International Journal of Food Science and Nutrition
www.foodsciencejournal.com
ISSN: 2455-4898
Received: 24-04-2025, Accepted: 25-05-2025, Published: 09-06-2025
Volume 10, Issue 3, 2025, Page No. 50-54

Looking forward to dietary nitrate and nitrite as preventive nutrition for special diseases

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Abstract
Excessive ingestion of nitrate and nitrite may pose a risk of methemoglobinemia in infants and gastrointestinal cancer in adults. These have driven regulatory action on dietary nitrate and nitrite. Current regulatory limits for dietary nitrate and nitrite are based on negative health effects without considering positive potential health benefits. The limits given by The World Health Organization's regulations limits on nitrate intake have been exceeded by a single food intake and recommended dietary pattern, have not caused any significant risk. This article reviews the foundation of current regulatory establishment and the problems faced by current regulatory and provides suggestions for current regulatory limits changes. It is very meaningful to develop scientific and reasonable guidelines for dietary ingestion of nitrate and nitrite as preventive nutrition for special diseases, thereby beneficial to public health.

Keywords: Nitrate, nitrite, accepted daily intake, health risks, regulatory limits

Introduction

The nitrate ingested by humans from plant foods can get into the food chain. Nitrate in vegetables is a main source of human diet, groundwater and surface water are secondary sources. The nitrate intake of vegetables depends on the types of vegetables being eaten, the nitrate concentration in vegetables, the intake of vegetables, and the nitrate level in the water supply [1]. Leaf vegetables have the highest nitrate content, while seeds or tubers have lower nitrate content [2]. Nitrite is mainly converted into endogenous nitrate through salivary circulation process [3,4]. The proportion of nitrate and nitrite consumed by humans from processed meat, dairy products, and poultry products is very small. Overall, nitrate in the diet mainly comes from dietary intake, while nitrite mainly comes from *in vivo* production.

The World Health Organization's regulations on nitrate ingestion have been exceeded by the intake of single foods and special dietary patterns for example soybean milk and spinach, and the Dietary Approaches to Stop Hypertension diet (DASH diet). Uncoordinated regulatory restrictions on dietary intake of nitrate and nitrite in meat products and vegetables may raise public concerns about the dietary recommendations from regulatory authorities. It is necessary to reassess the potential health effects of dietary nitrate and nitrite. The works can strengthen guidance on dietary nitrate and nitrite, thereby benefiting public health.

Current regulatory

Nitrate in potable water is a key factor limiting environmental eutrophication pollution. The nitrate and nitrite in contaminated potable water sources have a certain impact on human health. According to epidemiological and medical research, excessive intake of nitrate and nitrite may pose health risks, such as methemoglobinemia (MetHb), cancer, etc. The establishment of the current regulatory limits are based on the potential negative effects of nitrate and nitrite on health without considering potential health benefits（Figure 1 [5, 10]. Following the recommendations of the World Health Organization, the allowable content of nitrate in potable water in European Union is 50 mg/L and 44 mg/L in the United States [11]. The US Environmental Protection Agency sets human nitrate intake to 10 ppm and nitrite to 1 ppm [12]. The acceptable daily intake (ADI) of nitrate established by United Food and Agriculture Organization/World Health Organization is 3.7 mg/kg body weight and 0.06 mg/kg body weight for nitrite [13]. Considering the potential health benefits of nitrate and nitrite in the diet, it is necessary to renew the current regulatory.

