Al-Kitab Journal for Pure Sciences (2026); 10(2):132-142.
https://doi.org/10.32441/kjps.10.2.p10

Al-Kitab Journal for Pure Sciences
ISSN: 2617-1260 (print), 2617-8141(online)

https://isnra.net/index.php/kjps

The Role of Folic Acid in Avoiding Congenital Disabilities: A Review

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Citation: *Nawras Ali Hussein Al-Jubouri[1], Huda Saad Azzawi[2], zahraa hussein abdulateef[3]*. **The Role of Folic Acid in Avoiding Congenital Disabilities: A Review.**
Al-Kitab J. Pure Sci. [Internet]. 2025 Nov. 03 ;10(2):132-142 DOI.
https://isnra.net/index.php/kjps/article/view/2026.
https://doi.org/10.32441/kjps.10.2.p10

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Keywords: Congenital disabilities, Defects of neural tube, Folacin, Folic acid, Pregnant.

Article History

Received	11 Aug.	2025
Accepted	03 Nov.	2025
Available online	01 Nov.	2026

Abstract:

Folic acid (folacin, vitamin B9) is a vitamin with several significant functions in the human body. For this reason, too little or too much folic acid can increase the incidence of adverse health effects. This study reviewed current peer-reviewed scientific literature regarding folacin and the effects on pregnant women. We completed a systematic review of literature from peer-reviewed studies from 2018 to June 2025 from scientific databases. The succeeding utilized words and concoctions were used in the review - folacin, folate, folic acid supplements, folacin absence in pregnant women. The use of folacin, in regard to its biological action, has both direct and indirect actions on the metabolic system of the cell body of the pregnant woman as a whole since metabolism is for the mother and fetus specifically. Folic acid plays a role in avoiding megaloblastic anemia, and neural tube defects NTDs, and it is also helpful in the preservation of overall nervous system functionality and helps to decrease the risk of some types of malignant disease. It is presently being vigorously asserted that the use of folic acid is significant in supporting a normal pregnancy.

Keywords: Congenital disabilities, Defects of neural tube, Folacin, Folic acid, Pregnant.

مراجعة: دور حامض الفوليك في منع التشوهات الخلقية

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الخلاصة:

حمض الفوليك (فولاسين، فيتامين ب٩) هو فيتامين له العديد من الوظائف المهمة في جسم الإنسان. ولهذا السبب، فإن تناول القليل جدًا أو الكثير جدًا من حمض الفوليك يمكن أن يزيد من حدوث الآثار الصحية الضارة. استعرضت هذه الدراسة الأدبيات العلمية الحالية التي استعرضها النظراء فيما يتعلق بالفولاسين وتأثيراته على النساء الحوامل. لقد أكملنا مراجعة منهجية للأدبيات من الدراسات التي استعرضها النظراء من سنة ٢٠١٨ الى يونيو ٢٠٢٥ من قواعد البيانات العلمية. تم استخدام الكلمات والتركيبات المستخدمة التالية في المراجعة - الفولاسين، الفولات، مكملات حمض الفوليك، غياب الفولاسين لدى النساء قبل الولادة. إن استخدام الفولاسين، فيما يتعلق بعمله البيولوجي، له آثار مباشرة وغير مباشرة على النظام الأيضي لجسم خلية المرأة الحامل ككل لأن التمثيل الغذائي للأم والجنين على وجه التحديد. يلعب حمض الفوليك دورًا في الوقاية من فقر الدم الضخم الأرومات وعيوب الأنبوب العصبي، كما أنه مفيد في الحفاظ على وظائف الجهاز العصبي بشكل عام، ويساعد على تقليل خطر الإصابة ببعض أنواع الأمراض الخبيثة. ويُؤكد حاليًا بقوة على أهمية استخدام حمض الفوليك في دعم الحمل الطبيعي.

الكلمات المفتاحية: التشوهات الخلقية، عيوب الانبوب العصبي، الفولاسين ، حامض الفوليك، الحامل.

1. Introduction:

A balanced diet is vital for keeping human health and avoiding many diseases. Folic acid, also known as folacin or vitamin B9, plays a vital role in many biological processes, including DNA production, cell division, and blood cell formation. Its importance is particularly significant during periods of rapid growth, such as gestation. Folacin absence can lead to several health problems, most notably megaloblastic anemia and an increased risk of birth defects in fetuses. Both severe absence and excessive heights of folate can contribute to a higher risk of developing certain chronic illnesses, highlighting the need to maintain optimal levels through a balanced diet. [1].

