ELSEVIER

Food Chemistry 78 (2002) 273–280

Food Chemistry

www.elsevier.com/locate/foodchem

Dietary polyamines

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Received 8 November 2001; accepted 7 December 2001

Abstract

Dietary polyamines contribute to the total body polyamine pool. As polyamines are important in health and disease, it is of interest to obtain information on the food polyamine content, making it possible to calculate and manipulate the polyamine intake. In this study, meat was found to contain considerably higher amounts of polyamines than fresh fish, though the levels in fish increased rapidly upon storage and processing. Whereas some cheeses were generally high in polyamines, the content in other dairy products was low. Most fruits and vegetables normally contained low levels of polyamines, although spermidine was high in broccoli and cauliflower, and putrescine in citrus fruits. Cooking did not significantly alter the polyamine concentration. From a sensory and a nutritious point of view, these results provide a means to compose a diet high or low in polyamines.

Keywords: Polyamines; Putrescine; Cadaverine; Spermidine; Spermine; Food

1. Introduction

The polyamines putrescine, spermidine and spermine are intimately involved in cell proliferation and differentiation (Canellakis, Marsh, & Bondy, 1989; Heby, 1981; Heby et al., 1992; Jänne, Pösö, & Raina, 1978; Pegg & McCann, 1982).

Earlier it was believed that polyamines needed for growth were exclusively synthesized in situ. However, it is now apparent that polyamines are recruited from the diet and microorganisms residing in the intestinal tract (Bardócz, Grant, Brown, Ralph, & Pusztai, 1993, Bardócz, White, Grant, Brown, Duguid, & Pusztai, 1996; Moulinoux, Darcel, Quemener, Havouis, & Seiler, 1991; Osborne & Seidel, 1989, Sarhan, Knödgen, & Seiler, 1989). In chicks, small doses of orally administered putrescine promote whole body growth (Smith, 1990). In rats, exogenously supplied polyamines modulate mucosal growth, epithelial cell proliferation and ontological differentiation, activate brush border proteins (Seidel & Scemama, 1997), and change the intestinal postnatal enzyme pattern (Wild, Daly, Sauriol, & Bennett, 1993). In rat colon, polyamines also enhance the growth of azoxymethane induced aberrant crypt foci (Paulsen, Reistad, Eliassen, Sjaastad, & Alexander, 1997).

Uptake of polyamines by intestinal cells has been suggested to be an important regulatory mechanism of the intracellular polyamine concentration, and they are preferentially taken up by tumours and tissues with high demands for polyamines (Bardócz et al., 1993; Clark & Fair, 1975). Diamine oxidase, present in high concentrations in the intestinal mucosa, protects the animal against large amounts of histamine and putrescine from the intestinal lumen (Luk, Bayless, & Baylin, 1980, Nilsson, Kockum, & Rosengren, 1996; Shaff & Beaven, 1976). Aminoguanidine, a specific inhibitor of diamine oxidase, promotes the growth of large bowel tumours (Kusche, Horn, & Mennigen, 1992; Kusche, Menningen, Leisten, & Krakamp, 1988), demonstrating the importance of the enzyme.

Polyamines are strongly related to tumour growth (Seiler, Sarhan, Grauffel, Jones, Knödgen, & Moulinoux, 1990; Seiler, Atanassov, & Raul, 1998). The effect of polyamines in tumour promotion seems to come not only from a direct stimulating effect on growth and

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PII: S0308-8146(01)00405-8

differentiation, they also have an effect on the non-specific immune system specialized in tumour killing (Chamaillard, Quemener, Havouis, & Moulinoux, 1993), on the plasma concentration of interleukin-1 and -6, and on the tumour necrosis factor concentration (Kaouass, Deloyer, Gouders, Peulen, & Dandrifosse, 1997; Kaouass, Sulon, Deloyer, & Dandrifosse, 1994). Furthermore, putrescine and cadaverine can react with nitrite to form heterocyclic carcinogenic nitrosamines (Hotchkiss, 1989; Huis in't veld, Hose, Schaafsma, Silla, & Smith, 1990, Pfundstein, Tricker, Theobald, Spiegelhalder, & Preussmann, 1991; Silla Santos, 1996).