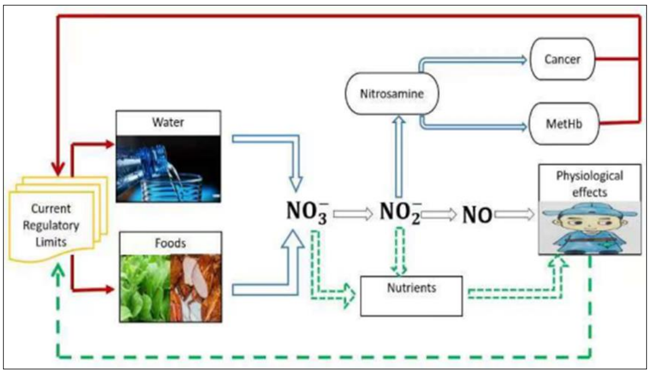

Figure 1 Overview diagram of current regulatory limits for dietary nitrate and nitrite. Current regulatory limits are based on negative health effects without considering positive potential health benefits. Current regulatory limits for dietary nitrate and nitrite should consider the potential beneficial physiological effects of dietary nitrate and nitrite.NO_3^-: nitrate; NO_2^-: nitrite; NO: nitric oxide; Methemoglobinemia: MetHb.

Diet exceeding WHO ADI Levels

The role of diet in preventing and controlling the incidence rate of non-communicable diseases and premature death has been fully confirmed through a large number of population-based epidemiological studies [14]. Research has shown that consuming some foods with high levels of nitrite and nitrate, especially leafy vegetables, can easily achieve beneficial effects. The Dietary Approaches to Stop

Hypertension (DASH) diet was developed by the National Institutes of Health in the United States to reduce hypertension without taking medication. Extensive research has proven that a DASH diet may reduce blood pressure, lower cholesterol, and increase insulin sensitivity [15]. Lord and Bryan have shown that people who follow the DASH diet have exceeded ADI by more than 500% [16, 17]. Human breast milk is the most suitable nutrient for infants and cannot be completely replaced by other foods such as infant formula. As is well known, breast milk has significant nutritional and immune benefits for infants [18, 19]. However, breast milk and colostrum contain high content of nitrite and nitrate [20, 23]. The nitrate content in 100 mL of colostrum consumed by infants is still equivalent to 42% of the World Health Organization's ADI [24].

It is worth noting that the intake of nitrate in a single food may approach or exceed the World Health Organization's ADI limit, for example breast milk, spinach, or dried vegetable supplements [25, 26]. In addition, when adults consume certain vegetables and fruits, their saliva nitrate concentration can reach three times the regulatory limit for drinking water [27]. The intake of nitrite and nitrate in some foods or healthy eating is higher than the World Health Organization's ADI limits, which has raised doubts about current recommended limits. Although nitrate levels in the diet exceed ADI, studies have shown significant health benefits and do not pose any significant risks. The fact indicates that the current regulatory limits are no longer suitable as guidance for dietary nitrate and nitrite.

Negative Potential Health Risks

Epidemiological and clinical studies have shown that the intake of nitrate and nitrite is associated with an increased risk of gastrointestinal cancer, thyroid dysfunction and thyroid cancer [10], chronic obstructive pulmonary disease in women and other diseases [6, 8]. The intake and consumption of nitrate and nitrite in pickled and processed meats are associated with the risk of gastrointestinal cancer [7, 9]. A recent meta-analysis questioned this conclusion. The existing epidemiological evidence is insufficient to support a clear and accurate positive correlation between independent consumption of processed meat and the risk of colorectal cancer [5]. Nitrates added to meat must be converted into nitrites to function. Sodium nitrite is used as a coloring agent, flavoring agent, and antibacterial agent in pickling and processing meats. The use of nitrates and nitrites in meat products is restricted by regulations from the US Food and Drug Administration (FDA) and the US Department of Agriculture (USDA). When using nitrite in bacon, it is necessary to simultaneously use sodium erythorbate or sodium ascorbate (vitamin C), which is an antioxidant that can inhibit the nitrification of secondary amines by nitrite [28]. Since the mid-1970s, the use of these antioxidants has reduced nitrate and nitrite levels in processed meat, resulting in a reduction of approximately 80% in residual nitrite levels in American cured meat products [29].