Vitamin B9 is logically present in the diet as folates, folic acid salts representing a collection of concoctions that differ in the number of glutamic acid residues and the degree of oxidation of the pteridine ring. This group consists of several derivatives, for example dihydrofolate

(DHF), tetrahydrofolate (THF), and methylfolate. Synthetic folic acid is the most stable and bioavailable form of these compounds. [2].

Notably the human body can synthesize this vitamin in small quantities, which are shaped by the contribution of intestinal microbes, especially Bifidobacterium (particularly B. solidiscentis and B. pseudocatenulatum), Lactobacilli, Bifidobacteria, Proteobacteria, Fusobacteria, and Actinomyces [3]. So, this vitamin must be obtained from external sources, i.e., through diet or suitable nutritional supplements [4].

Folic acid (vitamin B9) is an essential nutrient involved in DNA synthesis, methylation, and cell division, processes essential for fetal and placental development. Pregnant women who do not consume adequate amounts of folic acid are at greater risk of neural tube defects and an increased risk of miscarriage [5]. Although dietary sources of folate and folate supplements are the primary sources, the gut microbiome can also produce folate in the colon, particularly in Bifidobacterium and Lactobacillus bacteria, which may contribute to circulating folate levels. New research has shown that bacterial imbalances in the gut microbiome may affect folate production or its role in immune regulation, potentially impacting gestation [6].

2. Reasons and consequences of low folacin levels in the body:

One of the most common causes of folacin absence in the human body is dietary errors, especially not consuming enough vegetables, fruits, and whole grain products daily - they are a valuable source of folacin. Low folic acid content in the diet may also be attributed to high rates of loss through food processing and storage. Poor utilization, storage and absorption, of folic acid in the cells of the body may also be attributed to ingestion huge amounts of tea or coffee, alcoholism, and smoking [7].

The concentration of vitamins and minerals in the body, such as ascorbic acid (vitamin C), vitamin B12, iron, zinc, and others, in addition to adequate levels of methionine, can significantly impact the body's consumption of folacin. Vitamin B12 deficiency leads to decreased folic acid retention in cells. Vitamin c absence, in turn, leads to impaired folic acid absorption in low or metabolically energetic states. Impaired folic acid absorption can also result from functional and structural disorders of the small intestine, as well as deficiencies in enzymes that fail to form polyglutamine compounds [8].

Drugs such as Painkillers (e.g., ibuprofen or aspirin), antiepileptic drugs, antibiotics, corticosteroids, sulfonamides, and folic acid antagonists (such as trimethoprim and

methotrexate) also have a folate-lowering effect. Additionally, those at risk for folic acid deficiency include smokers, women using oral contraceptives, and alcoholics [9].

Regarding pregnancy, folic acid absence is closely linked to an increased occurrence of neural tube defects. A deficiency of this nutrient in the diet of pregnant women may raise the risk of the child developing and cleft palate and cleft lip, as well as increasing the incidence of Down syndrome [10].

Folic acid absence can negatively impact genome stability due to its vital role in the synthesis of thymines and purines. When folic acid levels are low, the availability of thymine, which is important for DNA polymerization and reparation, is reduced. As a result, incorrect incorporation of uracil instead of thymine can occur during replication, resulting in uracil-adenine conjugation. This defect can convert base pairs from GC to AT in the new DNA copy. This conversion is a potential source of serious genetic mutations. Severe folic acid absence, which is also essential for the synthesis of thymidine nucleotides, can lead to genome instability, connected with chromosomal abnormalities and DNA strand breaks. [11]. Research shows that the volume of uracil that is poorly bound to lymphocyte DNA is reduced in woman of reproductive age, which is associated with a daily intake of (400) micrograms of folacin, which in sequence underscores the need for folacin supplement through the reproductive time [12].

The genetic stability of a cell is also affected by the grade of genomic methylation, a compound known to play a chief role [13]. Therefore, a lack in nutritional folacin contributes to the disturbance of many critical metabolic processes and may lead to impaired cell growth and development. One of the most well-known roles of folate is the prevention of neural tube defects and pregnancy problems. It is also indicated for the prevention of, neurodegenerative diseases, cardiovascular disease, megaloblastic anemia and cancer [14, 8, 7].

3. Folacin and fetal growth illnesses:

Pregnant women are among the groups with the greatest need for folacin. An absence of this nutrient can cause many damaging consequences. Folacin is critical for the cell growth in the emerging embryo. The baby's brain and spinal cord develop from the neural tube; therefore, the timing of their development is crucial. Statistics indicate that central nervous system defects are a leading cause of neonatal mortality [15, 16].

