Oxidized nucleic acids as components potentially responsible for carcinogenic properties of thermally processed red meat

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Introduction: Processed red meat is classified by the International Agency for Research on Cancer to the Group 1 - "carcinogenic to humans"[1]. Several modified components may be formed during thermal processing of meat that are proposed as being involved in the process of carcinogenesis. Those are: heterocyclic amines, N-nitroso compounds, polycyclic aromatic hydrocarbons, lipid and protein oxidation products [2]. The formation of some of them is partly explained by oxidative properties of heme iron in red meat [2]. However, another type of molecules that may undergo oxidative modification in the presence of lipids and heme iron are nucleic acids. Some indications reinforce the conviction that addressing this trope is justified. One of them is increased availability of MTH1 enzyme in the alimentary tract [3]. The role of this protein is to hydrolyse oxidized purines and therefore it works as a natural protection against their incorporation into host's DNA. This study checked if there are grounds for assuming that oxidized nucleic acids may arise during heat treatment and may contribute to the carcinogenic properties of processed red meat.

Materials and methods: The oxidation of DNA isolates (50-100 bp) was carried out in the presence of bovine methaemoglobin as a source of heme iron and phospholipids which are main prone to oxidation lipid components of cellular membranes. Both methaemoglobin and phospholipids are abundant components of red meat. Additionally, to accelerate the induction of oxidation of DNA and phospholipids, ascorbic acid was added in some experiments. Ascorbic acid is an antioxidant used by meat industry, however it is also known to maintain Fe^{2+} level thereby to promote Fenton reaction producing ROS. The kinetics of the phospholipids oxidation reaction and the influence of different concentrations of DNA on it was followed spectrophotometrically.

Results: Preliminary experiments have shown that lower concentrations of DNA (up to 0.1 mg/mL in reaction mixture) seem to accelerate the kinetics of phospholipid oxidation. Addition of ascorbic acid further increased oxidation rate. In contrast, higher concentrations of DNA (0. 25 – 0.50 mg/mL) seem to prevent oxidation of phospholipids as indicated by lowered, almost inhibited, rate of methaemoglobin oxidation.

Conclusions: Nucleic acids exhibited high susceptibility to oxidation in the presence of heme iron. There is a risk that mechanisms protecting against their harmful effects (e.g. MTH1 activity) may not be sufficient if the amount of oxidized nucleic acids is significantly increased. The incorporation of oxidatively modified nucleotides released upon digestion may initiate mutations and impair epigenetic mechanisms. Considering the prooxidative role of ascorbic acid and susceptibility of nucleic acids to oxidation, more attention should be paid to properly design composition of meat products so as to protect their ingredients against excessive oxidation. Altogether, our results could be considered as the first step in the investigations of possible contribution of oxidised nucleic acids to the carcinogenicity of processed red meat.

Literature:

1. Domingo, J. L., & Nadal M. (2017) Carcinogenicity of consumption of red meat and processed meat: A review of scientific news since the IARC decision. Food and Chemical Toxicology, 105, 256-261
2. Chiang, V. S.-C., & Quek, S.-Y. (2017) The relationship of red meat with cancer: Effects of thermal processing and related physiological mechanisms. Critical Reviews in Food Science and Nutrition, 57(6), 1153-1173
3. Kakuma, T., Nishida, J., Tsuzuki T., & Sekiguchi, M. (1995) Mouse MTH1 Protein with 8-Oxo-7,8-dihydro-2'-deoxyguanosine 5'-Triphosphatase Activity That Prevents Transversion Mutation. The Journal of Biological Chemistry, 270(43), 25942–25948