Carbohydrate Polymers **21** (1993) 189–194

Cereal dietary fibers affect post-prandial lipoproteins in healthy human subjects

Christophe Dubois,[a] Louis Cara,[a] Patrick Borel,[a] Martine Armand,[a] Michele Senft,[a] Henri Portugal,[b] Pierre-Marie Bernard,[c] Huguette Lafont[a] & Denis Lairon[a]

[a]*Unité 130-INSERM (National Institute of Health and Medical Research), 18 Av. Mozart, 13009 Marseille, France*
[b]*Laboratoire central d'analyse, Hôpital Ste Marguerite, Marseille, France*
[c]*Service de médecine interne et endocrinologie, Hôpital Ste Marguerite, Marseille, France*

Normolipidemic males (six) ingested on separate days a low-fiber (2·8 g) test-meal (70 g fat, 0·75 g cholesterol), enriched or not with 10 g dietary fiber in the form of either oat bran, rice bran or wheat fiber or 4·2 g fiber as wheat germ. Fasting and post-meal blood samples were obtained for 7 h. Chylomicrons, VLDL, LDL and HDL were isolated from the baseline samples and the samples of the 2–3 h triglyceride peak. Chylomicron triglycerides were significantly ($p \leq 0{\cdot}05$) reduced with wheat fiber. All fiber sources reduced chylomicron cholesterol. VLDL lipid components were not markedly changed. LDL cholesterol decreased post-prandially and this was reversed after adding oat bran and wheat germ. HDL triglycerides were unchanged but the post-prandial HDL cholesterol decrease was significantly amplified after adding oat bran and wheat germ. In conclusion, dietary fiber-rich fractions from cereals can alter post-prandial lipoproteins in humans to a variable extent.

INTRODUCTION

The long-term beneficial effects of some cereal dietary fiber-rich fractions on lipid metabolism have been well documented (Anderson & Tietyen-Clark, 1986; Jenkins *et al.*, 1986; Kritchevsky & Story, 1986). It is likely that dietary fibers could basically exert some effects on cholesterol and triglyceride metabolism, either by altering dietary fat and cholesterol processing, or by increasing sterol and bile salt fecal excretion, or by changing some hormone profile, thus altering the post-prandial lipoprotein pattern. Another possibility is that dietary fibers should influence endogenous lipid synthesis, possibly due to the metabolic effects of some colon fermentation end-products such as short-chain fatty acids. All these possibilities could occur and have gained some experimental support (Anderson & Tietyen-Clark, 1986; Jenkins *et al.*, 1986; Kritchevsky & Story, 1986). However, the relative importance of these possible mechanisms has not yet been elucidated.

In this context, we aimed to study whether cereal dietary fiber-rich fractions affect post-prandial lipemia and lipoproteins. It seems important to study post-prandial lipemia and lipoproteins to elucidate some mechanisms but also because over a 24 h period, most of the time is usually spent in the post-prandial state (Patsch *et al.*, 1983; Cohn *et al.*, 1988*a*; Cara *et al.*, 1992*a*). The effects of cereal dietary fibers on post-meal lipemia have already been reported (Cara *et al.*, 1992*a*). The present work was dedicated to studying the effects of oat bran, rice bran, wheat fibers and wheat germ on post-prandial lipoproteins in healthy human subjects.

SUBJECTS AND METHODS

The detailed protocol of the study has been previously reported (Cara *et al.*, 1992*a*).

Subjects

Six adult male volunteers participated in the double-blind study after giving an informed consent to a protocol approved by the local Medical Ethics Committee. Their fasting blood concentrations of cholesterol (4·11–5·20 mmol/liter), triglycerides (0·62–

Carbohydrate Polymers 0144-8617/93/$06.00

1·04 mmol/liter), glucose (4·48–5·50 mmol/liter) and insulin (25·1–85·7 pmol/liter) were in the normal range. None were obese or diabetic.

