FOLIC ACID – THE OCCURRENCE AND THE ROLE IN HUMAN NUTRITION

Magdalena TUSZYŃSKA
Research Institute of Horticulture
Konstytucji 3-Maja 1/3, 96-100 Skierniewice, Poland
Received: June 1, 2012; Accepted: June 25, 2012

Summary
Folic acid occurs naturally in the salt form of folic acid - the so-called folate. The human body cannot synthesize it, and therefore it must be supplied from outside. Folic acid is involved in the synthesis and proper functioning of RNA and DNA acids. It is essential for growth and division of all body cells, which is particularly important during active growth or in the fetal and newborn life. In children and adults, folate along with vitamin B₁₂ are involved in the production of red blood cells. Current research indicate on the existence in Poland and in Central and Northern Europe of significant deficiencies of folic acid in the diet.

Deficiency of folic acid in our diet is due to the fact that we consume more highly processed food. Stored and heat-treated food loses a large part of folates. The most common pathological processes associated with a deficiency of folic acid in the body are neural tube defects, megaloblastic anaemia, disturbances in the functioning of the nervous and cardiovascular system, as well as the development of certain types of cancer. Effective methods to increase folate intake are still being searched for.

key words: folic acid, biological functions, consumption, neural tube defects, cardiovascular disease

INTRODUCTION
Folic acid, N-[4-(2-amino-4-hydroxypteridinyl)-(6)-methylamino]benzoyl]-L-aminoglutaric acid, also called pteroylglutamic acid (PGA) is an organic compound belonging to a group of water-soluble B vitamins (Bonechi et al. 2004). It is known under the names: folacin, vitamin B₉, vitamin M, vitamin B₁₁. It was first isolated in 1941 as a substance of an acid, which showed a growth-stimulating properties of the bacteria Streptococcus faecium and Lactobacillus casei (Mitchell et al. 1941). It was separated from the spinach leaves, hence its name. Latin word folium means leaf.

The commonly used term “folic acid” often includes the proper folic acid and a group of its derivatives with a very complex structure. These compounds are characterized by
a similar biological activity despite the structural differences of molecules. Formally, this compound has more than 150 forms, in nature there are about 20.

**Chemical structure and properties of folic acid**

Chemically, folic acid is made up of a bicyclic pterin linked by a methylene bridge (C9-N10) to para-aminobenzoic acid (PABA), which is joined by peptide linkage to a single molecule of L-glutamic acid (Hawkes & Villota 1989). The pteridine moiety of folates can exist in either oxidized or reduced states. There may be a one-carbon substituent group present in N5 or N10 positions of tetrahydrofolic acid, resulting in a number of folate derivatives (Gregory 1989). The structure of folic acid is shown in Fig.1.

![Fig. 1. Structure and numbering of N-[4-(2-amino-4-hydroxypteridinyl)-(6)-methylamino]-benzoyl]-L-aminoglutaric acid (Bonechi et al. 2004)](image)

Folic acid has molecular formula C19H19N7O6, molecular weight 441.4, and pure compound is in the form of yellow crystals. The compound is showing the optical rotation, and is dextrorotary (optical rotation angle of polarized light is equal to +20°). It has limited solubility in water, but is soluble in acidic and alkaline solutions and insoluble in organic solvents (Dick et al. 1948, Lund 1994). Acidic conditions, light and high temperatures increase the susceptibility of folic acid to cleavage (Dick et al. 1948). There is great variability in the thermal stability of folates (Mnkeni & Beveridge 1982, Day & Gregory 1983). The degree and rate of destruction is largely influenced by the pH of the medium, type of buffer, reducing agents in the buffer and folate derivatives. It has been reported that under identical heating conditions, folic acid and 5-formyltetrahydrofolic acid are quite stable, whereas 5-methyltetrahydrofolic acid and tetrahydrofolic acid are very labile (Paine-Wilson & Chen 1979, Hawkes & Villota 1986). Tetrahydrofolic acid is extremely labile to heat compared to 5-methyl-tetrahydrofolic acid with a half-life of 2.25 and 21.4 min. at
100°C, respectively. The stability of both folate derivatives drastically increased with the incorporation of ascorbic acid, thus showing the detrimental effect of molecular oxygen at higher temperatures (Chen & Cooper 1979). Folate compounds are susceptible to light. Hence, folate analysis is most often carried out in subdued light and glass-wares are wrapped with aluminium foil.

