THE ROLES OF DIETARY POLYAMINES IN HUMAN HEALTH AND THEIR OCCURRENCE IN FOODS

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Chapter 6

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PAVEL KALÁČ*
Department of Applied Chemistry, Faculty of Agriculture, University of South Bohemia, CZ-37005 České Budějovice, Czech Republic

ABSTRACT

The ubiquitous polyamines putrescine, spermidine and spermine fulfil an array of physiological roles in man. Particularly, their participation in cell growth and proliferation has been of great interest in relation to tumor growth. Both endogenous and dietary polyamines take part in such processes. Thus, reliable information on their content in foods is needed for dieticians. Available data from the literature for numerous food items are summarized in this chapter. Commonly, as the high and very high levels there are considered contents of tens mg kg-1 and above 100 mg kg-1, respectively. Among raw foods of animal origin, liver, kidney, spleen and heart of main warm-blooded slaughter animals have high and very high levels of spermine, higher than respective meats. Ripened cheeses are rich in putrescine as are fish roe and sauces. Foods of plant origin are the main dietary source of spermidine and/or putrescine. Soybean, fermented soy products, mushrooms, sauerkraut, ketchup, cauliflower, broccoli, oranges, grapefruits and their juices belong to items with the highest content. Nevertheless, it is not yet possible to set up credible “tabular values” for polyamines, as their contents vary widely within a food item and very limited information is available on their changes under various storage and processing conditions. Moreover, daily cellular requirements for the polyamines have not yet been established.

INTRODUCTION

The biologically active polyamines putrescine [PUT; butane-1,4-diamine], spermidine [SPD; N-(3-aminopropyl)-butane-1,4-diamine] and spermine [SPM; N,N’-bis(3-aminopropyl)-
butane-1,4-diamine) (Figure 1) are ubiquitous compounds widespread from bacteria to mammals. They have traditionally been classified within the group of biogenic amines. Nevertheless, they started to be considered as a self-reliant group during the 1990’s, because of their roles in normal cells and due to their mode of formation (Kusano et al., 2008). Recent classification of biologically active amines is given in Figure 2.

![Figure 1. Formulae of polyamines](image)

Putrescine, being structurally a diamine, has been classified in the both groups, as it is mostly formed as a “true” biogenic amine by the decarboxylation of corresponding amino acid (ornithine), however, it is the main precursor of physiologically active polyamines spermidine and spermine.

Among numerous biological roles, participation in cell growth and proliferation has been of primary interest, as polyamines, both formed endogenously and taken from diet, can be involved in tumor development. The physiological research of polyamines has been thus very extensive. To the contrary, an increased intake of dietary polyamines may be required in some cases, e.g. in wound healing. The main polyamine roles in health and disease were reviewed (Teti et al., 2002; Gugliucci, 2004; Moinard et al, 2005; Larqué et al., 2007). Recently, various aspects of the polyamine physiological roles were covered in a book (Dandrifosse, 2009a).

![Figure 2. Biologically active amines occurring in foods.](image)

Amines marked with * can be formed both as biogenic amines by non-specific decarboxylation of amino acids and during de novo biosynthesis as natural polyamines.

Three sources maintain the polyamine body pool: (i) endogenous (de novo) biosynthesis, (ii) production by intestinal bacteria or constituents of epithelial cells shed into the gut lumen,
and (iii) dietary intake. The proportion of diet was reported as higher than that provided by the biosynthesis (Bardócz, 1995). Thus, plausible data on polyamines content in foods and beverages are necessary for the estimation of their intake. Unfortunately, daily cellular requirements for the polyamines have not yet been determined.

The aim of the chapter is to review briefly recent knowledge on the biological implications of dietary polyamines for human health and to provide data on polyamines content in foods. Information available particularly during the five-year period since a review on the topic was published (Kalač and Krausová, 2005) will be presented including references.

**Polyamines Formation and Catabolism**

Polyamine biosynthesis is an ancient metabolic pathway present in all organisms. They are considered as essential compounds in living cells of all eukaryotic organisms due to their participation in cell proliferation, transcription and translation processes. Polyamine homeostasis is necessary for cell survival. Its deregulation is involved in such grave illnesses such as cancer or neurodegenerative disorders (Wallace et al., 2003; Rodriguez-Caso et al., 2006; Minguet et al., 2008; Pegg, 2009). In healthy cells, polyamine levels are intricately controlled by the biosynthetic and catabolic enzymes.

A simplified scheme of polyamine biosynthetic pathways is given in Figure 3. The biosynthesis from arginine and methionine are very effectively regulated by two key enzymes, ornithine decarboxylase and S-adenosyl-L-methionine decarboxylase, respectively. Moreover, aminopropyltransferases, preferably spermidine synthase, are the second important group (for a review see Ikeguchi et al., 2006). Cadaverine is formed in plants by the decarboxylation of lysine catalyzed by lysine decarboxylase (EC 4.1.1.18) as a secondary metabolic pathway.

Catabolism of SPD and SPM proceeds as oxidase-catalyzed oxidative deamination and consecutive transformation of the primary reaction products (Seiler, 2004; Wang and Casero, 2006). Some of the final products, namely hydrogen peroxide, acrolein, 3-aminopropanal, 3-acetamidopropanal and 4-aminobutanal, may contribute to the etiology of several pathological states, including cancer (Casero and Pegg, 2009), neurodegenerative diseases (Wood et al., 2007), stroke (Saiki et al., 2009) and renal failure (Igarashi et al., 2006).

