Differential effect of 3-hydroxy-3-methylglutarylcoenzyme A reductase inhibitors on plasma paraoxonase 1 activity in the rat.

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Statins (3-hydroxy-3-methylglutarylcoenzyme A reductase inhibitors), apart from lowering plasma cholesterol, modulate other processes involved in atherogenesis. The aim of this study was to investigate the effect of a natural statin, pravastatin, and of the synthetic one, fluvastatin, on plasma paraoxonase 1 (PON1), the antioxidant enzyme contained in plasma high-density lipoproteins. The adult male Wistar rats received either pravastatin (4 or 40 mg/kg/day) or fluvastatin (2 or 20 mg/kg/day) for 3 weeks. Then, plasma PON1 activity, lipid peroxidation products and total antioxidant capacity were assayed. Fluvastatin at a dose of 20 mg/kg/day decreased paraoxon-hydrolyzing activity of PON1 by 23.6% and its phenyl acetate-hydrolyzing activity by 17.4%. Lower dose of this drug as well as either dose of pravastatin had no effect on these activities. Fluvastatin at doses of 2 and 20 mg/kg/day decreased γ-decanolactone-hydrolyzing activity of plasma by 19.1% and 30.9%, respectively. Statins had no effect on either total or HDL-cholesterol but markedly reduced plasma triglycerides. Fluvastatin had a more marked antioxidant activity, as evidenced by significant reduction of plasma concentration of malonyldialdehyde + hydroxydialkenals and lipid hydroperoxides, as well as by elevation of total plasma antioxidant capacity and plasma concentration of reduced sulphydryl groups. These results suggest that fluvastatin but not pravastatin decreases plasma PON1 activity in normolipidemic rats, however, the former drug is more effective in reducing the level of oxidative stress.

Key words: pravastatin, fluvastatin, paraoxonase, lipid peroxidation, oxidative stress

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