Most animals cannot synthesize folic acid because they cannot synthesize PABA or attach the first glutamate to pteroic acid (Stryer 1981). They must derive folic acid from the diet, the best source being green leafy vegetables. There are several forms of folic acid and not all of them are biologically active (Martin 1983). In plants, folic acid exists as a polyglutamate conjugate with a γ-linked polypeptide chain of seven glutamic acids. In the gut, specific enzymes (folyl polyglutamate hydrolases) cleave these molecules. Only the form with one glutamate (monoglutamyl form) is absorbed in humans (Martin 1983).

Folate is as an acceptor and donor of one-carbon units for over 100 biochemical processes. Reduced folate or those without carbon substitution (dihydropteroylglutamates or tetrahydropteroylglutamates) are unstable (O’Broin et al. 1975, Cooper & Chen 1978, Gregory 1989, Hawkes & Villota 1989). The presence in foods of antioxidants (ascorbic acid) and reduced thiols protects folate against oxidant instability. Moreover, exposure to the peptic acid of the stomach increases folate instability (Malin 1977, Chen & Cooper 1979). Polyglutamylation of folate is probably necessary to concentrate and store folates in tissues. However, to be in the proximal one-third of the small intestine, polyglutamyl folates must be hydrolyzed to the respective monoglutamyl derivatives. This conversion is catalyzed by intestinal hydrolases (Godwin & Rosenberg 1975, Halsted et al. 1986, Keagy et al. 1988, Halsted 1989). A large proportion of folate delivered to the liver is secreted into the bile and redistributed to the peripheral tissues. The central folate acceptor molecule in the one-carbon cycle is a polyglutamyl form of tetrahydrofolate (Wagner 1995). The carbon can be carried as a methyl, methylene, formyl, formimino or methenyl group. Folate is particularly required for the methylation of homocysteine to form methionine and the biosynthesis of amino acids and deoxynucleotides needed for DNA replication and repair (Sellub & Rosenberg 1996). Biochemical changes associated with inadequate folate status trigger the onset of abnormalities in one-carbon metabolism.

**Importance of folates for the human nutrition**

In the early 1990s, several European countries carried out a campaign encouraging young women planning motherhood to increase their daily ration intake of foods rich in folate, as well as dietary supplementation with folic acid. They were informed about the consequences of folic acid deficiency during the first weeks of pregnancy, that is, during the formation of the neural tube, which then develops into the brain and spinal cord of the child. However, the campaign about associated with folate deficiency defects in the formation of the fetal cen-
Central nervous system did not achieve the expected results, as shown by statistics. Poland belongs to countries with the highest death rate due to congenital neural tube defects in Europe (Brzeziński & Mazurczak 1994). The incidence of neural tube defects in Poland is 8.61 per ten thousand live births, whereas the average in Europe is 2.97 per ten thousand live births. The incidence of spina bifida in newborns in Poland is 6.17 per ten thousand live births and is also among the highest in Europe (Brzeziński 1998, Szostak-Węgierek 2004). In most countries, prevention programmes are created, whose purpose is to promote consumption of folic acid by all women of childbearing age, not just those planning to increase their family. There is also the primary prevention of neural-tube defects programme in Poland.

It should be noted that pregnancy is not the only period when folate plays an important role for health. Folic acid is involved in the synthesis of purines, pyrimidines, nucleic acid formation and the metabolism of certain amino acids (for example: glycine, histidine, methionine). It plays an important role in tissues where cell division occurs, especially in fetal tissues, the hematopoietic system and gut epithelium. The presence of folic acid in appropriate amounts in the diet ensures the proper functioning of tissues and organs of our body. In many clinical and epidemiological studies, folate deficiency in the diet has been shown to favor the development of atherosclerosis (Ballal et al. 1997, Gerhard & Duell 1999) and some cancers (Rohan et al. 2000, Cole et al. 2007) and also to lead to the formation of many neuropsychiatric disorders (Morris et al. 2005, Ryglewicz & Graban 2005).

Dietary folate deficiency promotes the development of atherosclerosis. Homocysteine plays an important role in the pathogenesis of this disease. An excess of homocysteine with the deficiency folate and vitamin B12 causes vascular endothelial damage and a prooxidant effect, leading to an increased risk of atherosclerosis (Quinnivan et al. 2002). Several studies have shown an inverse correlation between the concentration of folate and homocysteine in the blood (Verhoef et al. 1997, Van Oort et al. 2003).