**Biological Roles in Man**

PUT, SPD and SPM under physiological conditions are flexible polycations exhibiting 2, 3 or 4 positive charges, respectively (see Figure 1). This determines them as essential factors for the growth, maintenance and function of normal cells.
Figure 3 A simplified scheme of polyamine biosynthetic pathways. The pathway via agmatin, known in bacteria and plants, was proposed also for mammals. Methionine is a donor of aminopropyl units for spermidine and spermine formation. Participating enzymes: ① arginase (EC 3.5.3.1); ② ornithine decarboxylase (EC 4.1.1.17); ③ arginine decarboxylase (EC 4.1.1.19); ④ agmatinase (EC 3.5.3.11); ⑤ spermidine synthase (EC 2.5.1.16); ⑥ spermine synthase (EC 2.5.1.22); ⑦ methionine adenosyltransferase (EC 2.5.1.6); ⑧ S-adenosyl-L-methionine decarboxylase (EC 4.1.1.50).

The available reviews of the partial topics will be preferably cited within this section. Further current information on various aspects of physiological roles of polyamines in animals is available in the proceedings of 11th International Congress on Amino Acids, Peptides and Proteins (Amino Acids, 37, S1-S127).

**Participation in Tumor Growth**

Due to the roles in cells, the polyamines accumulate in cancerous tissues and their level is elevated in the body fluids of cancer patients. Thus, drugs inhibiting biosynthesis of polyamines can prevent cancer and may also be used for therapeutic purposes (Oommen et al., 2009). Inhibitors of ornithine decarboxylase and polyamine structural analogues and derivatives have been the main investigated agents (Bachrach, 2004; Casero and Marton, 2007).

The second direction has been focused on polyamine catabolism and catabolic products. Among them, both carcinogenic and cytotoxic effects are ascribed to acrolein. As reported Toninello et al. (2006), a long-lasting imbalance of amine oxidases and antioxidant enzymes seems to be carcinogenic, while, for a short time, amine oxidases are cytotoxic for cancer cells. Moreover, the interest has been posed on spermine oxidase (EC 1.5.3.3), the only catabolic enzyme able to oxidize spermine specifically (Amendola et al., 2009).

However, tumor cells, which have a high requirement for polyamines, have the ability to uptake extracellular polyamines, both dietary and produced by intestinal bacteria, and to reduce the effects of the therapeutic agents mentioned above. Exogenous polyamines are
taken up to cells via polyamine transport system, an energy-dependent process that is upregulated in cancer cells (Gardner et al. 2004). Deprivation of exogenous polyamines therefore started as another approach in 1990’s (Bardóczi et al., 1999). The reduction of dietary polyamine intake and partial intestinal decontamination in preliminary clinical trials with prostate cancer patients show such way as a well-observed and tolerated therapeutic regimen (Cipolla et al., 2003, 2007). Some components of diet, namely flavonoids, polyphenols and probiotics, were reported to reduce hyperproliferative role of polyamines in colorectal cancer (Linsalata and Russo, 2008).

Effects on Intestinal Tract

As reviewed by Deloyer et al. (2001), dietary polyamines play a significant role in the growth and development of the digestive system of neonates. Since the intestinal epithelium has the highest cell turnover, polyamines are vital for the proper structure and maintenance of the entire digestive tract of adults. Polyamines in the gastrointestinal tract originate from intestinal bacteria, sloughed cells and intestinal secretions. Considerable polyamine concentrations were observed in the lumen of human gut during the fasting state, which suggests endogenous secretion. A significantly higher polyamine content was determined in the jejunum than in the ileum, most probably due to proximal absorption.

Dietary polyamines are almost completely absorbed in the small intestine. The proportion of the polyamines, which may affect the large intestinal mucosal tissue, is primarily of microbial rather than of dietary origin (Noack et al., 1999).

A great deal of this section of the physiological research has been carried out with laboratory animals. Maturation of the suckling rat intestine by polyamines was recently thoroughly reviewed by Dandrifosse (2009b). In early-weaned piglets, dietary polyamines did not significantly modify the gut mucosal levels of PUT, SPD and SPM (Sabater-Molina et al., 2009).

Effects as Antioxidants

Polyamines, preferably SPD and SPM, were proved to be the effective antioxidants participating in the reduction of cell membranes and DNA damage. The three polyamines and also cadaverine at physiological concentrations were reported as potent scavengers of hydroxyl radicals (\(\bullet\cdot OH\)). Moreover, SPD and SPM also partially quenched singlet oxygen (\(^1\text{O}_2\)). These radicals damage membranes and are involved in inflammation, lipid peroxidation and oxygen toxicity (Das and Misra, 2004). Antioxidative activity of SPD and SPM was found also against hydrogen peroxide (Farriol et al., 2003; Rider et al., 2007) and reactive aldehydes (Bellé et al., 2004). Nevertheless, SPD and SPM can act as pro-oxidants and enhance oxidative damage to DNA components in the presence of free iron ions and hydrogen peroxide (Mozdzan et al., 2006).

Further Effects

The polyamines are involved in events inherent to genetically programmed cell death. Numerous links were identified between the polyamines and apoptic pathways, however, a lot of unresolved questions have endured (Seiler and Raul, 2005). Exogenously administered polyamines were proved to possess anti-inflammatory activity in acute and chronic
inflammation. The effect can be attributed to their antioxidant and/or lysosomal stabilization properties (Lagishetty and Naik, 2008).

