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Dietary nitrate and nitrite: Benefits, risks, and evolving perceptions

Wendy Bedale [a], Jeffrey J. Sindelar [a,b], Andrew L. Milkowski [a,b,*]

[a] Food Research Institute, University of Wisconsin-Madison, Madison, WI, USA
[b] Muscle Biology Laboratory, Department of Animal Sciences, University of Wisconsin-Madison, Madison, WI, USA

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ABSTRACT

Consumers have an illogical relationship with nitrite (and its precursor, nitrate) in food. Despite a long history of use, nitrite was nearly banned from use in foods in the 1970s due to health concerns related to the potential for carcinogenic nitrosamine formation. Changes in meat processing methods reduced those potential risks, and nitrite continued to be used in foods. Since then, two opposing movements continue to shape how consumers view dietary nitrate and nitrite. The discovery of the profound physiological importance of nitric oxide led to the realization that dietary nitrate contributes significantly to the nitrogen reservoir for nitric oxide formation. Numerous clinical studies have also demonstrated beneficial effects from dietary nitrate consumption, especially in vascular and metabolic health. However, the latest wave of consumer sentiment against food additives, the clean-label movement, has renewed consumer fear and avoidance of preservatives, including nitrite. Education is necessary but may not be sufficient to resolve this disconnect in consumer perception.

1. Introduction

The 2015 Food & Health Survey by the International Food Information Council Foundation (International Food Information Council Foundation, 2015) provides an example of consumers' contrary relationship with food preservatives such as nitrite: Nearly equal numbers (36% vs. 34%) believe that "chemicals in foods" and "foodborne illness from bacteria", respectively, are the most important food safety issues at this time. Consumers worry about the same ingredients (chemical preservatives and antimicrobials) that protect them from something else that they fear (foodborne pathogens).

More specifically, consumers have developed an illogical relationship with nitrite (and its precursor, nitrate) in food. Nitrate and nitrite, despite many centuries of use in food preservation, were nearly banned from use in foods in the 1970s due to data suggesting possible health concerns (Cassens, 1990), and nitrite remains among food additives most feared by consumers (Downs, 2008). However, sales for bacon, arguably the food most commonly associated with nitrite, continue to grow 10% annually (Sax, 2014). Meanwhile, hot dogs containing celery powder (a rich natural source of nitrate) are erroneously touted in the popular press as being "by default healthier than nitrate-filled dogs" (Myers, 2014). Consumers seeking clean-label products will virtuously add celery, spinach, uncured bacon, and beet juice (popularized as an antidote for metabolic syndrome because of its high level of nitrate) to their shopping baskets, not realizing that all contain the same chemical that they assiduously avoid when added in the form of a purified chemical to foods.

Although nitrate and nitrite alone are regarded to have no or limited carcinogenic potential (Grosse et al., 2006), nitrite in combination with certain amines or amides could potentially form N-nitroso compounds (NOC), many of which are carcinogenic in animals. Some epidemiological studies have suggested an association between dietary nitrite and red or processed meats and cancer (Abid, Cross, & Sinha, 2014), while others have demonstrated conflicting results (Eichholzer & Gutzwiller, 1998), with reviews and meta-analyses sometimes coming to different conclusions (Alexander, Weed, Cushing, & Lowe, 2011; Alexander, Weed, Miller, & Mohamed, 2015). Adding to the confusion: vegetables and drinking water contribute large amounts of nitrate (and nitrite) to the diet, far more than cured meats (National Academy of Sciences, 1981). Diets rich in fruits and vegetables, which may contain 5 times the acceptable daily nitrate intake (Section 2.5) (Hord, Tang, & Bryan, 2009), have been associated with lower rates of certain cancers (Lee & Chan, 2011).

Within the last several decades the profound importance of nitric oxide (and its oxidative products nitrite and nitrate) in many physiological systems has been established. Dietary consumption of nitrate has been demonstrated in clinical studies to have numerous health benefits, especially related to improved cardiovascular function. Media coverage of these studies has resulted in consumers eschewing nitrate and nitrite in some foods while embracing other foods (such as beet juice) precisely because they contain nitrate.