Epidemiological and nutritional observations show that the consumption of fresh vegetables rich in folic acid protects against the formation of certain types of cancer (Choi & Mason 2000, Jones & Baylin 2002). Published results of cohort and case-control studies show that the deficit of folic acid in the body increases the risk of the emergence and development of certain cancers: colorectal, breast, ovary, uterus, lung, pancreas, etc. (Zhang et al. 1999, Su & Arab 2001, Terry et al. 2002). Recently, several papers have shown that high doses of folic acid may accelerate the development of cancers including colon, larynx and prostate (Kim 2004, Kim 2006, Rampersaud et al. 2002). Results obtained in the studies show that folate deficiency may induce neoplastic transformation. Moderate amounts may inhibit the cancer development but high doses of folic acid may accelerate it (Kim 2004). It is believed that excess folic acid leads to DNA hypermethylation, which may be a consequence of the inactivation...
of tumour suppressor genes responsible for the proper control of cell division (Jones & Baylin 2002).

In recent years, there is increasing evidence indicating the important role of folic acid in the functioning of the nervous system. Its beneficial effects on the function of this system is associated with its participation in the formation of neuro-stimulating substances in the body such as dopamine, norepinephrine and epinephrine (Paul et al. 2004, Coppen & Bolander-Gouaille 2005, Reynolds 2006). Many clinical and epidemiological studies have shown that folate deficiency in the diet leads to a number of neuropsychiatric disorders such as depression, psychosis, dementia and seizures (Quadri et al. 2004, Luchsinger et al. 2007).

A deficiency of folic acid and its derivatives in the human body may be due to an inadequate supply of products containing it. Increased folic acid demand during pregnancy and lactation, intestinal malabsorption, biochemical folic acid metabolism disorders due to its interaction with certain medications such as anti-epileptics, analgesics and neutralizing gastric acid, folic acid antagonists (eg. methotrexate, trimethoprim) or hormonal oral contraceptives may also be the reason for its deficiency (Kishi et al. 1997, Lewis et al. 1998, Olatunji & Soladoye 2008). Folic acid and its derivatives practically exhibit no toxic effects on the human body. Consumption of excessive quantities (eg. 15 mg daily) can only sometimes cause allergic skin reactions and disorders of the digestive and nervous systems. Some reservations about the safety of folic acid in humans may be raised by a few reports about the influence of large doses on the progression of adenomas and their transformation into colorectal cancers (especially colon).

**Sources and intakes of folates**

Folate are present in almost all food products – both vegetable and animal products. They are mostly in the form of polyglutamine compounds representing approximately 75% of total folate content (mainly from vegetables), while approximately 30% are monoglutamine, the main source of which is bread and meat. Folates are absorbed in the human gastrointestinal tract at the rate of 50-90%, averaging 80% (Melse-Boonstra et al. 2002, Winkels et al. 2007).

Raw and frozen vegetables, mainly: lettuce, spinach, cabbage, broccoli, asparagus, cauliflower, Brussels sprouts, beans, peas, tomatoes and beets are a rich source of folates in the human diet (Table 1). Valuable folate sources are also liver, yeast, eggs, cheese and wheat bran. Low levels of folates are meat, milk and dairy products (Table 2). Grain products are a major folate source in the diet of the citizen of Poland. They provide nearly 40% of the vitamin in relation to the total daily intake. Approximately 25% of folates is supplied by vegetables, 13% by potatoes and 6-7% by fruits, milk, dairy products and eggs (Wartanowicz 1997). Spinach is a vegetable, which besides having a high folic acid content, also contains an active enzyme which catalyzes the breakdown of polyglutamine folate derivatives.
Table 1. Content of folate in fruit and vegetables (Kunachowicz et al. 2005)