The polyamines are also implicated in bone growth and development. Tjabringa et al. (2008) reported that SPM regulates differentiation of adipose tissue-derived mesenchymal stem cells along the osteogenic lineage.

Etiology and pathology of mental disorders, namely schizophrenia, mood disorders, anxiety and suicidal behavior, are another field of the polyamine research. Fiori and Turecki (2008) conclude that the polyamine pathway represents an important frontier for the development of neuropharmacological treatments.

In a review, Rhee et al. (2007) concluded that the polyamines could function as primordial stress molecules from bacteria to mammals, and might play an essential role in regulation of pathogen-host interactions.

The polyamines, especially SPM, play an important role in the allergy prevention in children, mainly by the regulation of food-allergens uptake by the intestine. They affect both the innate and acquired immunity (Dandrifosse and Dandrifosse, 2009).

Toxicity, Risk of Nitrosamines Formation

Oral acute toxicity of the individual polyamines, determined in Wistar rats, was observed to be 2000, 600 and 600 mg kg\(^{-1}\) body weight for PUT, SPD and SPM, respectively. The no-observed-adverse-effect level (NOAEL) was 180, 83 and 19 mg kg\(^{-1}\) body weight for PUT, SPD and SPM, respectively (Til et al., 1997). Such extreme intakes of dietary amines cannot be imagined.

Spermidine or putrescine can react under acidic conditions with nitrous acid forming \(N\)-nitrosopyrrolidine. Nevertheless, information on this reaction in foods has been very scarce and nitrosamines formation from polyamines does not seem to pose a health risk.

Levels in Human Blood

As results from data collected by Ducros et al. (2009), usual concentrations are 8-14 and 5-8 nmol ml\(^{-1}\) of packed red cells for SPD and SPM, respectively. Levels of the polyamines in red blood cells change during the early stage of acute pancreatitis, correlating with the extent of pancreatic necrosis (Jin et al., 2009).

Different results were reported on the polyamine level changes in blood of volunteers following one-shot or long-term consumption of dietary polyamines. While polyamines contained in orange juice did not affect significantly the polyamine levels in blood during up to 3 hours after ingestion (Acheampong et al., 2009), daily intake of polyamine-rich fermented soybean product natto for two months increased blood polyamine levels by a factor of 1.39 (Soda et al., 2009).

Polyamines in Foods

Due to various biological roles of the polyamines mentioned above, reliable information on their content in foods and beverages has been needed for dieticians and physicians. Data available up to 2004 were collected in the review article (Kalač and Krausová, 2005) based on
comprehensive list of references. Only the more recently published papers, mostly with original results, will be therefore cited in the following sections.

Terms high and very high content or level will be used for tens mg kg\(^{-1}\) and above 100 mg kg\(^{-1}\) of the polyamines, respectively.

The polyamines are present in cells in free, bound and conjugated forms. In plant tissues, polyamines are bound covalently to a partner molecule such as phenolic compounds or membrane phospholipids and can be released by hydrolysis with a strong acid. Some binding, preferably with proteins, can be supposed in animal tissues; however, proven information is lacking. Most of the accessible data do not differentiate free and conjugated polyamines in foods.

Spermidine and spermine in foods originate from raw plant and animal tissues; a limited proportion may be formed by the present microbiota. Commonly, increased SPD and SPM levels may be supposed in young and quickly growing organisms and mainly in metabolically highly active tissues and organs (Nishimura et al. 2006). Higher PUT levels in fresh food raw materials are rare, but do exist in some items of plant origin. Putrescine contents increase, even considerably, due to the high activity of several groups of bacteria, mainly Enterobacteriaceae and Clostridium spp. under inappropriate storage and handling conditions.

The polyamines are very stable compounds which resist heat and survive acidic or alkaline conditions.

**Intake of Dietary Polyamines**

Mean daily intake of 18.7, 12.6 and 11.0 mg of PUT, SPD and SPM, respectively, was reported for the United Kingdom, Italy, Spain, Finland, Sweden and the Netherlands (Ralph et al. 1999). The values adopted for Japan were 9.9, 12.0 and 7.9 mg (Nishibori et al. 2007) and for a USA convenient sample diet 14.0, 7.9 and 7.2 mg were selected (Zoumas-Morse et al., 2007).

Comparing dietary polyamine intake in Europe (France, United Kingdom, Sweden, Italy, Germany and the Netherlands), USA and Japan, Weiger et al. (2005) reported high polyamine intake from similar European and USA diet (Western style of the nutrition), while the Japanese diet represented the significantly lower source. Putrescine was the major polyamine in all three diets, but at a lower level in Japan. Intake of SPM was comparable in all diets, and that of SPM was lowest again in Japan.

The cited papers state dairy products due to high PUT level as the main source of polyamines intake in Europe and USA, while vegetables in Japan, where is a low consumption of cheeses. Vegetables are the main source of SPD, while SPM originates mainly from meat and meat products.

The role of dietary polyamines intake increases in the young during intensive growth and in elderly people along with a decreasing ability to biosynthesize them due to diminishing activity of key enzyme ornithine decarboxylase (see Figure 3).