Test-meals

The interval between two test-meals was 7–15 days. The control low-fiber test-meal consisted of commercially available food, i.e. bread (50 g), pasta (50 g), tomato sauce (100 g) with sunflower oil (20 g), two hard-boiled eggs (140 g), butter (25 g), one yoghurt (125 ml), black coffee (150 ml) and water (100 ml). The control test-meal contained 70 g fat, 756 mg cholesterol and 2·8 g total dietary fibers. Energy (1280 kcal) was supplied by proteins (12·7%), carbohydrates (37·9%) and fat (49·4%).

To prepare the fiber-enriched test-meals, four different cereal sources of dietary fibers were incorporated in the tomato sauce. They were either wheat fiber (processed wheat bran containing 80% total dietary fiber) from ARD (Paris, France), wheat germ (Diepal, Villefranche/Saône, France), oat bran (Westhove, Arques, France) or rice bran (Rizerie du Petit Manusclat, Arles, France). All cereal sources used were ground to pass a 200 μm sieve. Ten grams of total dietary fibers were added to the test-meal in the form of either wheat fiber (12·5 g), oat bran (40 g) or rice bran (39·4 g), and 4·2 g in the form of wheat germ (40 g). These cereal fractions contained 20·0%, 51·4%, 11·6% and 11·9% total fibers in the form of soluble fibers, respectively.

After an overnight fast, in the morning, an antecubital vein was catheterized with an intravenous cannula equipped with disposable obturators. The subjects ingested the test-meal within 20 min. Blood samples were collected before the meal and every half-hour for 5 h and then 6 and 7 h after the meal.

Analytical determinations

Serum was separated from whole blood by centrifugation (4°C, 10 min, 910 g). Triglycerides (Buccolo & David, 1973), total and free cholesterol (Stahler *et al.*, 1973) and phospholipids (Takayama *et al.*, 1977) were assayed in all samples. Fasting samples and pooled aliquots of the three serum samples displaying the highest triglyceride concentrations (1·5–3 h post-prandial peak) were used for separation of lipoprotein fractions and for determination of apoproteins. Chylomicrons were isolated by ultracentrifugation at 10°C for 1 h at 27 000*g* in a Beckman 40·3 rotor (Cara *et al.*, 1992*a*). VLDL, LDL and HDL were quantitatively separated by ultracentrifugation on a KBr discontinuous density gradient (200 000*g*, 15°C, 24 h, SW 41 Ti rotor). Lipids were assayed as above for serum samples. Total serum ApoA1 and ApoB were assayed by immuno-nephelometry as reported elsewhere (Cara *et al.*, 1992*a*).

Statistical analysis

In this double-blind, randomized study, each subject was his own control. The values (mean ± SEM of six determinations) are expressed as variations of concentration over baseline. The statistical significance ($p \leqslant 0{\cdot}05$) of the differences observed between a fiber-enriched meal and the control test-meal was assessed by using Student's t test for paired values.

RESULTS

As previously reported (Cara *et al.*, 1992*a*), the addition of fibers to the test-meal did not markedly change the post-prandial variations in blood glucose and insulin concentrations.

Post-prandial triglyceride variations

Post-prandial triglyceride variations exhibited a 0–7 h bell-shaped curve with a maximum at 2–2·5 h (Cara *et al.*, 1992*a*). As shown in Fig. 1, the addition of wheat fiber, oat bran and rice bran significantly decreased the maximum post-prandial triglyceride concentration. As expected, the triglycerides secreted post-prandially into the serum mainly originated from chylomicrons (mean of five meals: 88·2%). Adding various dietary fibers did not markedly change the maximum chylomicron triglyceride concentration, although the 0–7 h area under the curve was significantly reduced in the presence of wheat fiber (Cara *et al.*, 1992*a*). Very low density lipoprotein (VLDL) triglycerides markedly increased post-prandially after the control test-meal. The addition of wheat fiber to the test-meal significantly reduced (−49·6%) the maximum post-prandial VLDL triglyceride concentration, whereas adding all other fiber sources only tended to lower this value. The post-prandial changes in the triglycerides transported in the form of low density lipoproteins (LDL) and high density lipoproteins (HDL) were very limited. Nevertheless, the addition of oat bran or rice bran to the test-meal significantly reduced the maximum LDL triglyceride concentrations. The HDL triglycerides were unchanged post-prandially.