Concerns about the risk of cancer associated with nitrite and nitrate are always accompanied by concerns about preformed N-nitrosamines or N-nitrosamines formed in the stomach due to the consumption of foods rich in nitrite and nitrate [30]. The reason for this concern is that some low molecular weight amines can react with nitrite to produce carcinogenic N-nitroso derivatives [3]. Nitrosamines were a class of compounds first described in chemical literature over 100 years ago, but they did not receive widespread attention until 1956. In 1956, two British scientists, John Barnes and Peter Magee, reported that dimethyl nitrosamine could produce liver tumors in rats [31]. Magee and Barnes' milestone discovery prompted scientists around the world to study the carcinogenic properties of other nitrosamines. About 90% of these compounds have been found to be carcinogenic in various experimental animals after testing approximately 300 of them. Most nitrosamines are mutagens, while some are transplacental carcinogens. Most of them are organ specific. The reason why nitrosamines occur is because their chemical precursors - amines and nitrifying agents - are widely present, and the chemical reaction formed by nitrosamines is reasonable.

In 1973, research showed that ascorbic acid can inhibit the formation of nitrosamines [32, 33, 34.] Antioxidants, α-Tocopherol (vitamin E) can also inhibit the formation of nitrosamines [35]. Ascorbic acid and α- Tocopherols inhibit the formation of nitrosamines due to their redox properties. For example, when ascorbic acid is oxidized to dehydroascorbic acid, nitrite is reduced to NO, which is not a nitrosation agent. Most vegetables rich in nitrate are also rich in antioxidants, such as vitamins C and E, which can prevent unnecessary nitrosation reactions. These antioxidants are now commonly added to cured and processed meats. On the other hand, the absence of such protective nitrosation inhibitors in drinking water may be a concern. Controlling the metabolic processes of nitrate and nitrite, keeping them away from nitrification and reducing them to NO, can provide a strategy to reduce health risks while promoting health benefits.

Positive Potential Health Benefits

Many research achievements have created the modern foundation for the health benefits of dietary nitrate and nitrite [36, 39]. The discovery of the nitric oxide pathway is of milestone significance. Nitric oxide (NO) is a gas signaling molecule that is crucial for regulating many physiological processes, including immune, nervous systems, and cardiovascular [40, 43]. NO is generated in the body through two main biological pathways. The first discovered is the L-arginine-NO- synthase pathway, in which nitric oxide synthase (NOS) catalyzes the reaction of L-arginine with oxygen to produce NO [44]. The second discovered is the nitrate-nitrite-NO pathway, which produces NO by reducing nitrate and nitrite through various reduction mechanisms, including nitrate and nitrite reductases [45, 46]. The half-life of NO is very short, and it is quickly oxidized to nitrite, which is then oxidized to nitrate. The unique feature of nitrite and nitrate is that they can serve as stable cycling storage forms of NO and can be quickly reduced to restore NO levels in the body. These two pathways can affect the production/homeostasis of NO in the human body. L-arginine pathway is a very complex pathway, and if any cofactors in the pathway are restricted, NOS will stop producing NO. In fact, the enzymatic production of NO is usually very effective. However, in many diseases, important NOS cofactors are oxidized, uncoupled, or oxygen limited under hypoxic conditions, making it impossible to maintain NO production. The nitrate-nitrite-NO pathway has been proven to be a backup system for ensuring NO supply when the L-arginine-NO synthase pathway is dysfunctional [47]. Both pathways produce NO with the same biological activity. Supplementing nitrate and nitrite through diet can serve as a protective measure to make up for insufficient NOS activity. The redundant system of NO production in tissues is of great significance for gastrointestinal, cardiovascular, and immune functions, which are related to providing dietary nitrate and nitrite. This process is regulated by reducing substrate, oxygen tension, pH, and nitrite level [48].

The discovery of nitrate - nitrite- NO pathway has greatly changed our view. The fact indicates that they can be spontaneously generated in the human body, not just by synthetic food additives. Before this discovery, most previous researchers have focused on the potential hazards of dietary nitrite and nitrate. Surprisingly, the effects of nitrite and nitrate in human diseases and health have not been fully recognized. Therefore, the potential beneficial effects of nitrate and nitrite on health require a new regulatory.