**Recent Original Papers with Overall Data**

Several papers dealing with polyamine content in wide range of food items were published during last years (Nishimura et al., 2006; Cipolla et al., 2007; Nishibori et al., 2007;
Saaid et al., 2009). Some of the published data confirmed previously available results, some of them brought new information, which will be inserted in the following sections.

However, the published data both in these and previously published papers give mostly results of analyses of a limited number of samples, usually 2-5, per food item. It should be noted here that polyamine contents vary widely within an item. Moreover, most of the data are given for fresh foods or raw materials, while information on the effects of various storage conditions and industrial and culinary treatments has been very limited.

Spermine contents are commonly higher in foods of animal origin than those of SPD, what is the inverse relation than that observed in most materials of plant origin.

### Polyamines in Foods of Animal Origin

#### Meat of Warm-Blooded Animals

Literature data on polyamines content in raw and processed beef, pork and in meat products available until 2005 were reviewed (Kalač, 2006). Thus, only new results with at least five samples per item are given in Table 1 for fresh meat and in Table 2 for fresh pluck/giblets and slaughter by-products. Putrescine contents were usually below the limit of detection of the used analytical methods with bovine liver being an exception.

Among various meats (Table 1), very low, often undetectable levels of SPD are characteristic for beef and pork. Data for veal and lamb have been yet limited. The elevated SPD levels of about 10 mg kg⁻¹ were reported for chicken meat. Mean SPD content of 27.4 mg kg⁻¹ in fresh chicken breasts (Moreira et al., 2008) exceeded the other reported values. Usual SPM contents vary between 20 and 30 mg kg⁻¹ in meats of big slaughter animals. Higher levels are reported in chicken meat, however, extremely low content of only 1.6 mg kg⁻¹ was determined by Cipolla et al. (2007).

The contents of both SPD and SPM in pluck, giblets and slaughter by-products (Table 2), which are consumed in some countries, are commonly higher than contents in meats. The extreme levels of both the polyamines were reported for porcine pancreas. These data are in accord with commonly accepted notion that metabolically active tissues have elevated polyamine levels. Pluck and giblets thus are among items with the highest polyamine contents observed in food. The higher SPD content than that of SPM in bovine liver and also in porcine pancreas, and comparable levels of both the polyamines in porcine spleen leave the usual line between SPD and SPM relation in foods of animal origin.

Data on polyamine changes in beef, pork, chicken meat and porcine liver and kidney under various storage conditions and thermal processing became available during the period since 2006.

Under cold conditions, three ways of storage were tested (i) aerobic packaging in a foil, simulating household practice, (ii) vacuum packaging and (iii) packaging under a modified atmosphere. A mixture of 70% N₂ and 30% CO₂, v/v, was used for beef and pork loins and porcine livers packaging, while a mixture of 20% CO₂ and 80% O₂, v/v, for chicken breasts. The overall results are given in Table 3. Both the polyamines were more stable in beef and pork than in chicken meat and especially than in porcine kidney and liver. Comparable results for SPD and SPM in chicken breasts stored aerobically or under modified atmosphere (30% CO₂ and 70% O₂, v/v) at 4 °C up to 17 days were reported by Balamatsia et al. (2006), while PUT level markedly increased.
The Roles of Dietary Polyamines in Human Health and their Occurrence in Foods

Table 1. Contents of polyamines (mg kg⁻¹) in fresh meat. Putrescine contents were only rarely quantifiable by the analytical methods used. Spermine contents were detectable only in a limited proportion of samples.

<table>
<thead>
<tr>
<th>Product</th>
<th>n</th>
<th>Spermidine</th>
<th>Spermine</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>x</td>
<td>sx</td>
<td>r</td>
<td>x</td>
</tr>
<tr>
<td>Beef</td>
<td>63</td>
<td>-</td>
<td>ND-2.9</td>
<td>21.7</td>
</tr>
<tr>
<td>Sirloin</td>
<td>57</td>
<td>-</td>
<td>ND-2.4</td>
<td>22.0</td>
</tr>
<tr>
<td>Rump</td>
<td>10</td>
<td>2.5</td>
<td>-</td>
<td>28.4</td>
</tr>
<tr>
<td>Unspecified</td>
<td>5</td>
<td>2.3</td>
<td>1.2-4.1</td>
<td>31.1</td>
</tr>
<tr>
<td>Veal</td>
<td>10</td>
<td>4.0</td>
<td>-</td>
<td>20.3</td>
</tr>
<tr>
<td>Leg</td>
<td>15</td>
<td>-</td>
<td>ND-6.6</td>
<td>26.1</td>
</tr>
<tr>
<td>Pork</td>
<td>12</td>
<td>-</td>
<td>ND-5.3</td>
<td>28.4</td>
</tr>
<tr>
<td>Loin</td>
<td>72</td>
<td>3.0</td>
<td>1.1</td>
<td>20.7</td>
</tr>
<tr>
<td>- gilts</td>
<td>12</td>
<td>-</td>
<td>ND-5.6</td>
<td>18.3</td>
</tr>
<tr>
<td>Leg</td>
<td>15</td>
<td>-</td>
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<td>28.4</td>
</tr>
<tr>
<td>- gilts</td>
<td>17</td>
<td>-</td>
<td>ND-5.6</td>
<td>18.3</td>
</tr>
<tr>
<td>Unspecified</td>
<td>5</td>
<td>1.2</td>
<td>0.7-1.7</td>
<td>26.1</td>
</tr>
<tr>
<td>Lamb</td>
<td>10</td>
<td>5.8</td>
<td>-</td>
<td>26.5</td>
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<td>10</td>
<td>7.6</td>
<td>-</td>
<td>15.4</td>
</tr>
<tr>
<td>Chicken</td>
<td>10</td>
<td>7.6</td>
<td>-</td>
<td>15.4</td>
</tr>
<tr>
<td>Wing</td>
<td>10</td>
<td>9.3</td>
<td>-</td>
<td>23.2</td>
</tr>
<tr>
<td>Breast</td>
<td>30</td>
<td>27.4</td>
<td>1.9</td>
<td>38.7</td>
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<tr>
<td>Thigh</td>
<td>10</td>
<td>13.4</td>
<td>-</td>
<td>1.6</td>
</tr>
<tr>
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<td>Wing</td>
<td>20</td>
<td>-</td>
<td>ND-49.7</td>
<td>8.5</td>
</tr>
</tbody>
</table>

