OXIDATION OF FISH LIPIDS DURING GASTROINTESTINAL IN VITRO DIGESTION

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ABSTRACT

Fish and many other marine organisms, contain long chain n-3 polyunsaturated fatty acids (LC n-3 PUFA), e.g. eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). EPA and DHA has shown beneficial effects in diseases related to inflammatory processes, such as cardiovascular diseases. Unfortunately, PUFA are prone to oxidation generating reactive oxidation products. Among them, malondialdehyde (MDA), 4-hydroxy-2-hexenal (HHE) and 4-hydroxy-2-nonenal (HNE), form adducts with proteins and DNA, which may impair functions of the cell. A series of earlier studies have revealed that oxidation of lipid containing foods like meat does not only take place during process and storage, but also during gastric conditions. Here, we hypothesized that digestion of the highly unsaturated marine lipids may therefore lead to increased levels of reactive oxidation products, which could counteract the documented positive effects of LC n-3 PUFA. The overall aim of this study was to investigate whether fish and fish oil oxidize during gastrointestinal (GI) *in vitro* digestion; what is causing this oxidation, what levels of oxidation products can be formed and what cellular impact oxidized digests, with varying amounts of oxidation products, can possess.

Presence of digestive enzymes and bile, particularly the latter, was decisive for the stepwise formation of aldehydes during GI digestion of cod liver oil. Oils containing different amounts of preformed lipid oxidation products maintained the same oxidation ranking order during static and dynamic digestion, even though the relative changes were not directly proportional to the initial oxidation level. Adding hemoglobin to emulsified oil strongly promoted GI oxidation. During dynamic digestion of raw herring mince and isolated herring oil (bulk or emulsified), aldehyde levels of gastric lumen ranked the samples as: raw mince >> emulsified oil > bulk oil. Herring mince with a lipid content of 17% generated higher aldehyde levels than herring mince with 4% lipids, and both herring minces formed higher aldehyde concentrations than raw salmon mince with 17% lipids. A high content of pro-oxidative heme-proteins and more preformed oxidation products of the herring mince, in combination with the antioxidative carotenoids of salmon are suggested explanations. Oven baking the fish had a slight pro-oxidative effect on GI oxidation. Maximum levels of non-protein bound MDA, HHE and HNE determined during dynamic digestion of fish lipids in this study were 27 µM, 1.6 µM and 0.07 µM, respectively.

Intracellular oxidation and cell energy metabolic activity were elevated in yeast (*Saccharomyces cerevisiae*) cells exposed to cod liver oil digests, compared to digested blanks. Also, proteins related to energy metabolism and oxidative stress response were differentially expressed in the presence of digested oils compared to digested blank. The presence of oil digests also affected both the maturation of dendritic cells and the ratio of secreted cytokines (IL-12p40/IL10), which suggest a pro-inflammatory effect. In conclusion, reactive aldehydes are formed during GI *in vitro* digestion of fish lipids, which may counteract the anti-inflammatory properties of LC n-3 PUFA. Fish lipids of good quality and inclusion of antioxidants to the meal may repress the formation of aldehydes during digestion.