique. Kolmogrov-smirinov test was used to check the normality of distribution of the variables. After normality was conformed, repeated-measures analysis of variance with SPSS version 13 was employed to analyze the changes across the time (weeks). Statistical significance was set at $p \leq 0.05$ for all statistical tests.

## RESULTS

The results indicated that coagulating factor VII was significantly increased following butter intake at the end of the 2nd and 4th week ($p<0.05$), but BT and serum fibrinogen decreased at the end of the 2nd and 4th week ($p<0.05$). There was no significant change of serum triglycerides after butter intake. Serum cholesterol was increased after buter intake, but there was no significant between groups. PT and PTT were changed at the end of 2nd and 4th week, which decrease significantly at the end of 2nd week and increases significantly at the end of 4th week ( $p<0.05$ ) (Table 1). Calorie and other nutrients intake ( exception fat ) of subjects were same during study (Table 2).

Table 1:Cagulating factors at before and after butter intake in male subjects

| Variable | Baseline | 2 weeks | 4 weeks |
|---|---|---|---|
| Triglyceride (mg $dL^{-1}$) | 115.2±54.7 | 111.6±41.5 | 114.5±46.3 |
| Cholesterol (mg $dL^{-1}$) | 160.7±24.6 | 161.3±27.1 | 162.7±26.4 |
| PT (sec) | 12.9±0.3 | 12.5±0.5* | 13.3 ±0.8*,+ |
| PTT (sec) | 36.3±2.5 | 35.2 ±2.2* | 39±4.3*,+ |
| Fibrinogen (mg $dL^{-1}$) | 243.7±40.4 | 232.1±33.9* | 209±23.5*,+ |
| BT (sec) | 145±27.9 | 140.6±34 | 128±25.2* |
| Factor VII % | 186.7±75.9 | 203.6±75.8 | 239.9±63.8*,+ |

Values are mean±SD, n = 23, *$p<0.05$ vs basline, +$p<0.05$ vs 2 weeks

Table 2: The mean of calorie and other nutrients (*Exception fat*) intake during study

| Variables | Mean±SD | Variables | Mean±SD |
|---|---|---|---|
| Calorie (Kcal) | 2517±510 | Folacin (µg) | 98±81 |
| Protein (g) | 76.1±22.4 | Vitamin B5 (mg) | 3±2 |
| Carbohydrate (g) | 315.1±93 | Vitamin C (mg) | 62±39 |
| Fiber (g) | 11.4±7.8 | Vitamin E (mg) | 3±2 |
| Fat (g) | 105.6±21.2 | Calcium (mg) | 526±320 |
| Saturated fat (g) | 27±10 | Copper (mg) | 0.7±0.3 |
| Mono unaturated fat (g) | 31±9 | Iron (mg) | 23±8 |
| Poly unaturated fat (g) | 10±3 | Magnesium (mg) | 128±76 |
| Cholestrol (mg) | 314±243 | Phosphoros (mg) | 740±306 |
| Vitamin B1 (mg) | 1.7±0.5 | Potacium (mg) | 1713±900 |
| Vitamin B2 (mg) | 1.2±0.4 | Selenium (µg) | 57±49 |
| Vitamin B3 (mg) | 22.2±8 | Sodium (mg) | 3267±1311 |
| Vitamin B6 (mg) | 0.8±0.4 | Zinc (mg) | 6±2 |
| Vitamin B12 (µg) | 6±3 | p/s* | 0.4±0.2 |