n ... number of samples; x ... mean; sx ... standard deviation; r ... range; ND ... content below limit of detection.

Table 2. Content of polyamines (mg kg⁻¹) in fresh pluck/giblets and by-products. Putrescine contents were often below limit of quantification of the analytical methods used.

<table>
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<tr>
<th>Product</th>
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<th>Spermine</th>
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<td>x</td>
<td>sx</td>
<td>r</td>
<td>x</td>
<td>sx</td>
</tr>
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<td>58</td>
<td>23.8</td>
<td>41.2</td>
<td>2.2-259</td>
<td>122</td>
</tr>
<tr>
<td>Young bull</td>
<td>19</td>
<td>25.4</td>
<td>17.8</td>
<td>4.1-63.0</td>
<td>161</td>
</tr>
<tr>
<td>Cow</td>
<td>19</td>
<td>32.1</td>
<td>11.6</td>
<td>13.5-56.6</td>
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<tr>
<td>Barrow</td>
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<td>31.8</td>
<td>11.5</td>
<td>14.3-56.5</td>
<td>114</td>
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<tr>
<td>Gilt</td>
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<td>31.2</td>
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<td>7.7-57.0</td>
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<td>ND-49.7</td>
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Table 2. (Continued)

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<td></td>
<td></td>
<td>x</td>
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<td>r</td>
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<td>Brown hare</td>
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<tr>
<td>Chicken</td>
<td>38</td>
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<td>-</td>
<td>56.9</td>
</tr>
<tr>
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<td>20</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Kidney Porcine</td>
<td>40</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>9.4</td>
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<td>-</td>
<td>-</td>
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<td>-</td>
<td>-</td>
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<td>-</td>
<td>-</td>
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<td>17.1</td>
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<td>Slaughter by-products</td>
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</tr>
<tr>
<td>Bovine tongue</td>
<td>10</td>
<td>1.1</td>
<td>-</td>
<td>-</td>
<td>6.6</td>
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<tr>
<td>Porcine lung</td>
<td>20</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>51.9</td>
</tr>
<tr>
<td>Porcine tongue</td>
<td>20</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>7.7</td>
</tr>
<tr>
<td>Porcine esophagus</td>
<td>20</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>11.8</td>
</tr>
<tr>
<td>Porcine pancreas</td>
<td>20</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>322.9</td>
</tr>
<tr>
<td>Chicken skin</td>
<td>10</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>11.4</td>
</tr>
</tbody>
</table>

n ... number of samples; x ... mean; sx ... standard deviation; r ... range; ND ... content below limit of detection.

Table 3. Losses of spermidine (SPD) and spermine (SPM) (% from the initial content in fresh packaged material) in meat and pluck after storage at 2-3 °C under different packaging conditions

<table>
<thead>
<tr>
<th>Storage period (d)</th>
<th>Aerobic packaging</th>
<th>Vacuum packaging</th>
<th>Modified atmosphere</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SPD</td>
<td>SPM</td>
<td>SPD</td>
<td>SPM</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>21</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Beef loin</td>
<td>min.</td>
<td>min.</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Pork loin</td>
<td>min.</td>
<td>min.</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>
The Roles of Dietary Polyamines in Human Health and their Occurrence in Foods

### Table 1

<table>
<thead>
<tr>
<th>Storage period (d) Material</th>
<th>Aerobic packaging</th>
<th>Vacuum packaging</th>
<th>Modified atmosphere</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SPD</td>
<td>SPM</td>
<td>SPD</td>
<td>SPM</td>
</tr>
<tr>
<td>Chicken breast</td>
<td>min.</td>
<td>min.</td>
<td>10</td>
<td>40</td>
</tr>
<tr>
<td>Porcine liver</td>
<td>20</td>
<td>20</td>
<td>40</td>
<td>25</td>
</tr>
<tr>
<td>Porcine kidney</td>
<td>30</td>
<td>40</td>
<td>60</td>
<td>60</td>
</tr>
</tbody>
</table>

min. ... minimal losses.

Results on polyamine changes during several-month storage at –18 °C are not uniform. Spermine content in beef loin slightly increased during initial two months of storage and then decreased by about 30% (in all referred values given as percentage from the initial content in fresh material prior to freezing) after six-month storage period (Kozová et al. 2009b), while in pork loin, the changes were insignificant (Krausová et al. 2008). Contradictory changes were reported for chicken meat. Kozová et al. (2009a) observed an increase of both SPD and SPM contents after six months of frozen-storage, whereas Moreira et al. (2008) determined heavy shrinkage of 70 and 80% for SPD and SPM, respectively, after three-month storage. Krausová et al. (2007) reported losses of about 30% in porcine liver frozen for six months. Thus, a further research is needed to elucidate the differing data.