Nitrates and Nitrites as Nutrients

Two national organizations, the International Agency for Research on Cancer (IARC) and the European Food Safety Authority (EFSA), have issued recommendations on the potential health impacts of dietary sources of nitrate and nitrite. IARC concluded that the carcinogenicity of nitrate and nitrite derived from drinking water and food is not strongly supported by epidemiological evidence. They believe that some factors present in food, such as flavonoids in vegetables, may be the reason why nitrate in food is not associated with cancer risk. Overall, IARC concluded that "ingested nitrate or nitrite under conditions that result in endogenous nitrosation is probably carcinogenic to humans (group 2A)" [49]. EFSA concluded that epidemiological studies have shown that nitrate intake from diet or drinking water is not associated with an increased risk of cancer [13]. EFSA believes that it is currently unclear whether high intake of nitrite may be associated with an increased risk of cancer. The inconsistent positions of IARC and EFSA on foods containing nitrate and nitrite may lead to confusion among consumers. Therefore, regulatory agencies must develop new dietary guidelines on dietary nitrate and nitrite.

The potential positive health benefits of dietary nitrate and nitrite have been identified [36, 39]. In addition to describing the risks and benefits of dietary nitrate and nitrite, according to their proven physiological functions, these dietary components can be considered nutrients [50]. Based on current research results, we consider that the U.S. Institute of Medicine's Dietary Reference Intake (DRI) paradigm may be a suitable guide for developing regulatory on dietary nitrates and nitrites. The DRI paradigm encompasses the concepts of physiological defects, adequacy, and excess.

Like all nutrients, excessive ingestion of nitrate and nitrite can also increase potential health risks. The Food and Nutrition Committee of the National Academy of Sciences has established a set of dietary reference intake (DRI) paradigms for basic nutrients to clearly define situations where intake is insufficient, safe, or potentially excessive. The process of developing nutritional DRI is very complex, requiring consideration of a series of physiological factors, including nutritional status and potential toxicity. If nitrate and nitrite are considered nutrients, researchers, health professionals, and regulatory agencies need to reach a consensus to determine low, sufficient, or excessive physiological concentrations. There is a significant difference in the treatment and beneficial dosage of nitrite and nitrate compared to the potentially toxic and harmful dosage, which provides sufficient space for developing nutritional recommendations and dietary guidelines on dietary nitrate and nitrite.

Nitration Chemistry of Nitrite and Nitrate

The main reason for paying attention to nitrite and nitrate is the possibility of nitrosation chemical reactions. The risk-benefit spectrum of nitrate and nitrite may depend on specific metabolism and the presence of other components that may be ingested simultaneously. Gradually reducing to nitrite and NO may be a beneficial factor, while pathways leading to low molecular weight amine or amide nitration may be a health risk factor. Understanding and influencing these pathways will help reduce risks.

Nitrates themselves are usually considered harmless at low concentrations. On the other hand, nitrite has reactivity, especially in the acidic environment of the stomach where it can undergo nitrosylation reactions with proteins, amines, and amides. The nitrite content in the environment is very low, and nitrite in the human body is converted by common symbiotic bacteria in saliva after ingestion of nitrate [51,52]. Concerns about the risk of cancer associated with nitrite and nitrate are always accompanied by concerns about pre-formed N-nitrosamines or N-nitrosamines in the stomach due to the consumption of foods rich in nitrite and nitrate. The reason for this concern is that some low molecular weight amines can react with nitrite to produce carcinogenic N-nitroso derivatives. Nitrosamines were a class of compounds first described in chemical literature over 100 years ago, but they did not receive widespread attention until 1956. About 90% of the approximately 300 compounds tested have been found to be carcinogenic in various experimental animals. In 1973, some studies reported that ascorbic acid inhibits the formation of nitrosamines [32, 35]. Antioxidants, α- Tocopherol (vitamin E) can also inhibit the formation of nitrosamines. Most vegetables rich in nitrate are also rich in antioxidants, such as vitamins C and E, which can prevent unnecessary nitrosation reactions. These compounds are now also added to processed meat products. On the other hand, the absence of such protective nitrosation inhibitors in drinking water may lead to the involvement of nitrosation reactions. The adverse health effects may be caused by the complex interactions between the intake of nitrite and nitrate, accompanying nitrification cofactors and precursors, and specific medical conditions that increase nitrification (such as chronic inflammation). Controlling these factors is crucial for determining the safety of nitrite and nitrate.

