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Oxygen radicals, lipid peroxidation and the coagulation system

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Lipid peroxidation is an oxidative fragmentation of unsaturated lipids which can proceed by controlled enzymic steps or as an uncontrolled radical chain reaction. Products of lipid peroxidation include numerous primary peroxides which, in the presence of suitable transition metal catalysts, decompose to give oxygen radicals and secondary carbonyl compounds. Oxygen radicals can cause molecular damage and both peroxides and aldehydes, in nanomolar concentrations, possess potent biological activities.

Tissue damage leading to degenerative disease processes can be caused by increased peroxide formation and decomposition. However, in most cases increased peroxide formation and decomposition may only reflect the consequences of enhanced tissue damage. Products resulting from the autoxidation of polyunsaturated fatty acids have been shown to promote thrombin generation in platelet-poor plasma [1], an activity enhanced by their inhibitory action on antithrombin III [2]. These autoxidation products act on plasma triglyceride-rich lipoproteins, especially chylomicra of dietary origin, to produce the procoagulant activity [3]. Thus, the products of lipid peroxidation, which may arise as a consequence of tissue damage, can themselves lead to the initiation of degenerative disease processes.

In the present study, we have focussed on the procoagulant activity of the phospholipid fraction of chylomicra.

Injections of heparin or pentosan polysulphate, drugs which release lipoprotein lipase (LPL) and hepatic triglyceride lipase (HTGL), into healthy volunteers, resulted in a 50% fall in lipid peroxide-induced thrombin generation. *In vitro* addition of purified HTGL gave a similar reduction, but LPL had little effect. HTGL has a strong phospholipase activity, and incubation of fatty plasma or isolated chylomicra with phospholipase A_2 or phospholipase C markedly reduced their procoagulant activity.

These results suggest that the phospholipid fraction of chylomicra is responsible for the procoagulant activity, and this was confirmed by isolation of the phospholipids from chylomicra by organic solvent extraction or freeze/thawing. Table 1 shows the results of an experiment in which the surface coat was separated by centrifugation from the core material after repeated freeze/thawing. The surface coat fraction contained virtually all the phospholipid and all the procoagulant activity.

Table 1
Phospholipid content and procoagulant activity of core and coat materials, isolated from chylomicra.

	Phospholipid %	Procoagulant activity %
Chylomicra	100	100
Core material	5	7
Surface coat	95	87

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