The effects of various culinary thermal treatments on changes in the polyamine contents were reported for beef loin (Kozová et al. 2009b), pork loin (Paulsen et al. 2006; Paulsen and Bauer 2007; Krausová et al. 2008), chicken breast (Kozová et al. 2009a), porcine liver (Krausová et al. 2007) and porcine kidney (Kozová et al. 2008). Overall, losses of both SPD and SPM were usually about 40 %. Shrinkage at lower temperature processing, such as boiling, stewing or grilling seems to be lower than that caused by frying or roasting. No polyamines were detected in broth and grease.

Unfortunately, no data are recently available on the nature of the polyamine losses during meat - and indeed all food - storage and processing. The knowledge available on the polyamines catabolism in living cells cannot be applied on processes in food materials.

**Meat Products**

As resulted from the mentioned review (Kalač, 2006), research reports on the polyamine changes during production and storage of various meat products brought miscellaneous information. There were articles reporting mostly an increase of PUT content, while a decrease, stability or an increase of SPD and SPM contents.

Only several original papers dealing with meat products were published on the topic during the period since 2006. The contents of SPD and SPM in freshly prepared products prior to fermentation and drying fit well with data of Table 1 for beef and pork. Putrescine content usually increased to levels of tens or hundreds mg kg\(^{-1}\) in final products. In several types of dry-fermented sausages, an increase of SPD and SPM during processing was reported. However, the increase could be due to water losses, as the contents of both polyamines were not corrected to original dry matter content (Ruiz-Capillas et al., 2007; Genccelep et al., 2007; Lorenzo et al., 2008; Kurt and Zorba, 2009). Nevertheless, Komprda et al. (2009) found in dry fermented sausages stable content of SPD, while a steady decrease of SPM from 35 to 20 mg kg\(^{-1}\) during ripening and following storage.
The effects of five experimental variants of storage at 4 °C (aerobic, under vacuum, packed in a barrier film, and under two modified atmospheres) was tested in smoked turkey breast fillets up to 30 days. Levels of PUT, SPD and SPM increased only slightly, with an exception of significant increase of SPM content under the aerobic storage conditions (Ntzimani et al., 2008).

**Fish, Shellfish and Seafoods**

As results from the reviewed data until 2004 (Kalač and Krausová, 2005), recent original papers (Nishimura et al., 2006; Cipolla et al., 2007; Nishibori et al., 2007; Saaid et al., 2009) and a review (Kržízek, 2009), the polyamine content in the flesh of both sea and freshwater fish is very low after capture. Elevated polyamine contents were reported in anchovies, dried sardines, scallops (PUT), shrimp sauce and mainly in roe and viscera. Kim et al. (2009) determined SPD and SPM contents in the order of tens mg kg⁻¹ in some squid and shellfish species.

Putrescine content can increase considerably during an inappropriate storage and handling conditions together with levels of histamine (HIM) and cadaverine (CAD), while contents of SPD and SPM remain relatively stable. Based on these changes, Mietz and Karmas proposed already in 1978 biogenic amine index (BAI) as a criterion of fish and shellfish quality:

\[
\text{BAI} = \frac{(\text{PUT} + \text{CAD} + \text{HIM})}{(1 + \text{SPD} + \text{SPM})},
\]

where the contents of amines are given in mg kg⁻¹. BAI value of 10 is the limit of fish acceptability.

**Milk and Milk Products**

As reviewed by Michaelidou (2008), the content of all polyamines in cow, ewe, goat and also in human milks are very low. It was proved by the recent data of Cipolla et al. (2007) and Nishibori et al. (2007). Thus, very low levels are typical also for many milk products. As in other proteinaceous materials, PUT content can increase considerably by bacterial activity not only due to inappropriate processing and storage conditions, but also by the activity of some lactic acid bacteria during the making of ripening cheeses. For an illustration see data of Table 4. Using of raw or pasteurized milk for a cheese production seems to be a very important factor affecting PUT content in cheese (for a review see Kalač and Glória, 2009). Spermidine contents in cheeses are commonly higher than that of SPM. Such situation is rather unusual in products of animal origin. It has not yet been known origin of the polyamines present, as a part of them may be a constituent of microbiota (e.g. of cultural molds used for the making of some cheeses).

Polyamine level is higher in mother milk than in milk powders for babies. Human milk has the most probably a protective effect against allergies.