A polyamine deprivation regime in combination with inhibitors of ornithine decarboxylase and polyamine oxidase, and antibiotics suitable for the partial decontamination of the gastrointestinal tract, have been shown to reduce the growth of several solid tumours (Sarhan, Knödgen, & Seiler, 1992). Furthermore, alternating treatment with well-established cytotoxic drugs and polyamine deprivation significantly enhanced the efficacy of chemotherapy (Quemener, Moulinoux, Havouis, & Seiler, 1992).

Since a significant amount of polyamines required for proliferation and differentiation is provided by the diet (Bardócz et al., 1995), and thus appears to be important for cancer development and growth, it is of interest to examine the contents of individual polyamines in food. Relatively limited information on the polyamine contents of foods, often based on 2–3 samples, has been published. In the present study, we have concentrated on types of food commonly used in Norwegian households, even though some of the items have been analysed previously by other groups. These results have been included for comparative reasons, since both storage and processing, which vary greatly from one region of the world to another, have been shown to influence the polyamine contents (Huis in't Veld et al., 1990). To gain insight into the effect that cooking has on the polyamine content, some cooked food samples were included.

2. Materials and methods

2.1. Collection of foods

The food samples were bought mainly in grocery stores and supermarkets. Red wines were purchased at the state liquor monopoly.

2.2. Chemicals

Putrescine dihydrochloride, cadaverine dihydrochloride, spermidine trihydrochloride, spermine tetrahydrochloride, DL-proline, dansyl chloride and hexanediamine were purchased from Sigma Chemicals Co., St. Louis, MO, USA.

2.3. Assay of polyamines

Duplicate samples (10 g) of each food were homogenized in 20 ml 5% trichloroacetic acid (TCA), using an Ultra Turrax© homogenizer (25,000 rpm, 30 s). For liquid samples, 0.5 g TCA was added to 10 ml of each sample. Hexanediamine was added as an internal standard, and the homogenate was kept on ice for 30 min, followed by centrifugation at 4°C for 10 min at 10,000 × ***g***. Polyamines in the supernatant were converted to their dansyl derivatives by the method of Seiler and Wiechmann (1967), including the modifications described by Smith and Best (1977), and then separated by high performance liquid chromatography (Seiler, Knödgen, & Eisenbeiss, 1978) on a Radial-Pac-A© column (Waters, Milford, MA, USA) using a linear methanol/water gradient (Brodal, Eliassen, Rønning & Osmundsen, 1999).

Unprocessed and processed foods in our investigation are directly comparable, as the food items were split into two parts prior to further treatment. One was treated with TCA directly, the other processed before treatment with TCA, both being followed by polyamine analyses.

Cooking was carried out as in regular Norwegian households, and polyamine concentrations of these samples are based on the weight of cooked food. Foods were weighed both before and after processing, and a small per cent reduction in weight was noted during the cooking procedure for some items. The results for the processed foods did not significantly differ from the unprocessed items; therefore, no further testing was performed.

2.4. Statistical analyses

The StatView SE + program (Abacus Concepts, Inc., Berkeley, CA, USA) was used for the statistical analyses.

3. Results

3.1. General

The results of the polyamine analyses are shown in Table 1. Unless otherwise stated, the results are shown for raw/unprocessed foods. If processed items were tested, the results immediately follow the figures for the unprocessed foods. Our results are presented in bold type, while results for the same items published by others are in italics. The list is not complete, as concentrations of polyamines in some investigations were not recorded in nmol/g, and insufficient information prevented recalculations.

Cooking did not significantly alter the composition and concentration of polyamines in most of the investigated foods (Table 1).