| Product     | Folate content μg·100g⁻¹ | Product         | Folate content μg·100g⁻¹ |
|-------------|--------------------------|-----------------|--------------------------|
| Fruit       |                          | Vegetables      |                          |
| Apple       | 6                        | Cabbage, Savoy  | 72                       |
| Avocado     | 62                       | Cabbage, Chinese| 77                       |
| Banana      | 22                       | Cabbage, white  | 57                       |
| Grapes      | 6                        | Cauliflower     | 55                       |
| Orange      | 30                       | Chicory         | 52                       |
| Orange juice| 24                       | Chives          | 64                       |
| Raspberries | 30                       | Kale            | 120                      |
| Sour cherries| 8                        | Leek            | 56                       |
| Strawberries| 17                       | Lentil sprouts  | 84                       |
| Water-melon | 3                        | Lettuce         | 75                       |
| Vegetables  |                          |                 |                          |
| Asparagus   | 150                      | Parsley, leaves | 170                      |
| Beetroot    | 87                       | Parsley, root   | 180                      |
| Broad beans | 145                      | Peas, green     | 62                       |
| Broccoli    | 119                      | Pepper, red     | 52                       |
| Brussels sprouts | 130 | Pepper, green | 36                       |
|              |                          | Potato          | 20                       |
|              |                          | Soya bean sprouts| 160                  |
|              |                          | Spinach         | 193                      |
|              |                          | String-beans    | 70                       |
|              |                          | Tomato          | 39                       |

Table 2. Content of folate in meat, cereals, dairy products and others (Kunachowicz et al. 2005)

| Product          | Folate content μg·100g⁻¹ | Product                  | Folate content μg·100g⁻¹ |
|------------------|--------------------------|--------------------------|--------------------------|
| Meat             |                          | Milk and dairy products  |                          |
| Beef             | 6-10                     | Brie cheese, whole fat   | 60                       |
| Pork             | 3                        | Cheddar cheese, whole fat| 18                       |
| Veal             | 5                        | Milk                     | 1-5                      |
| Chicken liver    | 590                      | Quark                    | 27                       |
| Ox’s liver       | 330                      |                          |                          |
| Pig’s liver      | 110                      |                          |                          |
| Cereals and cereal products |              |                          |                          |
| Rye grain        | 113                      | Baker’s yeast            | 1407                     |
| Rye brown bread  | 28.5                     | Chicken eggs, whole      | 65                       |
| Wheat bran       | 260                      | Chicken eggs, yolk       | 152                      |
| Wheat bread      | 30.7                     | Ice-cream                | 6-8                      |
| Wheat grain      | 145                      | Mackerel                 | 10                       |
Table 3. Folate retention in spinach and broccoli following typical cooking procedures (McKillop et al. 2002)

| Food    | Cooking method | Cooking duration (min) | Folate (μg·100g⁻¹) |
|---------|----------------|------------------------|---------------------|
|         |                |                        | Raw foods | Cooked foods |
| Spinach | Boiled        | 3.5                    | 191.8     | 94.4         |
| Spinach | Steamed       | 3.0                    | 218.5     | 189.5        |
| Broccoli| Boiled        | 10.0                   | 177.1     | 77.0         |
| Broccoli| Steamed       | 10.0                   | 172.0     | 156.2        |

Thermal processing of vegetables is the cause of large folic acid losses, which can reach 40-70% of their initial content. Cooking vegetables leads to partial decomposition and reduces the content of folic acid. Because of the high solubility in water, folic acid is washed out into the water used in cooking like other vitamins B and vitamin C (McKillop et al. 2002, McNulty & Pentieva 2004). The study conducted by McKillop et al. (2002) indicated significant reductions of 51% and 56% in the folate content of spinach and broccoli compared with raw values respectively, as a result of boiling for typical time periods. In contrast, the steaming of spinach or broccoli did not result in a significant loss of folate content, even after the maximum steaming periods of 4.5 min and 15.0 min respectively, which produced overcooked consistencies (Table 3). Steam blanching resulted in greater retention of folate compared with water blanching. Likewise, other forms of cooking that minimize the direct contact of food with the cooking water such as pressure cooking and microwave cooking have been found to be preferable to boiling in terms of folate retention. According to Polish standards, the recommended folate intake for adults is from 280 to 340 μg per day, depending on gender, age and physical activity (Table 4). The recommendations also included low bioavailability of natural polyglutamate and large losses that occur during storage and food processing. The negative folate balance during pregnancy is a physiological phenomenon. It is assumed that the demand for folic acid increases 2 to 4 times during pregnancy (Gawędzki & Hryniewiecki 2003). Statistical data show that the intake of natural folate is still insufficient in Poland. Nutritional education for people has been introduced and prevention programmes have been implemented to prevent the most common pathological processes associated with folate deficiency in the body such as fetal developmental disorders, megaloblastic anaemia, neurological disorders and cardiovascular disease. This action aims to increase the folate amounts from natural sources or from pharmaceutical supplementation.
Table 4. The recommended daily intake of folic acid in μg per person (Szostak-Węgierek 2004)