**Eggs**

Hen eggs contain only negligible levels of SPD and SPM and very low content of PUT, preferably in yolk (Cipolla et al., 2007; Nishibori et al., 2007; Ramos et al., 2009).
Table 4. Median values and ranges of polyamines (mg kg\(^{-1}\)) in five types of Spanish cheeses (n = 20 in each type). Adapted from Novella-Rodríguez et al. (2003)

<table>
<thead>
<tr>
<th>Cheese type / Polyamine</th>
<th>Putrescine Median</th>
<th>Putrescine Range</th>
<th>Spermidine Median</th>
<th>Spermidine Range</th>
<th>Spermine Median</th>
<th>Spermine Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unripened</td>
<td>0.0</td>
<td>ND-3.1</td>
<td>0.3</td>
<td>ND-0.8</td>
<td>0.0</td>
<td>ND-1.1</td>
</tr>
<tr>
<td>Hard-ripened from pasteurized cow milk</td>
<td>5.0</td>
<td>ND-612</td>
<td>5.7</td>
<td>ND-43.0</td>
<td>1.6</td>
<td>ND-18.7</td>
</tr>
<tr>
<td>Hard-ripened from raw cow and ewe milks</td>
<td>8.1</td>
<td>ND-670</td>
<td>0.1</td>
<td>ND-39.6</td>
<td>0.0</td>
<td>ND-21.5</td>
</tr>
<tr>
<td>Goat cheese from pasteurized milk</td>
<td>4.1</td>
<td>ND-192</td>
<td>0.9</td>
<td>ND-14.5</td>
<td>0.0</td>
<td>ND-3.6</td>
</tr>
<tr>
<td>Blue from pasteurized ewe milk</td>
<td>18.0</td>
<td>3.0-257</td>
<td>10.1</td>
<td>ND-71.6</td>
<td>0.0</td>
<td>ND-18.9</td>
</tr>
</tbody>
</table>

ND ... not detectable.

Polyamines in Foods of Plant Origin

As mentioned above, vegetables and fruits are the main sources of PUT intake, and vegetables that of SPD intake. Spermine levels are usually low in foods of plant origin. Data on the proportion of free, soluble and insoluble conjugated polyamines have been very limited. In a recent publication with such information, Righetti et al. (2008) reported free form as the prevailing in soybean and Jerusalem artichoke. A part of polyamines conjugates with hydroxycinnamic acids forming amides.

As in previous sections, data until 2004 were reviewed (Kalač and Krausová, 2005).

Cereals, Legumes and Potato

In cereals and cereal products, data until 2004 reported low levels of PUT and SPM and mean SPD content about 10 mg kg\(^{-1}\). Recent papers (Cipolla et al., 2007; Nishibori et al., 2007) give similar results. Contents of all polyamines are commonly very low in rice, while an initial information on black rice (Oryza sativa subsp. javanica) and rice bran point out considerably elevated levels (Nishimura et al., 2006). The same authors reported also relatively high PUT and SPD contents in corn and very high levels of SPD and SPM in wheat germ. According to Cipolla et al. (2007), soft wheat has higher contents of all polyamines than semolina.

Legumes contain commonly tens mg kg\(^{-1}\) of PUT and SPD, while SPM levels are lower. Soybean and some fermented soy products (e.g. natto or soy sauce) are very rich in all polyamines with prevailing SPD (Nishimura et al., 2006; Nishibori et al., 2007). The reported content of SPD often exceeds 100 mg kg\(^{-1}\).

Contents 10-20, 10-20 and below 5 mg kg\(^{-1}\) of PUT, SPD and SPM, respectively, are typical for potato tubers.

A proportion of polyamines, usually tens per cent of the initial content, leaches to cooking water. Unfortunately, no further recent information is available.

The increasing consumption of different germinated seeds induced a research on changes of biogenic amine and polyamine contents. Levels of all amines increased significantly during the germination. Spermidine and SPM accumulated in the cotyledone, whereas PUT in the radicle and hypocotyl of soybeans (Glória et al., 2005). Similar trend was observed in alfalfa sprouts, but in fenugreek (Trigonellum foenum-graecum) slightly increased only PUT, while SPD and SPM contents remained stable (Frias et al., 2007).
Fruits and Vegetables

Some of vegetal foods and beverages have a considerably high mean PUT level (above 30-40 mg kg\(^{-1}\)), namely oranges, mandarins and the processed vegetables sauerkraut, ketchup and frozen green peas.

Spermidine levels in fruits and vegetables, both of temperate and tropical origin, are commonly higher than SPM contents. For instance, SPD and SPM contents in 16 fresh vegetables varied in the ranges of 4-45 and traces-7 mg kg\(^{-1}\), respectively (Moret et al., 2005). Pear, broccoli and cauliflower belong to food items with elevated SPD content, usually above 30 mg kg\(^{-1}\).

Both SPD and SPM contents decreased, roughly by a half, during three-week storage of parsley, zucchini, broccoli and cucumber under refrigeration (Moret et al., 2005). Similar trend was observed in a study with spinach leaves stored at 6 °C for up to 15 days (Lavizzari et al., 2007). Initial mean contents were 28.9 ± 9.6 and 3.6 ± 1.8 mg kg\(^{-1}\) for SPD and SPM, respectively. While both SPD and SPM decreased considerably during storage, PUT level increased.

In broccoli and radish seeds, germinated for three and five days under conditions of minimally processed sprouts, content of all three polyamines increased as did levels of histamine and tyramine. However, no cytotoxic effect was observed (Martínez-Villaluenga et al., 2008). The changes are similar to those mentioned above for soy and alfalfa sprouts.

Mushrooms

Very high contents of SPD, often over 100 mg kg\(^{-1}\) fresh weight, were reported from Japan for several species of cultivated mushrooms (Nishimura et al., 2006; Nishibori et al., 2007). In 17 European species of wild-growing edible mushrooms, PUT was the prevailing amine, sometimes exceeding 150 mg kg\(^{-1}\) fresh weight, mainly in species of the family Boletaceae. Spermidine contents were usually at level of tens mg kg\(^{-1}\), sporadically above 100 mg kg\(^{-1}\) (Dadáková et al., 2009). All the papers reported low levels of spermine.