*poly unsaturated fatty acid/ unsaturated fatty acid

## DISCUSSION

Butter fat is one of the most complex dietary lipids both in terms of fatty acid (predominantly palmitic, myristic, stearic, oleic acids) and triacylglycerol components and its physico-chemistry. In this study, we modified the dietary fat mainly through adding of butter fat to diet of subjects. Despite the large fat bolus of almost 30 g given to the women in this trial, the absolute change in dietary poly unsaturated fatty acids and mono unsaturated fatty acids was relatively small. Total saturated fat were increased by approximately 24.9 g. This moderate change had small effect on serum cholesterol, but had not effect on serum triglyceride. Several hemostatic factors are influenced by dietary components (Pearson, 1997; Marckmann, 1995) For example, when a high-fat diet is replaced by a lower-fat, higher-fiber diet, the activity of factor VII decreases and the capacity of the

endogenous fibrinolytic system increases. The fat quantity had a marked impact on the FVII. How dietary fat promotes the acute activation of FVII is not clear, but a relation to the plasma triglyceride concentration (Silveira *et al*., 1994; Kapur *et al*., 1996) or to lipolytic degradation of Triglyceride-Rich Lipoproteins (TRLP) have been suggested (Mitropoulos *et al*., 1994). In our study the serum FVII% after butter fat intake were approximately 16.9 and 53.2 higher than besline at the end of second and fourth week, respectively. The results of present trial is disagreement with study of Sanders that suggest the consumption of a stearic acid-rich triacylglycerol do not increases FVII in middle-aged men and women (Sanders *et al*., 2001). A significant improvement in cardiovascular risk can be achieved by moderate changes in dietary fatty acid profile, achieved through a common and well accepted food source, butter-fat (Poppitt *et al*., 2002). The study of Tholstrup showed that intake of the butter resulted in 6% lower total cholesterol (Tholstrup *et al*., 2006) but we did not observe decrease in serum cholesterol after butter intake. The content of total fats in the diet is known to influence the concentrations of FVII (Marckmann *et al*., 1998). Kirsty showed short-term intake of diets with similar fat content (38% as energy) but with distinctly different fatty acid compositions have no influence on plasma concentration of FVII (Kirsty *et al*., 2000) that with present study is disagreement. Fasting triglyceride concentrations are reported to be positively associated with factor VIIc (Scarabin *et al*., 1985; Mennen *et al*., 1996). The butter diet resulted in slightly higher levels of fibrinogen. Increased levels of fibrinogen have been recognized as an independent risk factor for both cardiovascular morbidity and mortality (Ernst and Reeh, 1993; Ridker, 1992). Fibrinogen was not reduced on a low-fat diet in a long-term study (Marckmann *et al*., 1993) or in a short-term study (Marckmann *et al*., 1991) have postulated that 10 study days or less may be too short for detection of effects on fibrinogen. During a 3-week study period, however, fibrinogen increased on a diet high in stearic acid compared with a diet high in myristic and lauric acid (Bladberg *et al*., 1995) There is no previous evidence of either total fat or fatty acid composition having an effect on circulating levels of fibrinogen (Freese and Mutanen, 1995) that was disagreement with present study. Our trial showed a decrease in serum fibrinogen following fat butter intake. We conclude that high saturated fat diet (butter) intake specially can be increase clotting factor (factorVII) and decrease BT and fibrinogen in short time for healthy individuals in lifelong but the had not effect on serum cholestrol and triglycerides.

## REFERENCES


Bladberg, E.M., P. Marckman, B. Sandstrom and J. Jespersen, 1994. Nonfasting Factor VII Coagulant activity (FVII:C) increased by high fat diet. Thromb Haemost, 71: 755-758.

Bladberg, E.M., T. Tholstrup, P. Marckmann, B.M. Sandström and J. Jespersen, 1995. Dietary changes in fasting levels of Factor VII Coagulant activity (FVII:C) are accompanied by changes in factor VII protein and other vitamin K-dependent proteins. Thromb Haemost, 73: 239-242.

Connelly, J.B., P.J. Roderick, J.A. Cooper, T.W. Meade, G.J. Miller, 1993. Positive association between self-reported fatty food consumption and factor VII coagulant activity, a risk factor for coronary heart disease, in 4246 middle-aged men. Thromb Haemost, 70: 250-252.