The goal of this review is to summarize recent literature related to risks and benefits of dietary nitrate and nitrite while attempting to address evolving consumer perceptions. Other excellent reviews on the risks and benefits of nitrate and nitrate have been published

* Corresponding author at: Food Research Institute, University of Wisconsin-Madison, Madison, WI, USA.
E-mail address: milkowski@wisc.edu (A.L. Milkowski).

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(Bryan & Ivy, 2015; Butler, 2015; Clements, Lee, & Bloomer, 2014; Gilchrist, Winyard, & Benjamin, 2010; Habermeyer et al., 2015; Hord et al., 2009; Kobayashi, Ohtake, & Uchida, 2015; McNally, Griffin, & Roberts, 2015; Milkowski, Garg, Coughlin, & Bryan, 2010; Sindelar & Milkowski, 2012), so in this paper the most recent research and consumer's evolving perceptions will be highlighted.

2. History of use, chemistry, and metabolism of nitrate and nitrate

2.1. Why are nitrate and nitrite used in meat?

Nitrite (and its precursor, nitrate) positively affects the appearance, flavor, safety, and quality of cured meats (Pearson & Gillett, 1996). Nitrite is responsible for the characteristic reddish-pink color (Fox, 1966) and flavor of cured meats (Macdonald, Gray, Stanley, & Usborne, 1980). Importantly, nitrite improves safety of meat by inhibiting the growth of microorganisms, notably *Clostridium botulinum* (Christiansen & Foster, 1965; Duncan & Foster, 1968a, 1968b; Sofos, Busta, & Allen, 1979). Finally, nitrite preserves and may even be considered to improve flavor in preventing rancidity by inhibiting lipid peroxidation (Pearson & Gillett, 1996) (Freybler et al., 1993) (Richards, 2013).

2.2. History and regulation of nitrate and nitrite in meat

Salt has been used in meat preservation since at least 3000 BC (Binkerd & Kolari, 1975). By around 200 BC, the Romans recognized that salt from some sources contained contaminants that contributed a reddish-pink color and flavor to cured meats. Eventually this contaminant was identified to be potassium nitrate (Honikel, 2008). Until the 20th century when large scale synthetic methods were developed, saltpeter was mined, obtained from natural sources (such as accumulated bat guano in caves) or could be made from manure or urine when combined with wood ashes, earth, and organic matter (Cressey, 2013). Potassium nitrate (saltpeter, also used in gunpowder) was used as a curing agent in meat for many centuries. Meat curing was as much an art as a science, with much inconsistency in finished products in terms of flavor and preservation (and safety).

In the early 1900s, an understanding of how nitrate actually worked in curing meats was developed. The nitrate, it was learned, was reduced to nitrite during curing. This reduction was promoted by bacteria introduced in handling meat or by reducing activity of the meat itself during the curing process. Nitrite was demonstrated to be the compound responsible for the color and flavor of cured meats. Importantly, nitrite was also identified as the chemical that inhibited the growth of certain pathogens such as *Clostridium botulinum* (which is named after “botulus”, the Latin word for sausage, because of the microbe's close association with sausages and sausage poisoning prior to this time). When nitrate was used as the curing agent, the conversion of nitrate to nitrite during curing was not always efficient, leading to sometimes inadequate or sometimes excessive levels of nitrite in the finished product.

The identification of nitrite as the responsible agent in the curing process led the USDA to undertake a series of experiments beginning in 1923 to determine the minimal level of sodium nitrite sufficient to promote curing (in terms of color formation and quality attributes) of hams and bacon. The studies established that nitrate was not required for curing, and that use of nitrite instead of nitrate could promote faster curing. The USDA approved nitrite as a meat curing agent in 1925.