Post-prandial cholesterol variations

As previously described in detail (Cara *et al.*, 1992*a*), cholesterolemia significantly decreased 1 h after the test-meal ingestion and remained low for the next 5 h. This is also observed herein (Fig. 2) for the serum cholesterol concentration measured at the maximum of the post-prandial triglyceride rise. Among the cereal fibers tested, only oat bran significantly amplified the post-prandial cholesterolemia decrease. The post-prandial decrease in the serum total cholesterol con-

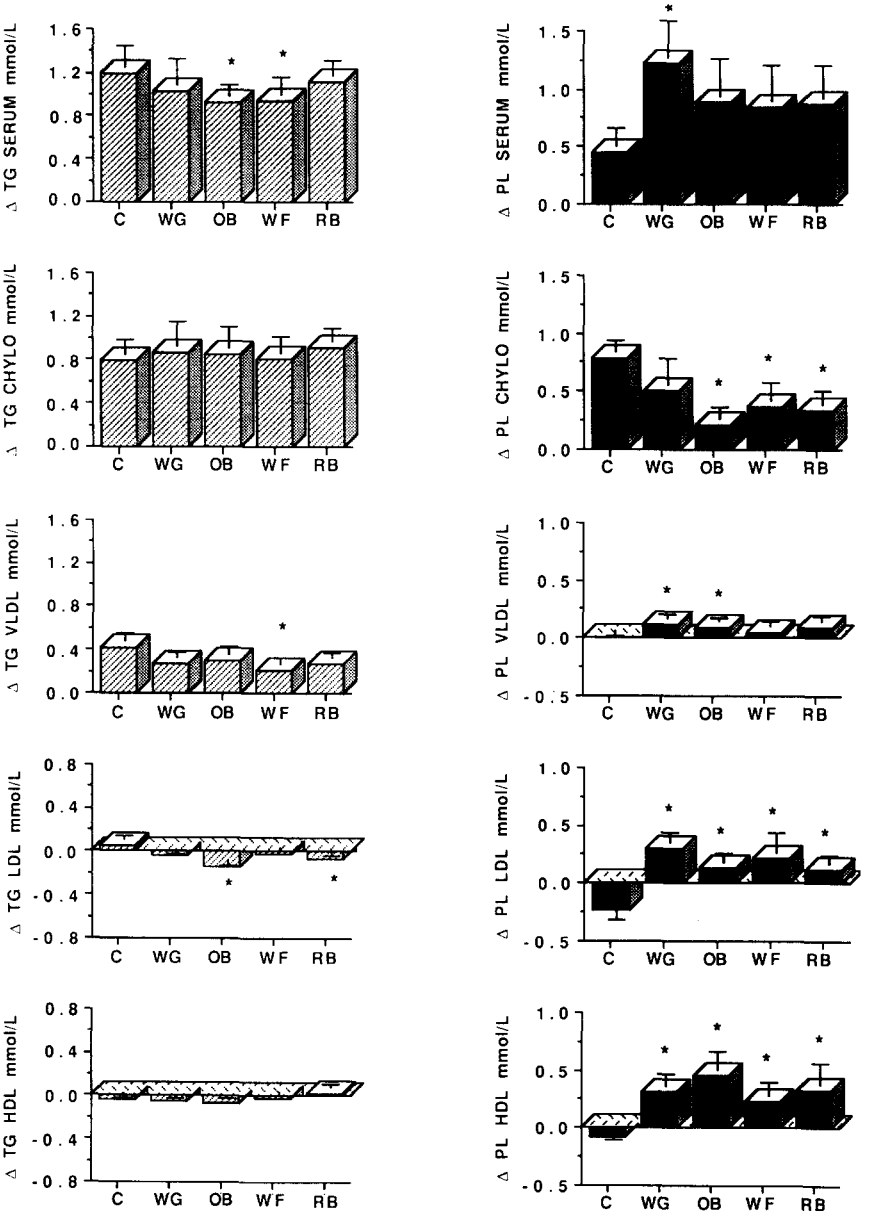

Fig. 1. Left column: triglyceride concentration change from fasting value (Δ). Right column: phospholipid concentration change from fasting value (Δ). Values are means ± SEM for six subjects. A significant difference ($p \leqslant 0{\cdot}05$) between a fiber-enriched meal (WG: wheat germ; OB: oat bran; WF: wheat fiber; RB: rice bran) and the control test-meal (C) is marked by an asterisk. Chylo: chylomicrons; VLDL: very low density lipoproteins; LDL: low density lipoproteins; HDL: high density lipoproteins.

centration was basically due to a decrease in serum esterified cholesterol and resulted from variations in different lipoprotein fractions (Fig. 2). After the intake of the control test-meal, a marked increase in the chylomicron cholesterol concentration occurred. Compared to the control low-fiber test-meal, all fiber sources tested significantly decreased the maximum chylomicron total cholesterol concentration but not the esterified fraction. The VLDL total and esterified cholesterol concentrations slightly decreased post-prandially and this pattern was not changed in the presence of dietary fibers. The LDL total and esterified cholesterol concentrations markedly decreased after ingestion of the control test-meal. This was observed to a comparable extent when supplementing the test-meal with wheat fiber or rice bran. A significantly different positive variation in total cholesterol and a markedly reduced decrease in esterified cholesterol were observed after adding oat bran or wheat germ. The HDL total and esterified cholesterol concentrations slightly decreased after ingestion of the control test-meal. This pattern was unchanged after adding wheat fiber or rice bran. Conversely, the addition of wheat germ, and more markedly oat bran, significantly amplified the