| Population group | Safe level | Recommended level |
|------------------|------------|-------------------|
| Gender, years    |            |                   |
| Infants          |            |                   |
| 0-0.5            | 25         | 35                |
| 0.5-1.0          | 50         | 70                |
| Children         |            |                   |
| 1-3              | 55         | 70                |
| 4-6              | 75         | 90                |
| 7-9              | 85         | 105               |
| Girls            |            |                   |
| 10-12            | 160        | 190               |
| 13-15            | 170        | 200               |
| 16-18            | 185        | 220               |
| Boys             |            |                   |
| 10-12            | 170        | 200               |
| 13-15            | 180        | 220               |
| 16-18            | 200        | 240               |
| Men over 18 years old of moderate physical activity | 280 | 300 |
| Women over 18 years old of moderate physical activity | 240 | 290 |
| Pregnancy        | 400        | 450               |
| Lactation        | 480        | 530               |
| Over 60 years old |            |                   |
| Women            | 300        | 320               |
| Men              | 320        | 340               |

In many countries, enriching some food products in folic acid for mass consumption, such as flour and bread, is being considered. This programme implementation would effectively prevent the occurrence of neural tube defects in a high proportion of the population and overcome the limitations associated with individual prevention. The preparation of a program for folic acid enrichment of certain mass consumption foods would require a significant increase in research on nutritional habits in order to balance the supply of folate fortification technology and the social acceptance of this kind of massive preemptive intervention. In the United States the fortification of flour, rice, pasta and other cereal products has been applied since early 1998 and after its introduction the number of newborns with congenital neural tube defects has decreased by almost 47% and the number of older people with ischemic stroke has also decreased (Honein et al. 2001, Williams et al. 2002, Bazzano et al. 2006). In the UK, since 2000, 0.24mg folic acid per 100g flour has been added. Quite a small dose of folic acid added to flour products is subject to concerns about exceeding the maximum daily level of this vitamin in certain population groups. High folic acid doses in the diet of older people may mask the symptoms of anaemia associated with B12 deficiency and consequently damage the nervous system, whereas in people with cancer, it can affect the course of treatment. In recent years, food enrichment is the most frequently chosen solution to dietary deficiencies. However, food fortification with folic acid is not accepted in most European countries.

New solutions to increase folate intake from natural sources are being sought. Among other things, the Folate FuncHealth foundation has proposed the following ways to increase levels of natural folate in foods (Jägerstad et al 2005):

- Increasing the folate concentration in fermented products like bread,
beer and wine by using yeast strains rich in folate;
• Increasing the folate content in fermented dairy products (cheese, yogurt, etc.) by the appropriate selection of lactic acid bacteria strains;
• Elaboration and application of production technology methods to minimize the loss of folate;
• Increasing folate content in processed foods such as soup concentrations, vegetable and fruit juices, through using varieties of fruit and vegetables rich in folate;
• Increasing the folate content in flour by grinding the whole grain and bran.

In Poland folic acid food fortification is voluntary and applies to most cereal products and confectionery. The consumer can make an informed choice between the products enriched with folic acid or unenriched ones.

In the near future can be expected that new food products fortified with folic acid will appear on the market and that food producers meeting the expectations of consumers will use methods of increasing levels of natural folate in foods promoted by the Folic FuncHealth.

REFERENCES

Ballal R.S., Jacobsen D.W., Robinson K. 1997. Homocysteine: update on a new risk factor. Cleve. Clin. J. Med. 64: 543-549.

Bazzano L.A., Reynolds K., Holder K.N., He J. 2006. Effect of folic acid supplementation on risk of cardiovascular diseases; a meta-analysis of randomized controlled trials. Jama 296: 2720-2726.

Bonechi C., Donati A., Lampariello R., Martini S., Picchi M. P., Ricchi M., Rossi C. 2004. Solution structure of folic acid: Molecular mechanics and NMR investigation. Spectrochim. Acta, Part A 60 (7): 1411-1419.