Conclusion

At present, public awareness of nitrate and nitrite is still influenced by current recommended ingestion limits. As the potential positive health benefits of nitrate and nitrite are gradually recognized, how to balance the basic physiological functions and potential negative health risks of dietary nitrate and nitrite will drive changes in current regulatory limits. It is necessary to hire an independent expert group from academia, industry, government, and non-governmental sectors to comprehensively evaluate the potential health risks and benefits of dietary nitrate and nitrite. It will help to redefine dietary guidelines and design optimal preventive nutrition plan for specific diseases.

Experts from various fields need to gather and develop nutritional guidelines for nitrite and nitrate, as for other recognized nutrients. Now, the data and facts of this initiative are available, and the ground for such studies is also very fertile. These works will be beneficial to public health.

Acknowledgment: Individuals who contribute articles that do not meet the criteria for authorship, including those who provide professional writing services or materials.

Disclosure of interest : The authors report no conflict of interest.

References

1. Pennington J. Dietary exposure models for nitrates and nitrites. Food Control,1998:(9)385–95.
2. Santamaria P. Nitrate in vegetables; content, toxicity and EC regulation. J Sci Food Agric,2005:86(1):10–7.
3. Spiegelhalder B, Eisenbrand G, Preussmann R. Influence of dietary nitrate on nitrite content of human saliva: possible relevance to *in vivo* formation of N-nitroso compounds. Food Cosmet Toxicol,1976:14(6):545–8.
4. Petersson J, Carlstrom M, Schreiber O, Phillipson M, Christoffersson G, Jagare A, *et al*. Gastroprotective and blood pressure lowering effects of dietary nitrate are abolished by an antiseptic mouthwash. Free Radic Biol Med,2009:46(8):1068–75.
5. Alexander DD, Miller AJ, Cushing CA, Lowe KA. Processed meat and colorectal cancer: a quantitative review of prospective epidemiologic studies. Eur J Cancer Prev,2010:19(5):328–41.
6. Jiang R, Camargo Jr CA, Varraso R, Paik DC, Willett WC, Barr RG. Consumption of cured meats and prospective risk of chronic obstructive pulmonary disease in women. Am J Clin Nutr,2008:87(4):1002–8.
7. Norat T, Bingham S, Ferrari P, Slimani N, Jenab M, Mazuir M, *et al*. Meat, fish, and colorectal cancer risk: the European Prospective Investigation into cancer and nutrition. J Natl Cancer Inst,2005:97(12):906–16.
8. Panesar NS. Downsides to the nitrate-nitrite-nitric oxide pathway in physiology and therapeutics? Nat Rev Drug Discov,2008:7(8):710.
9. Santarelli RL, Pierre F, Corpet DE. Processed meat and colorectal cancer: a review of epidemiologic and experimental evidence. Nutr Cancer,2008:60(2):131-44.
10. Ward MH, Kilfoy BA, Weyer PJ, Anderson KE, Folsom AR, Cerhan JR. Nitrate intake and the risk of thyroid cancer and thyroid disease. Epidemiology,2010:21(3):389–95.
11. World Health Organization. Recommendations; nitrate and nitrite. In: Guidelines for drinking water quality, 2004, 417–20.
12. National Primary Drinking Water Regulations: Final Rule, 40. Federal Register,1991:(56):141–143