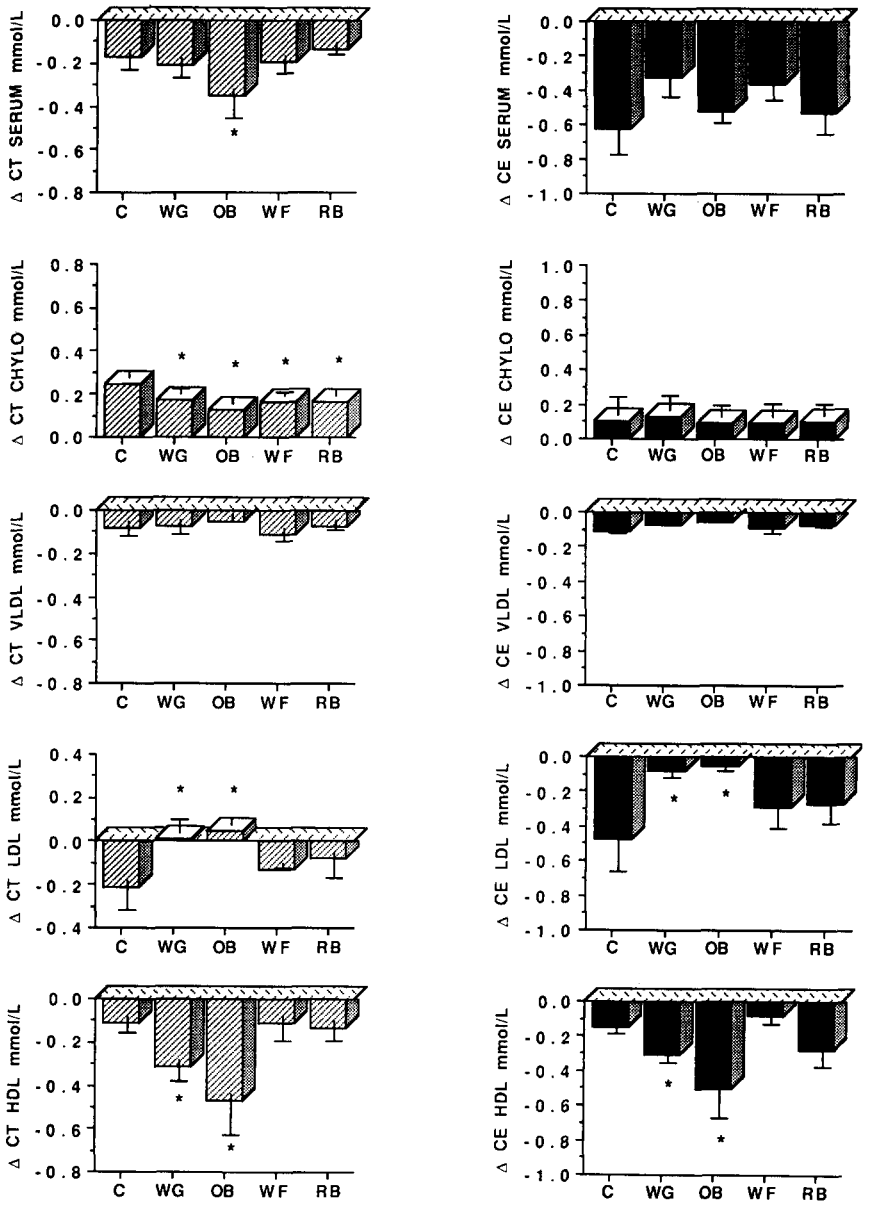

Fig. 2. Left column: total cholesterol concentration change from fasting value (Δ). Right column esterified cholesterol concentration change from fasting value (Δ). Values are means ± SEM for six subjects. A significant difference ($p \leqslant 0{\cdot}05$) between a fiber-enriched meal (WG: wheat germ; OB: oat bran; WF: wheat fiber; RB: rice bran) and the control test-meal (C) is marked by an asterisk. Chylo: chylomicrons; VLDL: very low density lipoproteins; LDL: low density lipoproteins; HDL: high density lipoproteins.

post-prandial decrease in the HDL total and esterified cholesterol concentrations. The extent of these variations was very large.

Post-prandial phospholipid variations

As shown in Fig. 1, the serum phospholipid concentration increased post-prandially. Only wheat germ addition significantly raised the value obtained after the control test-meal. The phospholipid concentration in chylomicrons increased post-prandially but with a lesser amplitude in the case of oat bran, wheat fiber and rice bran. VLDL phospholipids were significantly increased after addition of oat bran and wheat germ. After the control test-meal, LDL phospholipids decreased and this was reversed after addition of all the fiber sources tested. Comparable significant changes were observed with HDL phospholipids but to a greater extent, especially after addition of oat bran.

DISCUSSION

In addition to the data previously reported on 0–7 h post-prandial lipemia (Cara *et al.*, 1992*a*), the results obtained herein demonstrate that some cereal dietary

fibers alter the post-prandial lipoprotein pattern in healthy human subjects. Such changes were not observed during another study performed in healthy males and females with a test-meal supplemented with a mixture of guar gum and oat bran (Redard *et al.*, 1990).