During gravidity, folate deficiency leads to birth defects and problems such as abortion, placenta previa, prematurity, premature placental abruption, low birth weight, fetal death, and megaloblastic anemia [17].

Throughout gestation, the need for folacin rises and can only be partially met by consuming suitable nutrients that are sources of this nutrient. It is estimated that the nourishment covers (50%) of the daily necessity for these nutrients. Used for this purpose, nutritional supplements are recommended, which is especially important during pregnancy planning and in the first stages. The daily necessity for folate during pregnancy is 600 micrograms. References emphasize the need for all females of age to consume folic acid-rich products in their diet, in addition to fortified foods [18]. Females planning to become pregnant should take folacin supplements for at least (12) weeks before conception at a dose of 400 micrograms daily. Through the first trimester of gravidity—until the 12th week—folacin supplements should be taken at a dose of 400–800 micrograms daily. After the 12th week, females without further danger factors should take folate supplements at a dose of (600–800) micrograms daily. [19] Suitable folic acid intake stops the advance of neural tube faults.

These are inborn syndromes that emerge during fetal development and are extremely severe, disturbing the nervous system of child. Neural tube faults apparent for example spina bifida, anencephaly, microcephaly, or herniation of the nervous system, which causes, among other effects, bladder and rectal dysfunction, hydrocephalus, epilepsy, mental retardation, leg paralysis, and in severe cases can lead to death. The neural tube is an organ that forms initially during gestation, during the fetal period, approximately in the fourth week. regrettably, at the moment, a lot of women are ignorant of their pregnancy. A folic acid absence throughout this time will negatively affect the development of the child's nervous system and the closure of the neural tube [20]. According to the study, it was found that females who give birth to children with central nervous system defects have lower plasma folic acid levels and higher homocysteine levels [10].

All healthcare professionals must be fully aware of the importance of educating pregnant women about the role of folacin in avoiding congenital disabilities, especially those related to the neural tube. Failure to provide this basic information may constitute gross medical negligence and could lead to legal action, especially in cases where the child is born with a neural tube defect that could have been prevented through prior prevention. [7].

Despite the well-known benefits of folic acid, scientific evidence urges caution, especially in cases of megaloblastic anemia, as folic acid supplements can mask vitamin B12 deficiency, complicating diagnosis and treatment. In cases where the liver is impaired in folic acid metabolism, 5-MTHF supplementation is recommended. This non-activating supplement

immediately provides active folic acid to both mother and fetus without harmful accumulation in the blood, making it the ideal choice to ensure the safety of both [16].

Several epidemiological studies have shown that adding folate to the diet of mother before and during the first weeks of gestation, can be a key factor of the primary inhibition of congenital cardiac and vascular defects in the child. Studies on selected forms of these defects have demonstrated that folic acid supplementation meaningfully decreases the risk of cardiac septal defects (especially ventricular septal defects), as well as cone-shaped defects, and truncus arteriosus defects (specifically transpositon of the great vessels and Fallot syndrome) [21].

Obese females have been found to have double the danger of embryonic neural tube faults compared to females of standard weight. Furthermore, folic acid supplementation has been shown to reduce the danger of neural tube faults, which was chiefly evident in females with a BMI >25 kg/m2 compared to females with a BMI <25 kg/m2 [22]. Furthermore, fetal nervous system defects have been found to significantly affect women with type 1 or type 2 diabetes. [23] found a lower rate of neural tube faults in a group of diabetic women who took folate supplements at a dose greater than 400 µg/day.

4. Defects of neural tube

It is now accepted that supplementing with 400 mcg of folic acid close to gestation will stop most NTDs [24]. The advice for preventing recurrence in women with a history of neural tube defects remains 4.0 mg/day, given the significantly increased danger in such patients and because this is the dose used in the most rigorous trial [25]. Given the poor bioavailability and stability of folic acid in food, a diet high in folic acid would not be optimal for prevention. One study suggested that the risk of neural tube defects is 10 times higher in people with folate deficiency compared to those with high natural folate levels [26]. Another study suggests that an additional 200 mcg per day, or perhaps 100 mcg per day, as a routine intake in fortified foods would prevent most, if not all, of the NTDs that are preventable by folic acid [27].

