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Nitrates, Nitrites and Nitrosamines from Processed Meat Intake and Colorectal Cancer Risk

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Abstract

The International Agency for Research on Cancer reported that eating processed meat can increase a person's risk for colorectal cancer and classified processed meat as carcinogenic to humans. Nitrate and nitrite are used as additives to improve food quality and protect against microbial contamination and are sources of N-nitroso compounds (NOCs) which are known carcinogens. This review outlines the association between processed meat intake and colorectal cancer risk and discusses the use of nitrates and nitrites in processed meat as well as healthier alternatives. A wide range of factors affect the formation of NOCs including the amount of nitrite added, meat quality, fat content, processing, maturation and handling at home. Factors related to processing include additives, precursors (added *via* wood smoke, spices or other ingredients), heat applied during drying or smoking, storage/maturation conditions and packaging. NOC formation can be inhibited by the addition of ascorbic acid and α-tocopherol ingredients which are often added to processed meats. Studies have shown that plant polyphenols and alpha-tocopherol significantly decreased pH, lipid oxidation and residual nitrite content of processed meat. Plant polyphenols, especially green tea polyphenols can be used as alternatives to nitrates and nitrites to process meat improving the quality, shelf life and safety of processed meat products. These innovative meat products could potentially contribute to a reduction in cancer risk by means of nitrite reduction and phytochemical addition and should be explored further.

Keywords: Colorectal cancer; Nitrosamines; Processed meat

Introduction

Processed meat and colorectal cancer

The International Agency for Research on Cancer (IARC) recently reported that eating processed meat can increase a person's risk for colorectal cancer [1] and classified processed meat as carcinogenic to humans (Group1) based on sufficient evidence from epidemiological studies. It was estimated that each 50 g portion of processed meat eaten daily (approximately 2 bacon rashers), increased colorectal cancer risk by 18 per cent [1]. Subsequent publications have confirmed these findings. For example, a meta-analysis as part of the World Cancer Research Fund International Continuous Update Project (WCRF-CUP) confirmed a positive dose-response between intake of processed meat and colorectal cancer risk with an overall 12% increased risk of colorectal cancer for each 100 g/day increase of processed meat intake, although there was large variation found (95% CI = 4-21%) and a high degree of heterogeneity between study findings (I2=70%, p heterogeneity <0.01) [2]. One of the proposed mechanisms whereby processed meat can increase colorectal cancer is the formation of N-nitrosamines (NOC), which result from the reaction between a nitrosating agent, originating from nitrate (NO3)/nitrite (NO2) or smoke and a secondary amine, derived from protein [3].

The WCRF defined processed meat as meat which has been smoked, cured or had salt or chemical preservatives added rather than having just been cooked or reformed (like most sausages and burgers). This includes bacon, salami, chorizo, corned beef, pepperoni, pastrami, hot dogs and all types of ham.

Experimental

Nitrate, nitrite and nitrosamines

Nitrite and nitrate are used as additives to improve food quality and protect against microbial contamination. Nitrate and nitrite from processed meat are exogenous sources of N-

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nitroso compounds (NOCs) and precursors of endogenously formed NOCs which are known carcinogens [4]. endogenous formation of NOC by nitrosation of secondary amines *via* nitrite under acidic conditions and it is estimated to contribute 45%–75% of the total NOC exposure [5]. The richest food sources of nitrosamines are bacon, luncheon meats, hot dogs and sausages with added nitrates/nitrites such as chorizo and salami.Nitrite is an active ingredient used as a food additive to extend shelf life, to provide protection against the bacteria Clostridium botulinum and to give processed meat its typical pink colour. Studies have indicated that there is a positive though not necessarily linear correlation, between the amount of nitrite added and the amount of NOC formed [7-9].

Results and Discussion

Findings from the European Prospective Investigation into Cancer (EPIC), a large prospective study which investigated the association between dietary NOCs and cancer risk, showed that gastrointestinal cancer incidence and more specifically with risk of rectal cancer was associated with dietary NDMA (HR: 1.13; 95% CI: 1.00, 1.28; HR: 1.46; 95% CI: 1.16, 1.84 per 1-SD increase respectively) but not with endogenous NOCs or nitrite [10].

Variability in formation of nitrosamines

A wide range of factors affect the formation of NOCs including the amount of nitrite added, meat quality, fat content, processing, maturation and handling at home. Factors related to processing include additives, precursors (added *via* wood smoke, spices or other ingredients), heat applied during drying or smoking, storage/maturation conditions and packaging [11-13]. Moreover, NOC formation can be inhibited by the addition of ascorbic acid and α-tocopherol (vitamin E) [14,15] ingredients which are often added to processed meats.

The impact of vitamin C on the effects of NOC exposure can be seen clearly from the results of a study by DellaValle et al. [16] for example. They investigated the association between dietary nitrate and nitrite intake and risk of colorectal cancer in the Shaghai Women's Health Study, a cohort of 73, 118 women ages 40-70 residing in Shanghai. Overall nitrate intake was not associated with colorectal cancer risk. However, among women with vitamin C intake below the median (83.9 mg/day) and hence higher exposure to NOCs, risk of colorectal cancer increased with increasing quintile of nitrate intake) (HR=2.45; 95% CI 1.15-5.18).