Lipoprotein lipase and hepatic lipase activities have not been determined herein, but it is unlikely that these values markedly changed since only dietary fibers were added to the test-meal.

The first modification was observed in the chylomicrons originating from the small intestine. The dietary fiber sources tested generally lowered chylomicron phospholipids and free cholesterol (and triglycerides in the case of wheat fibers), thus suggesting that the chylomicron surface components have been particularly altered. This also suggests that these fiber sources may have reduced the amount of cholesterol absorbed and/or secreted by the small intestine and mainly transported by chlomicrons.

As for chylomicrons, VLDL triglycerides markedly increased post-prandially and adding fibers to the test-meal tended to reduce (or significantly reduced with wheat fibers) this rise. Since no marked change was observed for the variations in VLDL cholesterol and phospholipid concentration or total ApoB (Cara *et al.*, 1992*a*), it seems that VLDL particles were not profoundly affected by adding fibers to the meals, except in the case of wheat fibers.

The magnitude of LDL triglyceride changes was very low but the variations in LDL total and esterified cholesterol concentrations were much more marked; the drop observed post-prandially was reversed (or suppressed) when supplementing the control test-meal with wheat germ or oat bran. At the same time, the LDL phospholipid concentration increased. Since total ApoB was unchanged (Cara *et al.*, 1992*a*), we can assume that LDL particles were enriched in cholesterol esters and phospholipids in these cases.