13. European Food Safety Authority. Nitrate in vegetables: scientific opinion of the panel on contaminants in the food chain,2008:689:1–79.
14. World Health Organization. Report on diet, nutrition and the prevention of chronic diseases, 2003.
15. Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, *et al*. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. N Engl J Med,1997:336(16):1117–24.
16. Hord NG, Tang Y, Bryan NS. Food sources of nitrates and nitrites: the physiologic context for potential health benefits. Am J Clin Nutr,2009:90(1):1–10.
17. Karl JM, Alaverdashvili M, Cross AR, Whishaw IQ. Thinning, movement, and volume loss of residual cortical tissue occurs after stroke in the adult rat as identified by histological and magnetic resonance imaging analysis. Neuroscience,2010:170(1):123–37.
18. Hoddinott P, Tappin D, Wright C. Breast feeding. BMJ,2008:336(7649):881–7.
19. James DC, Lessen R. Position of the American Dietetic Association: promoting and supporting breastfeeding. J Am Dietetic Assoc,2009:109(11):1926–42.
20. Cekmen MB, Balat A, Balat O, Aksoy F, Yurekli M, Erbagci AB, *et al*. Decreased adrenomedullin and total nitrite levels in breast milk of preeclamptic women. Clin Biochem,2004:37(2):146–8.
21. Hord NG, Ghannam JS, Garg HK, Berens PD, Bryan NS. Nitrate and nitrite content of human, formula, bovine and soy milks: implications for dietary nitrite and nitrate recommendations. Breastfeed Med,2011:6(6):393–9.
22. Iizuka T, Sasaki M, Oishi K, Uemura S, Koike M, Shinozaki M. Non-enzymatic nitric oxide generation in the stomachs of breastfed neonates. Acta Paediatr,1999:88(10):1053–5.
23. Ohta N, Tsukahara H, Ohshima Y, Nishii M, Ogawa Y, Sekine K, *et al*. Nitric oxide metabolites and adrenomedullin in human breast milk. Early Hum Dev,2004:78(1):61–5.
24. Hord NG, Ghannam J, Garg H, Tang YP, Bryan NS. Nitrate and nitrite content of human, formula, bovine and soy milks: implications for dietary nitrite and nitrate recommendations Breastfeed Med, 2010. [Epub ahead of print].
25. Hord NG, Tang Y, Bryan NS. Food sources of nitrates and nitrites: the physiologic context for potential health benefits. Am J Clin Nutr,2009:90(1):1–10.
26. Lundberg JO, Feelisch M, Bjorne H, Jansson EA, Weitzberg E. Cardioprotective effects of vegetables: is nitrate the answer? Nitric Oxide,2006:15(4):359–62.
27. Li H, Thompson I, Carter P, Whitely A, Bailey M, Leifert C, *et al*. Salivary nitrate–an ecological factor in reducing oral acidity. Oral Microbiol Immunol,2007:22(1):67–71.
28. Rao GS, Osborn JC, Adatia MR. Drug-nitrite interactions in human saliva: effects of food constituents on carcinogenic N-nitrosamine formation. J Dent Res,1982:61(6):768–71.
29. Cassens RG. Residual nitrite in cured meat. Food Technol,1997:51:53–5.
30. Refai HM, Sebaei AS. Daily intake of nitrate and nitrite via meat nd poultry in Egypt. Food additives & contaminants: Part B,2020:13:292-297.
31. Magee PN, Barnes JM. The production of malignant primary hepatic tumours in the rat by feeding dimethyl nitrosamine. Br J Cancer,1956:10(1):114–22.
32. Fan TY, Tannenbaum SR. Natural inhibitors of nitrosation reactions: the concept of available nitrite. J Food Sci,1973:38(6):1067–9.
33. Fiddler W, Pensabene JW, Piotrowski EG, Doerr RC, Wasserman AE. Use of sodium ascorbate or erythorbate