Brzeziński Z.J. 1998. Kwas foliowy w zapobieganiu wadom wrodzonym cewy nerwowej. Med. Wieku Rozw. 2: 453-461. [in Polish]

Brzeziński Z.J., Mazurczak T. 1994. Propozycje wprowadzenia profilaktyki pierwotnej wad rozwojowych cewy nerwowej w Polsce. Pediat. Pol. 69: 684-686. [in Polish]

Chen T.S., Cooper R.G. 1979. Thermal destruction of folacin: effect of ascorbic acid, oxygen and temperature. J. Food Sci. 44: 713-716.

Choi S.W., Mason J.B. 2000. Folate and carcinogenesis: an integrated scheme. J. Nutr. 130: 129-132.

Cole B.F., Baron J.A., Sandler R.S., Haile R.W., Ahnen D.J., Bresalier R.S., et al. 2007. Folic acid for the prevention of colorectal adenomas: a randomized clinical trial. JAMA. 297: 2351-2359.

Coppen A., Bolander-Gouaille C. 2005. Treatment of depression time to consider folic acid and vitamin B12. J. Psychopharmacol. 19: 59-65.

Cooper R.G, Chen T.S., King M.A. 1978. Thermal destruction of folacin in microwave and conventional heating. J. Am. Diet. Assoc. 73: 406-410.

Day B.P.F Gregory J.F. 1983. Thermal stability of folic acid and 5-methyltetrahydrofollic acid in liquid model food systems. J. Food Sci. 48: 581-587.

Dick M., Harrison I.T., Farreer K.T.H. 1948. The thermal stability of folic acid. Aust. J. Exp. Biol. Med. Sci. 26: 239.

Gawędzki J., Hryniewiecki L. 2003. Żywienie człowieka. Podstawy nauki o żywieniu. Cz.I, PWN, Warszawa. [in Polish]
Gerhard G.T., Duell P.B. 1999. Homocysteine and atherosclerosis. Curr. Opin. Lipidol. 10: 417-428.
Godwin H.A., Rosenberg I.H. 1975. Comparative studies of the intestinal absorption of [3H] pteroylmonoglutamate and [3H] pteroylheptaglutamate in man. Gastroenterology 69: 364-373.
Gregory J.F. 1989. Chemical and nutritional aspects of folate research: analytical procedures, method of analysis, stability and bioavailability of dietary folates. Adv. Food Nutr. Res. 33: 1-11.
Halsted C.H. 1989. The intestinal absorption of dietary folates in health and disease. J. Am. Coll. Nutr. 8: 650-658.
Hawkes J.G., Villota R. 1986. Kinetics of folate degradation during food processing. In: Food engineering and process applications. LeMaguer M., Jelen P. (Eds.), vol. 1. Transport phenomenon (p. 323). Amsterdam, Netherlands: Elsevier Applied Science.
Hawkes J.G., Villota R. 1989. Folates in foods: Reactivity, stability during processing and nutritional implications. Crit. Rev. Food Sci. Nutr. 28: 439-539.
Honein M.A., Paulozzi L.J., Mathews T.J., Ericson J.D, Wong L.Y. 2001. Impact of folic acid fortification of the US food supply on the occurrence of neural tube defects. JAMA. 285: 2981-2986.
Jägerstad M., Piironen V., et al. 2005. Increasing natural food folates through bioprocessing and biotechnology. Trends Food Sci. Technol. 16: 298-306.
Jones P.A., Baylin S.B. 2002. The fundamental role of epigenetic events in cancer. Nat. Rev. Genet. 3: 415-428.
Keagy P.M., Shane B., Oace S. 1988. Folate bioavailability in humans: effect of wheat bran and beans. Am. J. Clin. Nutr. 47: 80-88.
Kim Y.I. 2004. Will mandatory folic acid fortification prevent or promote cancer? Am. J. Clin. Nutr. 80: 1123-1128.
Kim Y.I. 2006. Does a high folate intake increase the risk of breast cancer? Nutr. Rev.64: 468-475.
Kishi T., Fujita N., Eguchi T., Ueda K. 1997. Mechanism for reduction of serum folate by antiepileptic drugs during prolonged therapy. J. Neurol. Sci. 145: 109-112.
Kunachowicz H., Nadolna I., Przygoda B., Iwanow K. 2005. Tabele składu i wartości odżywczej żywności. Wydawnictwo Lekarskie PZWL, Warszawa. [in Polish]
Lewis D.P., Van Dyke D.C., Stumbo P.J., Berg M.J. 1998. Drug and environmental factors associated with adverse pregnancy outcomes. Part I: Antiepileptic drugs, contraceptives, smoking and folate. Ann. Pharmacother. 32: 802-817.
Luchsinger J.A., Tang M.X., Miller J., Green R., Mayeux R. 2007. Relation of higher folate intake to lower risk of Alzheimer disease in the elderly. Arch. Neurol. 64: 86-92.
Lund W. 1994. Pharmaceutical codex (12th ed.) Principles and practice of pharmaceuticals. London: Pharmaceutical Press: 73-75.
Malin J.D. 1977. Total folate activity in Brussels sprouts: the effect of storage, processing, cooking and ascorbic acid content. J. Food Technol. 12: 623-632.
Martin D.W. 1983. Water-soluble vitamins. Martin D.W., Mayes P.A., Rodwell V.W. (Eds), Harper’s review of biochemistry, Lange, Los Altos, CA: 97-113.
McKillop D.J., Pentieva K., Daly D., McPartlin J.M., Hughes J., Strain J.J., Scott J.M., McNulty H. 2002.
The effect of different cooking methods on folate retention in various foods that are amongst the major contributors to folate intake in the UK diet. Br. J. Nutr. 88: 681-688.