After the ingestion of the control test-meal, the HDL total and esterified cholesterol were lower than in the fasting state, in agreement with others (Patsch *et al.*, 1983; Cohn *et al.*, 1988*a*, *b*). HDL triglycerides and phospholipids and ApoA1 (Cara *et al.*, 1992*a*) concentrations only tended to slightly lower values. This was not changed (except for phospholipids) after adding rice bran or wheat fiber to the meal. Conversely, the addition of wheat germ or oat bran drastically changed this pattern. HDL triglycerides were unchanged but total and esterified cholesterol significantly dropped while phospholipids markedly increased. With oat bran supplementation, the post-prandial ApoA1 concentration decreased more markedly than with the control meal ($-17{\cdot}4$ vs $-7{\cdot}6\%$; Cara *et al.*, 1992*a*). Thus, the addition of oat bran or wheat germ to the test-meal markedly altered the composition of HDL particles and probably the HDL2/HDL3 ratio (Patsch *et al.*, 1983). The depletion of HDL in esterified cholesterol was previously shown post-prandially (Patsch *et al.*, 1983; Cohn *et al.*, 1988*a*) and can be explained by the CETP-mediated transfer of esterified cholesterol from HDL (especially HDL2) to triglyceride-rich particles (Tall, 1986). In fact, in the case of oat bran and wheat germ, the HDL cholesterol markedly decreased while the relative (VLDL + LDL) esterified cholesterol was markedly enhanced ($-0{\cdot}15$–$0{\cdot}30$ vs $0{\cdot}70$ mmol/liter). The post-prandial variations in HDL cholesterol esters were negatively correlated to those of LDL cholesterol esters ($r = 0{\cdot}78$, $p \leqslant 0{\cdot}05$). A first possibility is that the reduced chylomicron cholesterol concentration induced by some fibers has led to a reduced post-prandial transfer of surface components such as free cholesterol and phospholipids, from chylomicrons to HDL particles. In fact, the post-prandial variations in HDL phospholipids were negatively corelated to those of chylomicron phospholipids ($r = -0{\cdot}93$). This was also observed for the variations of total cholesterol ($r = -0{\cdot}61$) but not for cholesterol esters ($r = -0{\cdot}07$). The decrease in post-prandial HDL cholesterol concentration observed with oat bran and wheat germ cannot be explained by the inverse relationship previously found between post-prandial triglyceridemia and HDL cholesterol (Patsch *et al.*, 1983), since post-meal triglyceridemia did not increase in these cases. A second explanation could be that the cholesterol turnover from HDL markedly increased after oat bran and wheat germ supplementation. This could be related to the fact that HDL cholesterol serves as a preferential precursor for bile acid synthesis in the liver (Gregg-Halloran *et al.*, 1978; Esnault-Dupuy *et al.*, 1987) and cholesterol secretion in bile (Schwartz *et al.*, 1978), and that some studied sources of dietary fibers increase bile acids or sterol excretion (Bosaeus *et al.*, 1986; Anderson & Gustafson, 1988; Cara *et al.*, 1991*a*). This could occur during the first and second hour after meal intake, following gall bladder emptying and bile salt reabsorption from the intestine.

In conclusion, from the present data it is evident that in healthy human subjects, oat bran and wheat germ markedly affect post-prandial lipoproteins. It is noteworthy that among the fiber sources tested, oat bran (Anderson & Tietyen-Clark, 1986; Anderson & Gustafson, 1988; Anderson *et al.*, 1990; Kestin *et al.*, 1990) and wheat germ (Lairon *et al.*, 1987; Cara *et al.*, 1991*b*, 1992*b*) display documented hypocholesterolemic effects after chronic intake in human subjects. Thus, we can point out that long-term effects of dietary fibers on lipid metabolism can basically originate from an alteration of lipemia and lipoproteins in the post-prandial state.