to inhibit formation of N-nitrosodimethlyamine in frankfurters. J Food Sci.mn,1973:38(6):1084.
34. Mirvish SS. Blocking the formation of N-nitroso compounds with ascorbic acid *in vitro* and *in vivo*. Ann N Y Acad Sci,1975:258:175–80.
35. Mirvish SS. Inhibition by vitamins C and E of *in vivo* nitrosation and vitamin C occurrence in the stomach. Eur J Cancer Prev,1996:51:131–6.
36. Dejam A, Hunter CJ, Schechter AN, Gladwin MT. Emerging role of nitrite in human biology. Blood Cells Mol Dis,2004:32(3):423–9.
37. Bryan NS, Fernandez BO, Bauer SM, Garcia-Saura MF, Milsom AB, Rassaf T, *et al*. Nitrite is a signaling molecule and regulator of gene expression in mammalian tissues. Nat Chem Biol,2005:1(5):290–7.
38. Lundberg JO, Govoni M. Inorganic nitrate is a possible source for systemic generation of nitric oxide. Free Radic Biol Med,2004:37(3):395–400.
39. Zhang H, Qin L. Positive Feedback Loop Between Dietary Nitrate Intake and Oral Health. Nutrition Research,2023:115:1-12.
40. Hegesh E, Shiloah J. Blood nitrates and infantile methemoglobinemia. Clin Chim Acta,1982:125(2):107–15.
41. Hibbs Jr JB, Taintor RR, Vavrin Z. Macrophage cytotoxicity: role for L-arginine deiminase and imino nitrogen oxidation to nitrite. Science,1987:235(4787):473–6.
42. Palmer RMJ, Ferrige AG, Moncada S. Nitric oxide release accounts for the biological activity of endothelium-derived relaxing factor. Nature,1987:327(6122):524-6.
43. Garthwaite J, Charles SL, Chess-Williams R. Endothelium-derived relaxing factor release on activation of NMDA receptors suggests role as intercellular messenger in the brain. Nature,1988:336(6197):385–8.
44. Reutov VP, Sorokina EG. NO-synthase and nitrite-reductase components of nitric oxide cycle. Biochemistry,1998:63(7):874–84.
45. Lundberg JO, Weitzberg E. NO generation from inorganic nitrate and nitrite: role in physiology, nutrition and therapeutics. Arch Pharm Res,2009:32(8):1119–26.
46. Torregrossa AC, Aranke M, Bryan NS. Nitric oxide and geriatrics: implications in diagnostics and treatment of the elderly. J Geriatr Cardiol,2011:8(4):230–42.
47. Lundberg JO, Gladwin MT, Ahluwalia A, Benjamin N, Bryan NS, Butler A, *et al*. Nitrate and nitrite in biology, nutrition and therapeutics. Nat Chem Biol,2009:5(12):865–9.
48. Zweier JL, Li H, Samouilov A, Liu X. Mechanisms of nitrite reduction to nitric oxide in the heart and vessel wall. Nitric Oxide,2010:22(2):83–90.
49. Grosse Y, Baan R, Straif K, Secretan B, El Ghissassi F, Cogliano V. Carcinogenicity of nitrate, nitrite, and cyanobacterial peptide toxins. Lancet Oncol.2006:7(8):628–9.
50. Nathan S. Bryana, John L. Ivy. Inorganic nitrite and nitrate: Evidence to support consideration as dietary nutrients. Nutr Res,2015:35(8):643–54.
51. Hyde ER, Andrade F, Vaksman Z, Parthasarathy K, *et al*. Metagenomic analysis of nitrate-reducing bacteria in the oral cavity: implications for nitric oxide homeostasis. PLoS One,2014:9(3);88645.
52. Tannenbaum SR, Weisman M, Fett D. The effect of nitrate intake on nitrite formation in human saliva. Food Cosmet Toxicol,1976:14(6);549–52.