Table 1
Polyamine contents in various foods[a]

Food item	*n*	Polyamine concentration (nmol/g)								Reference
		Putrescine		Cadaverine		Spermidine		Spermine		
		Mean ± S.D.	Range	Mean ± S.D.	Range	Mean ± S.D.	Range	Mean ± S.D.	Range	
MEAT										
Beef	**5**	**115 ± 162**	**9–437**	**286 ± 251**	**3–648**	**38 ± 22**	**18–83**	**135 ± 22**	**116–179**	
Beef	*2*	*6*		*100*[b]		*18*		*140*		Okamoto et al. (1997)
Beef	*1*		*169–187*				*19–21*		*175–197*	Bardócz et al. (1995)
Beef	*3*		*63–67*				*126–136*		*152–208*	Bardócz et al. (1993)
Beef, fried	**2**	**144**	**16–343**	**271**	**20–555**	**29**	**18–39**	**150**	**129–179**	
Beef, cooked	*1*		*56–58*				*26–28*		*104–122*	Bardócz et al. (1995)
Beef, cooked	*3*		*22–32*				*39–47*		*113–165*	Bardócz et al. (1993)
Sirloin	**7**	**24 ± 36**	**7–145**	**34 ± 52**	**0–197**	**15 ± 4**	**7–21**	**84 ± 33**	**30–144**	
Sirloin, fried	**1**	**16**	**15–17**	**21**	**19–23**	**14**	**9–19**	**132**	**123–141**	
Ground beef	**8**	**46 ± 65**	**9–212**	**97 ± 126**	**0–386**	**21 ± 5**	**15–33**	**103 ± 18**	**66–132**	
Ground beef	*3*		*100–101*				*487–503*		*229–235*	Bardócz et al. (1993)
Ground beef, fried	**2**	**27**	**17–31**	**28**	**25–34**	**27**	**20–33**	**145**	**116–168**	
Pork chops	**5**	**2 ± 3**	**0–8**	**1 ± 3**	**0–9**	**19 ± 5**	**14–28**	**111 ± 37**	**72–171**	
Pork	*2*	*13*		*< 5*[b]		*32*		*140*		Okamoto et al. (1997)
Pork	*3*		*34–35*				*20–34*		*149–348*	Bardócz et al. (1993)
Pork	*10*	*8*[c]	*n.d.–8*[c]	*23*[c]	*n.d.–46*[c]	*16*[c]	*12–31*[c]	*152*[c]	*95–198*[c]	Nakamura, Wada, Sawaya, and Kawabata (1979)
Pork chops, fried	**1**	**21**	**9–32**	**28**	**0–55**	**19**	**17–21**	**151**	**146–155**	
Sausage, wiener	**5**	**10 ± 3**	**4–13**	**33 ± 47**	**4–121**	**16 ± 5**	**8–24**	**49 ± 10**	**25–62**	
Sausage, meat	*3*		*157–165*				*40–44*		*119–128*	Bardócz et al. (1993)
Chicken	*2*	*< 5*		*< 10*[b]		*20*		*310*		Okamoto et al. (1997)
Chicken	*3*		*32–33*				*63–65*		*291–296*	Bardócz et al. (1993)
Chicken, grilled	**5**	**23 ± 5**	**15–31**	**34 ± 19**	**0–68**	**119 ± 27**	**91–177**	**220 ± 30**	**167–263**	
FISH										
Cod	**9**	**16 ± 10**	**6–35**	**27 ± 23**	**1–72**	**4 ± 6**	**0–26**	**3 ± 4**	**0–11**	
Cod	*3*		*300–337*				*7–11*		*15–32*	Bardócz et al. (1993)
Cod, salted	**5**	**56 ± 34**	**24–109**	**327 ± 257**	**85–685**	**10 ± 7**	**0–17**	**13 ± 8**	**0–19**	
Cod roe	**6**	**1033 ± 202**	**901–1469**	**289 ± 528**	**21–1422**	**94 ± 29**	**54–130**	**99 ± 32**	**49–133**	
Salmon	**9**	**31 ± 11**	**18–52**	**25 ± 34**	**0–114**	**10 ± 5**	**3–23**	**4 ± 4**	**0–16**	
Salmon	*9*	*57 ± 35*[c]		*166 ± 228*[c]		*19 ± 7*[c]		*34 ± 30*[c]		Mietz and Karmas (1978)
Salmon, cooked	**1**	**29**	**28–30**	**8**	**6–9**	**31**	**29–33**	**24**	**20–27**	

(continued on next page)