Beverages

According to reviewed literature data (Kalač and Glória, 2009), wines have limited PUT content, commonly below 10 mg l\(^{-1}\) (mostly below 5 mg l\(^{-1}\)), and negligible SPD and SPM levels. Very similar state was reported for several hundreds beer samples by numerous papers reviewed by Kalač and Křížek (2003) and Kalač and Glória (2009). Consonant results were currently published for Chinese beers (Tang et al., 2009).

Even lower levels of all the polyamines are typical for black tea (Palavan-Unsal et al., 2007), coffee (Oliveira et al., 2005; da Silveira et al., 2007) and cocoa. Thus, their infusions represent only negligible intake. To the contrary, orange and grapefruit juices have been usually ranked among putrescine-rich products. Recently, Vieira et al. (2007) reported mean PUT content 33.6 mg l\(^{-1}\) in orange juices of seven different brands. Nevertheless, some papers give low PUT content in these juices (e.g. Cipolla et al., 2007; Saaid et al., 2009).

Limited data on spirits indicate very low levels of all the polyamines.

Other Foods

Plant oils contain non-detectable levels of all the polyamines.
As follows from limited data, confectionery seems to be a very limited source of the polyamines. It goes also for chocolate, sometimes classed among putrescine-rich items.

**CONCLUSION**

Reliable recommendations on the dietary polyamine intake are so far complicated due to several limitations:

- daily cellular requirements for the polyamines have not yet been established,
- the polyamine content in a food item usually varies in a wide range,
- most of available data deal with fresh raw food materials, data on changes in the polyamine contents during storage and processing have been limited,
- data on the rate of the dietary polyamines absorption in the small intestine are limited. Nevertheless, it seems that they are readily taken up from the gut lumen.

**Table 5. List of foods with high polyamine content, which should be avoided or restricted in the nutrition of tumor-bearing patients.**

The foods within a group are arranged by decreasing polyamine content. The items with limited data or with awaited high polyamine contents are written in italic. The prevailing polyamines are given in parenthesis

<table>
<thead>
<tr>
<th>Foods of animal origin</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Meat and meat products</td>
<td>Pluck / giblets</td>
<td>Fish / seafood</td>
<td>Milk products</td>
</tr>
<tr>
<td>Chicken (SPM)</td>
<td>Bovine liver (SPD, SPM)</td>
<td>Roe (SPM, PUT)</td>
<td>Ripened cheeses (PUT)</td>
</tr>
<tr>
<td>Other poultry (SPM)</td>
<td>Liver of warm-blooded animals (SPM)</td>
<td>Viscera (SPM, PUT)</td>
<td></td>
</tr>
<tr>
<td>Beef (SPM)</td>
<td>Chicken giblets (SPM, SPD)</td>
<td>Fish and shrimp sauces (PUT)</td>
<td></td>
</tr>
<tr>
<td>Pork (SPM)</td>
<td>Kidney (SPM)</td>
<td>Dried sardines (SPD, SPM)</td>
<td></td>
</tr>
<tr>
<td>Meat products (SPM)</td>
<td>Spleen (SPM, SPD)</td>
<td>Scallops (PUT)</td>
<td></td>
</tr>
<tr>
<td>Meat of other warm-blooded animals</td>
<td>Other inner organs of warm-blooded animals</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Foods of plant origin</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cereals</td>
<td>Legumes</td>
<td>Vegetables</td>
<td>Fruits</td>
</tr>
<tr>
<td>Wheat germ (SPD)</td>
<td>Fermented soy products (SPD)</td>
<td>Mushrooms (SPD, PUT)</td>
<td>Oranges and juices (PUT)</td>
</tr>
<tr>
<td>Rice bran (SPM)</td>
<td>Soybean (SPD)</td>
<td>Sauerkraut (PUT)</td>
<td>Grapefruits and juices (PUT)</td>
</tr>
<tr>
<td>Black rice (PUT)</td>
<td>Green peas (SPD, PUT)</td>
<td>Ketchup (PUT)</td>
<td>Mandarins (PUT)</td>
</tr>
<tr>
<td></td>
<td>Cauliflower (SPD)</td>
<td>Broccoli (SPD)</td>
<td>Pears (SPD)</td>
</tr>
<tr>
<td></td>
<td>Spinach (SPD)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Bardócz et al. (1999), using data available until 1998, recommended a diet with low polyamine level and itemized foods and beverages, which should be avoided by patients with tumors. Based on the current state of knowledge, foods with high polyamine contents are listed in Table 5. Naturally, for the assessment of polyamine intake it is necessary to take into consideration quantity of each consumed food item. Some staple foods such as bread or
potato can thus contribute considerably to total daily polyamine intake despite their relatively low polyamine contents. Plant-based foods account for crucial part of human diet. As they contain relatively great amounts of putrescine and/or spermidine, they are a major contributor of polyamines to the body pool.

It is not easy to select polyamine-low food items, since there are not many foods with a really low polyamine content.

An increased availability of dietary polyamines is advantageous during periods where intensive growth is required, namely in wound healing, post-operative recovery, liver regeneration or compensatory growth of the lung or the gut.

Unfortunately, a possibility to set up credible “tabular values” of the polyamines even for staple foods remains still very constricted.

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**REFERENCES**


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