Variation in residual nitrate and nitrite content of processed meat

The levels of residual nitrite and nitrate in processed meat products are also variable depending on the time and temperature used during processing and storing, the initial addition of nitrite and nitrate, the composition of the meat, pH, addition of antioxidant components such as ascorbate and the presence of micro-organisms [17,18]. For example, Yalcin [19] measured the residual nitrate and nitrite content of dry fermented sausages, salamis and sausage samples from Istanbul; the reported average nitrate concentration was 87.0 mg/kg (range 0-362.9) in dry fermented sausage (n=65), 102.4 mg/kg (range 0-390) in salami (n=83) and 147.4 mg/kg (range 0-370.9) in sausage (n=60). The average nitrite concentrations were 42.8 mg/kg (range 0-375) in dry fermented sausage, 87.6 mg/kg (range 0-375) in salami and 102.8 mg/kg (range 0-420) in sausage. Furthermore, the authors note that 3% of dry fermented sausage, 15.6% of salami and 20% of sausages wee above 150 mg/kg nitrite, higher than the concentrations indicated by the Regulations of food additives which may be detrimental to health. In comparison, fresh meats such as beef medallions or minced beef are shown to contain low levels of nitrate (estimated at 38.5 mg/kg and 18.7 mg/kg respectively) [20].

Leth et al. [21] also reported on the nitrate and nitrite levels of processed meat on the Danish and Belgian markets. They showed that the five highest levels of nitrate were found in a sample of ham (129 mg/kg), flank pork (124 mg/kg) and three salami samples (71 mg/kg-120 mg/kg) while the five highest levels of nitrite were found in two samples of kassler (smoked pork chops) (36 mg/kg and 19 mg/kg), a sample of meat sausage (luncheon meat) (28 mg/kg) and in two dinner sausages (26 mg/kg and 20 mg/kg). In general, they found that salamis contained low levels of nitrite (3 mg/kg) and accounted for the majority of the samples with a high content of nitrate (15 mg/kg-120 mg/kg).

Alternatives to nitrates and nitrites

Manufacturers are continuing to look for alternatives to sodium nitrate/nitrite as preservatives for products which are currently cured such as bacon and cooked ham. For example, manufacturers of some processed meats have begun to use 'natural' sources of nitrates, such as celery juice or spinach extract, as an alternative to sodium nitrate/nitrite. However, the nitrates present in celery juice or spinach extract are reduced to nitrites by the addition of starter bacterial cultures and as a result contribute to nitrosamine formation. The use of sodium nitrite in cooked ham results in a residual nitrite level of around 90 mg/kg compared to the use of celery juice as a source of nitrite which results in a residual level of nitrite between 30 mg/kg and 60 mg/kg [22]. Indeed the European Union considers the use of plant extracts containing high levels of nitrate with an intended technological purpose of preservation to be a deliberate use of a food additive and suggests that manufacturers must label their product as containing nitrate or nitrite [23]. Furthermore they have suggested that labelling these products as a "natural" source is misleading to consumers. It is also likely these products are less safe as the nitrite content may vary where high levels increase nitrosamine formation and lower levels lower the protection against pathogens such as Clostridium botulinum. The Food Additives Legislation Guidance to Compliance provides "advice on the legal requirements of Council Regulation (EC) No. 1333/2008." It expressly refers to the use of vegetable extract nitrites and states: "The indirect addition of nitrates to foods *via* nitrate rich extracts of vegetables such as spinach or celery should be considered an additive use and not a food use. In such cases the extract is being added for preservation as it contains a standardized level of nitrate and consequently such use would not be permitted by Regulation 1333/2008 as these extracts have not been approved as preservatives".

Healthy and safe alternatives to nitrates and nitrites

Healthier preservatives for processed meats such as bacon and cooked ham need to be explored to reduce exposure to N-nitrosamines to humans from these products. Several studies have shown that it is both feasible and possibly beneficial to use natural alternatives to nitrates and nitrites. For example plant extracts, including herbs and berries are natural preservatives [24-28]. In addition, Deda et al. [29] and have shown a promising example of reducing the nitrite level without compromising the processing and quality characteristics of frankfurter sausages by the addition of tomato paste.

Conclusion

The effects of plant polyphenols (green tea polyphenols and grape seed extract (GSE)) and alpha-tocopherol on physicochemical parameters, lipid oxidation, residual nitrite, microbiological counts, biogenic amines and N-nitrosamines were determined in bacons during dry-curing and storage by Wang et al. [30]. Results showed that plant polyphenols and alpha-tocopherol significantly decreased pH, lipid oxidation (formation of thiobarbituric acid reactive substances) and residual nitrite content compared with control ($P<0.05$) at the end of the ripening process. These findings suggest that plant polyphenols, especially green tea polyphenols, could be utilized for processing dry cured bacons to improve the quality, shelf life and safety of the finished products [30]. These innovative meat products could potentially contribute to a reduction in cancer risk by means of nitrite reduction and phytochemical addition and should be explored further.

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