Food item	n	Polyamine concentration (nmol/g)								Reference
		Putrescine		Cadaverine		Spermidine		Spermine		
		Mean±S.D.	Range	Mean±S.D.	Range	Mean±S.D.	Range	Mean±S.D.	Range	
Mackerel	**7**	**27±8**	**15–40**	**39±25**	**10–82**	**18±6**	**11–28**	**15±12**	**0–38**	
Mackerel–in–tomato, canned	**5**	**84±24**	**44–110**	**24±27**	**0–76**	**21±8**	**10–30**	**7±7**	**0–21**	
Tuna, canned	**10**	**64±81**	**15–289**	**111±52**	**16–202**	**37±11**	**13–55**	**39±8**	**26–51**	
Tuna	*2*	*n.d.*		*n.d.*[b]		*30*		*34*		Okamoto et al. (1997)
Crab, canned	**2**	**1386**	**1245–1526**	**43**	**38–48**	**9**	**8–10**	**11**	**10–11**	
FRUITS AND VEGETABLES										
Mandarin	**10**	**1382±502**	**765–2269**	**70±9**	**0–212**	**16±9**	**0–31**	**2±4**	**0–15**	
Mandarin orange	*1*		*13–15*				*18–20*		*2–3*	Bardócz et al. (1995)
Orange	**5**	**1556±128**	**1353–1733**	**n.d.**	**n.d.**	**28±27**	**3–80**	**1±2**	**0–7**	
Orange	*2*	*1330*		*n.d.*[b]		*13*		*8*		Okamoto et al. (1997)
Orange	*3*		*1081–1579*				*61–67*		*0*	Bardócz et al. (1993)
Tomato	**5**	**251±92**	**108–375**	**1±2**	**0–5**	**28±5**	**22–37**	**1±2**	**0–7**	
Tomato	*2*	*120*		*45*[b]		*12*		*n.d.*		Okamoto et al. (1997)
Tomato	*3*		*106–1386*				*11–17*		*0*	Bardócz et al. (1993)
Cucumber	**5**	**78±16**	**62–99**	**4±2**	**0–6**	**51±11**	**37–71**	**6±4**	**0–14**	
Cucumber	*3*		*36–37*				*10–11*		*1–3*	Bardócz et al. (1993)
Lettuce	**3**	**64±15**	**51–83**	**n.d.**	**n.d.**	**63±10**	**51–71**	**4±4**	**0–9**	
Lettuce (Iceberg)	*2*	*33*[c]		*n.d.*[c]		*31*[c]		*<1*[c]		Simon-Sarkadi and Holzapfel (1994)
Lettuce	*3*		*37–55*				*29–57*		*0*	Bardócz et al. (1993)
Carrot	**6**	**17±8**	**8–31**	**n.d.**	**n.d.**	**46±16**	**25–82**	**3±6**	**0–19**	
Carrot	*2*	*40*		*n.d.*[b]		*55*		*n.d.*		Okamoto et al. (1997)
Carrot	*3*		*14–20*				*53–57*		*10–14*	Bardócz et al. (1993)
Carrot, cooked	**4**	**17±9**	**7–31**	**n.d.**	**n.d.**	**46±13**	**36–67**	**4±7**	**0–17**	
Broccoli	**5**	**73±33**	**39–123**	**5±4**	**0–12**	**285±63**	**169–357**	**49±16**	**29–79**	
Broccoli, cooked	**4**	**64±33**	**29–101**	**1±2**	**0–5**	**188±44**	**119–228**	**35±7**	**26–44**	
Cauliflower	**5**	**60±24**	**37–101**	**5±4**	**0–10**	**195±45**	**147–271**	**30±8**	**23–44**	
Cauliflower	*3*		*35–51*				*150–192*		*48–64*	Bardócz et al. (1993)
Cauliflower, cooked	**4**	**45±14**	**30–67**	**2±2**	**0–5**	**181±73**	**131–312**	**31±14**	**22–56**	