Ernst, E. and K.L. Resch, 1993. Fibrinogen as a cardiovascular risk factor: A meta-analysis and review of the literature. Ann. Int. Med., 118: 956-963.

Fair, D.S., 1983. Quantitation of factor VII in plasma of normal and warfarin-treated individuals by radioimmunoassay. Blood, 62: 784-791.

Freese, R. and M. Mutanen, 1995. Postprandial changes in platelet function and coagulation factors after high-fat meals with different fatty acid compositions. Eur. J. Clin. Nutr., 49: 658-664.

Heinrich, J., L. Balleisen and H. Schulte, G. Assmann and J. Van de Loo, 1994. Fibrinogen and factor VII in the prediction of coronary risk: Results from the PROCAM Study in healthy men. Arterioscler Thromb, 14: 54-59.

Kapur, R., C.J. Hoffman, V. Bhushan and M.B. Hultin, 1996. Postprandial elevation of activated factor VII in young adults. Arterioscler. Thromb. Vasc. Biol., 16: 1327-1332.

Kelleher, C.C., 1992. Plasma fibrinogen and factor VII as risk factors for cardiovascular disease. Eur. J. Epidemiol., 1: 79-82.

Khaw, K.T. and E. Barret-Connor, 1987. Dietary fiber and reduced ischemic heart disease mortality rates in men and women: A 12-year prospective study. Am. J. Epidemiol., 126: 1093-1102.

Kirsty, H.A., C.C. Lynn, A. Weir, G.J. Miller and A.K. Dutta-Roy, 2000. A residential study comparing the effects of diets rich in stearic acid, oleic acid and linoleic acid on fasting blood lipids, hemostatic variables and platelets in young healthy men. J. Nutr. Biochem., 11: 408-416.

Kromhout, D., E.B. Bosschieter and C.L. de Coulander, 1982. Dietary fibre and 10 year mortality from coronary heart disease, cancer and all causes: The Zutphen study. Lancet, II: 518-522.

Kushi, L.H., R.A. Lew, F.J. Stare, C.R. Ellison, M. ElLozy, G. Bourke, L. Daly, I. Graham, N. Hickey and R.R. Mulcahy, 1985. Diet and 20 year mortality from coronary heart disease: The Ireland-Boston Diet-Heart Study. N. Eng. J. Med., 312: 811-818.

Marckmann, P., 1995. Diet, blood coagulation and fibrinolysis. Dan. Med. Bull., 42: 410-425.

Marckmann, P., J. Jespersen, T. Leth and B.M. Sandström, 1991. Effect of fish diet versus meat diet on blood lipids, coagulation and fibrinolysis in healthy young men. J. Int. Med., 229: 317-323.

Marckmann, P., E.M. Bladberg and J. Jespersen, 1998. Diet and blood coagulation factor VIIa key protein in arterial thrombosis. Eur. J. Clin. Nutr., 52: 75-84.

Marckman, P., B. Sandstrom and J. Jespersen, 1990. Effects of total fat content and fatty acid composition in diet on factor VII coagulant activity and blood lipids. Atherosclerosis, 80: 227-233.

Marckmann, P., B.M. Sandström and J. Jespersen, 1993. Favorable long-term effect of a low-fat/high-fiber diet on human blood coagulation and fibrinolysis. Arterioscler Thromb, 13: 505-511.

Meade, T.W., S. Mellows, M. Brozovic, G.J. Miller, R.R. Chakrabarti and R.R. North *et al*., 1986. Haemostatic function and ischeamic heart disease: Principal results of the Northwick Park Heart Study. Lancet., 2: 533-537.

Mennen, L.I., E.G. Schouten, D.E. Grobbee and C. Kluft, 1996. Coagulation factor VII, dietary fat and blood lipids: A review. Thromb. Haemost, 76: 492-499.