McNulty H., Pentieva K. 2004. Folate bioavailability. Proc. Nutr. Soc. 63: 529-536.

Melse-Boonstra A., de Bree A., Verhoef P., Bjorke-Monsen A.L., Verschuren W.M. 2002. Dietary monoglutamate and poliglutamate folate are associated with plasma folate concentrations in Dutch men and women aged 20-65 years. J. Nutr. 132: 1307-1312.

Mitchell H.K., Snell E.E., Williams R.J. 1941. The concentration of "folic acid". J. Am. Chem. Soc. 63 (8): 2284

Makeni A.P., Beveridge T. 1982. Thermal destruction of pteroylglutamic acid in buffer and model food systems. J. Food Sci. 47: 2038-2041.

Morris M.C., Evans D.A., Bienias J.T., Tangney C.C., Hebert L.E., Scherr P.A., Schneider J.A. 2002. Dietary folate and vitamin B12 intake and cognitive decline among community-dwelling older persons. Arch. Neurol. 62: 641-645.

O'Brien J.D., Temperley I.J., Brown J.P., Scott J.M. 1975. Nutritional stability of naturally occurring monoglutamyl folate derivatives of folic acid. Am. J. Clin. Nutr. 8: 438-444.

Olatunji L.A., Soladoye A.O. 2008. Low dietary folate impairs glucose tolerance and plasma lipid profile in oral contraceptive-treated rats. Pathophysiology 15 (3): 167-171.

Paine Wilson B., Chen T.S. 1979. Thermal destruction of folacin: effect of pH and buffer ions. J. Food Sci. 44: 717-722.

Paul R.T., McDonnell A.P., Kelly C.B. 2004. Folic acid: neurochemistry, metabolism and relationship to depression. Hum. Psychopharmacol. 19: 477-488.

Quadri P., Fragiaccomo C., Pezzati R., Zanda E, Forlone G., Tettamanti M., Lucca U. 2004. Homocysteine, folate and vitamins B12 in mild cognitive impairment, Alzheimer disease and vascular dementia. Am. J. Clin. Nutr. 80: 114-122.

Quinlivan E.P., McPartlin W., McNulty H., Ward M., Strain J.J., Weir D.G., Scott J.M. 2002. Importance of both folic acid and vitamin B12 in reduction of risk of vascular disease. Lancet 359: 227-228.

Rampersaud G.C., Bailey L.B., Kauwell G.P. 2002. Relationship of folate to colorectal and cervical cancer: review and recommendation for practitioners. J. Am. Diet. Assoc. 102: 1273-1282.

Reynolds E.H. 2006. Vitamin B12, folic acid and the nervous system. Lancet Neurol. 5: 949-960.

Rohan T.E., Jain M.G., Howe G.R., Miller A.B. 2000. Dietary folate consumption and breast cancer risk. J. Natl. Cancer Inst. 92: 266-269.