Potato	**6**	**110±24**	**66–145**	**7±4**	**0–13**	**78±12**	**57–94**	**13±6**	**4–20**	
Potato	*2*	*200*		*12*[b]		*93*		*n.d.*		Okamoto et al. (1997)
Potato	*3*		*108–112*				*76–78*		*14–16*	Bardócz et al. (1993)
Potato, cooked	**4**	**97±26**	**64–141**	**6±6**	**0–18**	**75±15**	**63–108**	**11±6**	**0–17**	
Potato, cooked	*3*		*229–261*				*101–109*		*24–28*	Bardócz et al. (1993)
DAIRY PRODUCTS AND BREAD										
Bread, whole grain	**5**	**39±5**	**28–46**	**1±2**	**0–6**	**90±10**	**70–102**	**31±10**	**17–43**	
Bread, whole wheat grain	*3*		*6–10*				*147–189*		*35–45*	Bardócz et al. (1993)
Yoghurt, plain	**5**	**3±4**	**0–10**	**2±3**	**0–8**	**5±4**	**0–9**	**4±5**	**0–11**	
Yoghurt, plain	*2*	*<5*		*n.d.*[b]		*n.d.*		*n.d.*		Okamoto et al. (1997)
Brown cheese	**5**	**1±2**	**0–5**	**n.d.**	**n.d.**	**1±2**	**0–5**	**0±1**	**0–2**	
Cheese, yellow:										
Norvegia	**5**	**30±54**	**0–131**	**30±13**	**7–50**	**5±5**	**0–12**	**8±5**	**2–14**	
Norvegia, matured	**1**	**83**	**81–84**	**90**	**79–100**	**n.d.**	**n.d.**	**14**	**13–14**	
Gouda	*2*	*n.d.*		*n.d.*[b]		*n.d.*		*n.d.*		Okamoto et al. (1997)
Cheddar, fresh	*3*		*115–227*				*557–751*		*118–194*	Bardócz et al. (1993)
Cheddar, matured	*3*		*7409–7427*				*1361–1392*		*115–198*	Bardócz et al. (1993)
Cheese, blue:										
Saga	**2**	**137**	**74–212**	**58**	**42–69**	**103**	**16–193**	**10**	**0–20**	
Normanna	**3**	**186±31**	**143–230**	**294±62**	**248–413**	**164±28**	**139–202**	**2±4**	**0–10**	
Blue	*2*	*77*		*n.d.*[b]		*140*		*n.d.*		Okamoto et al. (1997)
Woodward's Stilton	*3–6*	*782*[c]		*66*[c]		*23*[c]		*3*[c]		Baker, Wong, Coutts, and Pasutto (1987)
BEVERAGES										
Juice, orange:										
Fresh, w/ pulp	**3**	**966±129**	**870–1139**	**n.d.**	**n.d.**	**17±6**	**13–26**	**n.d.**	**n.d.**	
Preserved	**3**	**621±30**	**583–652**	**n.d.**	**n.d.**	**13±1**	**12–14**	**n.d.**	**n.d.**	
Wine, red	**8**	**132±167**	**22–557**	**10±4**	**5–19**	**5±3**	**0–9**	**n.d.**	**n.d.**	
Wine, red	*2*	*33*		*11*[b]		*<5*		*n.d.*		Okamoto et al. (1997)

[a] Our results are presented in bold. Results from the literature are in italics. n.d., not detected.
[b] Cadaverine and/or histamine.
[c] Results recalculated from μg/g.

3.2. Meat

Beef contained higher, yet variable, concentrations of polyamines, especially putrescine and cadaverine, as compared to other types of meat. Spermine and spermidine were fairly uniformly distributed among the various meat types, with higher spermine values than in most of the other foods examined. Meat from grilled chicken was high also in spermidine.

3.3. Fish

Fresh fish was low in all polyamines, but apparently vulnerable to storing and preservation, since increased polyamine concentrations could be found in salted cod. Cod roe, however, was especially high in putrescine.

3.4. Fruits and vegetables

Orange and mandarin were the only fruits investigated, both containing very high amounts of putrescine. As for meat and fish, only small differences in polyamine concentrations were noted between raw and cooked vegetables. As expected, they were almost devoid of cadaverine, a product of mainly microbial origin. Carrots were low in all polyamines, while the spermidine content in broccoli and cauliflower was higher than in either meat or fish.

3.5. Dairy products and bread

Plain yoghurt was practically devoid of polyamines, while the contents in blue cheeses were rather high. The special Norwegian brown "cheese", which is made from whey and thus not a genuine cheese, was almost devoid of polyamines. Whole wheat bread (Kneipp) contained some spermidine, with only low concentrations of the other polyamines.