REFERENCES

Anderson, J.W. & Gustafson, N.J. (1988). *Am. J. Clin. Nutr.*, **48**, 749.

Anderson, J.W. & Tietyen-Clark, J. (1986). *Am. J. Gastroenterol.*, **81,** 907.
Anderson, J.W., Spencer, D.B., Hamilton, C.C., Smith, S.F., Tietyen, J., Bryant, C.A. & Oeltgen, P. (1990). *Am. J. Clin. Nutr.*, **52,** 661.
Bosaeus, I., Carlsson, N.G., Sandberg, A.S. & Andersson H. (1986). *Hum. Nutr.: Clin. Nutr.*, **40C,** 429.
Buccolo, G. & David, H. (1973). *Clin. Chem.*, **19,** 476.
Cara, L., Borel, P., Armand, M., Senft, M., Riottot, M., Ferezou, J. & Lairon, D. (1991*a*). *Nutr. Res.*, **11,** 907.
Cara, L., Borel, P., Armand, M., Senft, M., Lafont, H., Portugal, H., Pauli, A.M., Boulze, D., Lacombe, C. & Lairon, D. (1991*b*). *Plant. Food. Hum. Nutr.*, **41,** 135.
Cara, L., Dubois, C., Borel, P., Armand, M., Senft, M., Portugal, H., Pauli, A.M., Bernard, P.M. & Lairon, D. (1992*a*). *Am. J. Clin. Nutr.*, **55,** 81.
Cara, L., Armand, M., Borel, P., Senft, M., Portugal, H., Pauli, A.M., Lafont, H. & Lairon, D. (1992*b*). *J. Nutr.*, **122,** 317.
Cohn, J.S., McNamara, J.R., Cohn, S.D., Ordovas, J.M. & Schaeffer, E.J. (1988*a*). *J. Lipid Res.*, **29,** 469.
Cohn, J.S., McNamara, J.R., Cohn, S.D., Ordovas, J.M. & Schaeffer, E.J. (1988*b*). *J. Lipid Res.*, **29,** 925.
Esnault-Dupuy, C., Chanussot, F., Lafont, H., Chabert, C. & Hauton, J. (1987). *Biochimie,* **69,** 45.
Gregg-Halloran, L., Schwartz, C.C., Vlahcevic, Z.R., Gregory, D.H. & Swell, L. (1978). *Surgery,* **84,** 1.
Jenkins, D.J.A., Rainey-McDonald, C.G., Jenkins, A.L. & Benn, G. (1986). In *CRC Handbook of Dietary Fiber in Human Nutrition,* ed. G.A. Spiller. CRC Press, Boca Raton, FL, pp. 327–44.
Kestin, M., Moss, R., Clifton, P.M. & Nestel, P.J. (1990). *Am. J. Clin. Nutr.*, **52,** 661.
Kritchevsky, D. & Story, J.A. (1986). In *CRC Handbook of Dietary Fiber in Human Nutrition,* ed. G.A. Spiller. CRC Press, Boca Raton, FL, pp. 129–42.
Lairon, D., Lacombe, C., Borel, P., Corraze, G., Nibbelink, M., Chautan, M., Chanussot, F. & Lafont, H. (1987). *J. Nutr.*, **117,** 838.
Patsch, J.J., Karlin, J.B., Scott, L.W. & Smith-Gotto, A.M. (1983). *Proc. Natl. Acad. Sci.*, **80,** 1449.
Redard, C.L., Davis, P.A. & Schneeman, B. (1990). *Am. J. Clin. Nutr.*, **52,** 837.
Schwartz, C.C., Hallogran, L.G., Vlahcevic, Z.R., Gregory, D.H. & Swell, L.L. (1978). *Science,* **200,** 62.
Stahler, F., Gruber, W., Stinshoff, K. & Roschla, P. (1973). *Med. Lab.*, **30,** 29.
Takayama, M., Itoh, S., Nagasaki, T. & Tanimizu, I. (1977). *Clin. Chim. Acta,* **79,** 93.
Tall, A.R. (1986). *J. Lipid Res.*, **27,** 361.