Miller, G.J., J.C. Martin, K.A. Mitropoulos, B.E.A. Reeves, R.L. Thompson, T.W. Meade, J.A. Cooper and J.K. Cruickshank, 1991. Plasma factor VII is activated by postprandial triglyceridaemia, irrespective of dietary fat composition. Atherosclerosis, 86: 163-171.

Miller, G.J., J.C. Martin, J. Webster, H. Wilkes, N.E. Miller, W.H.Wilkinson and T.W. Meade, 1986. Association between dietary fat intake and plasma factor VII coagulant activity: A predictor of cardiovascular mortality. Atherosclerosis, 60: 269-277.

Miller, G.J., Y. Stirling, D.J. Howarth, J.C. Cooper, F.R. Green, A. Lane and S.E. Humphries, 1995. Dietary fat intake and plasma factor VII antigen concentration. Thromb. Haemost, 73: 893.

Mitropoulos, K.A., M.P. Esnouf and T.W. Meade, 1987. Increased factor VII coagulant activity in the rabbit following diet-induced hypercholesterolaemia: Evidence for increased conversion of VII to αVIIa and higher flux within the coagulation pathway. Atherosclerosis, 63: 43-52.

Mitropoulos, K.A., G.J. Miller, J.C. Martin, B.E.A. Reeves and J. Cooper, 1994. Dietary fat induces changes in factor VII coagulant activity through effects on plasma free stearic acid concentration. Arterioscler and Thromb, 14: 214-22.

Pearson, T.A., J. LaCava and H.F. Weil, 1997. Epidemiology of thrombotic-hemostatic factors and their associations with cardiovascular disease. Am. J. Clin. Nutr., 65: 1674-1682.

Ridker, P.M., 1992. An epidemiologic assessment of thrombotic risk factors for cardiovascular disease. Curr Opin Lipidol., 3: 285-290.

Scarabin, P.Y., L. Bara, M. Samama and G. Orssaud, 1985. Further evidence that activated factor VII is related to plasma lipids, Br. J. Haematol., 61: 186-187.

Silveira, A., F. Karpe, M. Blombäck, G. Steiner, G. Walldius and A. Hamsten, 1994a. Activation of coagulation factor VII during alimentary lipemia. Arterioscler Thromb, 14: 60-69.

Silveira, A., F. Green, F. Karpe, M. Blombäck, S. Humphries and A. Hamsten, 1994b. Elevated levels of factor VII activity in the postprandial state: Effect of the factor VII Arg-Gln polymorphism. Thromb Haemost, 72: 734-739.

Sanders, T.A.B., F.R. Oakley, J.A. Cooper and G.J. Miller, 2001. Influence of a stearic acid-rich structured triacylglycerol on postprandial lipemia, factor VII concentrations and fibrinolytic activity in healthy subjects. Am. J. Clin. Nutr., 73: 715-721.

Sanders, T.A., G.J. Miller, T. de Grass and N. Yahia, 1996. Postprandial activation of coagulant factor VII by long-chain dietary fatty acids. Thromb Haemost, 76: 369-371.

Sanders, T., 1996. Effects of unsatuarated fatty acids on blood clotting and fibrinolysis. Curr. Opin. Lipidol., 7: 20-23.

Poppitt, S.D., G.F. Keogh, T.B. Mulvey, B.H. McArdle, A.K.H. MacGibbon and G.J.S. Cooper, 2002. Lipid-lowering effects of a modified butter-fat: A controlled intervention trial in healthy men. Eur. J. Clin. Nutr., 56: 64-71.

Tholstrup, T.M. Raff, S. Basu, P. Nonboe, K. Sejrsen and E.M. Straarup, 2006. Effects of butter high in ruminant trans and monounsaturated fatty acids on lipoproteins, incorporation of fatty acids into lipid classes, plasma C-reactive protein, oxidative stress, hemostatic variables and insulin in healthy young men. Am. J. Clin. Nutr., 83: 237-243.