The realization in the 1960s that most nitrosamines were carcinogens, and subsequently in the 1970s that nitrosamines formed when bacon was fried at high temperatures, created a political, scientific and societal controversy that almost resulted in the banning of bacon and nitrites, as detailed in Professor Robert Cassens, 1990 book “Nitrite-cured meat: A food safety issue in perspective (Cassens, 1990). It seems possible that intense media coverage from this era is still responsible for some of the negative perception of nitrite and nitrates by consumers today. The legacy may have been further perpetuated by the education that health professionals received in that era that is carried forward to this day.

Several factors likely reduced the intense anti-nitrite sentiment. USDA scientists demonstrated that reducing nitrite levels in bacon and including ascorbate or its isomer erythorbate or tocopherols (Vitamin E) during curing could inhibit formation of nitrosamines during bacon frying (Fiddler, Pensaben, Kushnir, & Piotrows, 1973). In 1978 USDA regulations for pumped bacon were changed to reduce nitrite levels and require either ascorbate or erythorbate be added (U.S. Department of Agriculture). Later, in 2001, results of animal studies from the National Toxicology Program were released which showed that dietary nitrite showed at best equivocal potential to be carcinogenic in bioassays in rodents (National Toxicology Program, 2001).

Finally, the discovery in the 1980s that nitric oxide (endogenously synthesized from arginine or potentially produced by reduction of nitrite) is a key metabolic signaling molecule affecting a huge number of physiological processes led to a profound need to reconsider the effects and importance of nitrate and nitrite in the body. Media mentions of nitrite and nitrosamine decreased (Cassens, 1990), and an uneasy truce was thus established for most consumers in their relationship with nitrite and cured meats.

In parallel to and also expanding from the nitrate/nitrite controversy, consumers have also become much less trusting of all food additives and have greatly embraced “clean labels”. The origins of the clean-label movement may be related to the nitrite story, but other factors certainly played important parts, including passage of the U.S. Delaney Clause legislation in 1958, which restricted the use of any food additives that were shown to cause cancer upon ingestion by man or in animals (Weisburger, 1996). Environmental concerns related to pollution and use of pesticides were also prominent in the post-war era, contributing to more concern about risks of new technologies, especially those involving chemicals. In the 1970s, the allergist Benjamin Feingold espoused the removal of food additives including preservatives to treat or prevent hyperactivity (Smith, 2011). The Ames test was established in the 1970's as a quick and inexpensive method to assess mutagenic potential of chemicals, although high doses of many compounds that are non-carcinogenic to humans may be mutagenic in that assay. However, the simplicity of the test during the “War on Cancer” era may have led to its overuse, enhancing consumer suspicion to “chemicals”.

More recently, Michael Pollan's, 2008 book “In Defense of Food: An Eater's Manifesto” (Pollan, 2008) put forth the mantra “don't eat anything with more than five ingredients, or ingredients you can't pronounce”. The internet, and the rise of the “mommy blogger”, have certainly allowed fears regarding food (whether scientifically vetted or not) to be spread easily to a wide audience. Scientific reports that receive extensive media coverage such as the IARC report on the carcinogenicity of red and processed meats (Bouvard et al., 2015) lead to consumer confusion, especially in a world where everyone can read, repackage, and discuss information online (Brossard & Scheufele, 2013), and where a consumer can chose to live within his own echo chamber, reinforcing existing beliefs (Del Vicario et al., 2016). Meanwhile, the relative rarity of botulism outbreaks in the modern era (Shapiro, Hatheway, & Swerdlow, 1998) has likely fostered nonchalance about the key role that nitrite plays in preventing *C. botulinum* growth. Industry, always looking for novel marketing messages, has embraced clean label as a way of differentiating their products from others. A combination of these and other factors, along with the lingering legacy of anti-nitrite sentiment, has likely led to a re-emergence in consumer avoidance of foods with preservatives, including nitrite and nitrate.

In the last two decades, the clean-label and the anti-nitrite movements have come together to spawn the development of “uncured” bacon and other processed meats. The USDA does not allow the addition of synthetic chemicals, including sodium nitrite or sodium erythorbate, to be added to meat products that are labeled as “natural” or “organic (Sebranek, Jackson-Davis, Myers, & Lavieri, 2012). Cured meats such