Ryglewicz D., Graban A. 2005. Zaburzenia metabolizmu homocysteiny w chorobach zwyrodnieniowych ośrodowego układu nerwowego. Czynniki Ryzyka. 11: 20-22. [in Polish]

Selhub J., Rosenberg I.H. 1996. Folic acid. E.E Ziegler, L.J Filer Jr (Eds.), Present knowledge in nutrition (7th), International Life Sciences Institute Press, Washington, DC 206-219.

Stryer L. 1981. Biosynthesis of amino acids and heme. Biochemistry, Freeman, San Francisco. 485-510.

Su L.J., Arab L. 2001. Nutritional status of folate and colon cancer risk: evidence from NHANES I epidemiologic follow-up study. Ann. Epidemiol. 11: 65-72.

Szostak-Węgierek D. 2004. Znaczenie prawidłowego żywienia kobiety w czasie ciąży. Żyw. Człow. Metab. 31: 160-171. [in Polish]
Terry P., Jain M., Miller A.B., Howe G.R., Rohan T.E. 2002. Dietary intake of folic acid and colorectal cancer risk in cohort of women. Int. J. Cancer 97: 864-867.
Van Oort F.V., Melse-Boonstra A., Brouwer I.A., Clarke R., West C.E., et al. 2003. Folic acid and reduction of plasma homocysteine concentrations in older adults: a dose-response study. Am. J. Clin. Nutr. 77: 1318-1323.
Verhoeft P., Kok T.J., Kuliylmans L.A. 1997. The 667C/T mutation in the methylenetetrahydrofolate reductase gene associations with plasma total homocysteine levels and risk of coronary atherosclerotic disease. Atherosclerosis 132: 105-112.
Wagner C. 1995. Biochemical role of folate in cellular metabolism L.B Bailey (Ed.), Folate in health and disease, Marcel Dekker, New York 23-42.
Wartanowicz M. 1997. Foliany w żywieniu (przegląd piśmiennictwa). Żyw. Człow. Metab. 24: 81-89. [in Polish]
Williams L.J., Mai C.T., Edmonds L.D., Shaw G.M., Kirby R.S., Hobbs C.A., et al. 2002. Prevalence of spina bifida and anencephaly Turing the transition to mandatory folic acid fortification in the United States. Teratology 66: 33-39.
Winkels R.M., Brouwer J.A, Siebelink E., Katan M.B., Verhoef P. 2007. Bioavailability of foods is 80%. Am. J. Clin. Nutr. 85: 465-473.
Zhang S., Hunter D.J., Hankinson S.E., Giovannucci E.L., Rosner B.A., et al. 1999. A prospective study of folate intake and the risk of breast cancer. JAMA. 281: 1632-1637.

KWAS FOLIOWY - WYSTĘPOWANIE I ROLA W ŻYWIENIU CZŁOWIEKA

Streszczenie
Kwas foliowy występuje naturalnie w postaci soli kwasu foliowego – tzw. folianów. Organizm ludzki nie potrafi go syntetyzować i dlatego musi on być dostarczany z zewnątrz.
Kwas foliowy bierze udział w syntezie i prawidłowym funkcjonowaniu kwasów RNA i DNA. Jest niezbędny do wzrostu i podziału wszystkich komórek organizmu, co jest szczególnie istotne w okresie intensywnego wzrostu, czyli w życiu płodowym i niemowlęcym. U dzieci i dorosłych foliany razem z witaminą B12 biorą udział w produkcji czerwonych krwinek. Aktualne badania wskazują na występowanie znacznych niedoborów folianów w diecie mieszkańców Europy Środkowej i Północnej. Niedobór kwasu foliowego w naszej diecie wynika z tego, że spożywamy coraz więcej żywności wokoł przetworzonej. Żywność przechowywana i poddawana obróbce cieplnej traci w dużej części foliany. Najczęstsze procesy patologiczne związane z niedoborem kwasu foliowego w organizmie to: wady cewy nerwowej, niedokrwistość megaloblastyczna, zaburzenia w działaniu układu nerwowego i sercowo-naczyniowego, jak również rozwój niektórych typów nowotworów. Poszukiwane są wciąż skuteczne metody, służące zwiększeniu spożycia folianów.

Unauthentifiziert | Heruntergeladen 14.03.20 04:41 UTC