3.6. Beverages

Fresh orange juice was high in putrescine, and only slightly lower than that of the fruit itself, while the polyamine level in preserved juice was about 30% lower.

Two of the eight red wines tested contained rather high concentrations of putrescine; otherwise, the polyamine levels were at or below the detection level.

4. Discussion

The polyamine concentration of each food item varied somewhat from sample to sample, most likely due to conditions related to production, transport and storage.

In the present study, the polyamine analyses of fish, meat and meat products confirmed the results obtained from previous investigations for most of the food items (Bardócz et al., 1993; 1995, Okamoto, Sugi, Koizumi, Yanagida, & Udaka, 1997). However, we found a significantly lower level of spermidine and spermine in ground beef, and of putrescine in cod than did Bardócz et al. (1993), probably due to the different levels of bacterial contamination, as indicated in our analyses by the presence of cadaverine, which is not normally found in mammalian tissues (Pegg, 1986).

Bardócz et al. (1993) found relatively high levels of putrescine in cod, while our results showed that fresh fish was low in all polyamines. On the other hand, lightly salted cod had a relatively high content of cadaverine, indicating that treatment and storage influence the amine levels. The present study also included a few fish samples where the effect of storage was examined. Four to five days storage at 4 °C of fresh and lightly salted cod resulted in a significant increase in the putrescine and cadaverine levels, while similar treatments of salmon and mackerel resulted in only slight changes in the polyamine concentrations (results not shown). However, in rainbow trout, Dawood, Karkalas, Roy, and Williams (1988) found that the concentrations of putrescine, cadaverine and histamine increased during storage, while those of spermidine and spermine decreased following an initial rise. The present study, however, does not provide an answer as to why the polyamine content in some fish species changed differently during storage. One may speculate whether this could be caused by bacterial contamination.

High putrescine levels in canned crabs and fresh cod roe suggest bacterial contamination. However, the level of cadaverine was high in only one of the cod roe samples, indicating that the putrescine concentration may be naturally high in cod roe. To confirm this, roe must be removed from the cod immediately after catching, and analysed.

Milk was low in polyamines, while some cheeses contained substantial amounts (Table 1). The fermentation process applied in cheese production may explain the difference. In agreement with this, a nonfermented product, the Norwegian brown "cheese", was low in polyamines (Table 1).

Substantial quantities of putrescine, and low levels of spermine may be characteristic of citrus fruits (Table 1), as mandarin, orange, as well as orange- and grapefruit juices tested (Bardócz et al., 1993), showed such patterns.

Furthermore, the present results also confirmed the results of Bardócz et al. (1993, 1995) and Okomoto et al. (1997), who showed that fruits and vegetables, with the exception of broccoli and cauliflower, were generally low in all polyamines. Our study also confirmed the relatively high level of putrescine in tomatoes (Bardócz et al., 1993; Table 1).

A balanced diet with respect to nutrients, low or high in polyamines, should be possible to compose from food items with known concentrations of polyamines. However, it must be borne in mind that storage, transport and handling, will influence to some extent, the polyamine variety and concentrations (Klausen & Lund, 1986; Luten et al., 1992). Cooking, on the other hand, did not seem to alter the polyamine concentrations significantly (Table 1). However, we have analysed too few samples to allow a strong conclusion.

Upon calculating the contribution of polyamines from the diet, one should consider that only a limited fraction of the dietary polyamines are absorbed from the intestinal tract, as they can also be metabolised during the passage through the intestinal wall. Furthermore, the degree of absorption will be partly determined by the presence of other amines, e.g. histamine and cadaverine, as they compete with putrescine for the degrading enzyme diamine oxidase.

Estimated amounts of daily-ingested polyamines range between 100 and 500 μmol (Bardócz, 1993, Bardócz et al., 1995; Canellakis, Viceps-Madore, Kyriakidis, & Heller, 1979). However, this information does not provide insight into the individual's intake of polyamines. Should this be of interest, it must be based on the actual food polyamine content.

Dietary polyamines have both beneficial and harmful effects, but present knowledge is too sparse to allow recommended restrictions on intake in health or disease. Before any recommendations are given, the effect of dietary polyamines should be further elucidated, and more foods examined for their content of polyamines.

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