Ideally, an additional 400 micrograms per day should be offered, as this is the quantity used in numerous intervention trials [28], and can be accomplished through dietary supplements. This quantity cannot be provided through fortification, because exposure to large amounts of folate by people who consume huge amounts of flour may put older adults at risk of pernicious anemia. It is likely that, dependent on the chosen staple food, it would be probable to raise the intake of most women by 100 micrograms per day without causing very high exposure in other groups. It is proposed that this quantity, although not ideal, would stop greatest NTDs.

Studies have shown that pregnant women's exposure to pesticides is associated with an increased risk of several congenital malformations, particularly neural tube defects, indicating that environmental pollution is an important factor in human health and fetal well-being (Figure 1). Of the 229 articles, 8 evaluated pesticide exposure during pregnancy. Various methods were used, including biological sample analysis and questionnaires. The pesticides studied included insecticides, herbicides, fungicides, and nematicides. Insecticides were the most studied, and concentrations were measured at different exposure periods (preconception and prenatal). Different data collection techniques and different types of biological samples were used. The main pesticides studied included DDT, DDE, HCH, and endosulfan. The results showed different levels of pesticides in maternal serum, placenta, and umbilical cord. Maternal serum showed the highest concentrations of pesticides, but their detection in placental and umbilical cord tissues confirms fetal exposure [29].

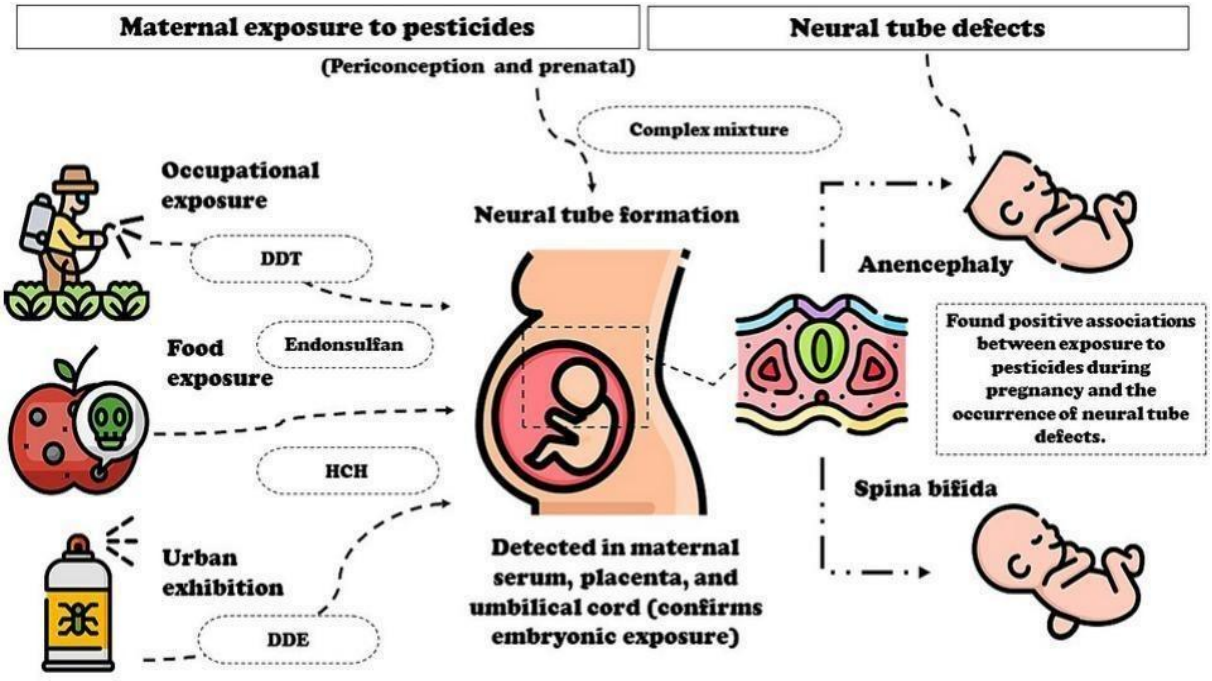


Figure 1: the exposure of pregnant women to pesticides

5. Conclusions

In conclusion, based on the presented data, it can be confirmed that folacin plays a critical and multifaceted role in the body and is a vital nutrient for maintaining proper bodily functions. It is imperative to highlight the role of folacin in pregnant women, as both its absence and excess are connected with an increased risk of several health problems, most notably congenital

abnormalities in the embryo, mainly neural tube defects, in addition to nervous system disorders, cardiovascular diseases, and some cancer types.

To prevent these birth defects and the associated health risks, women who are pregnant or planning pregnancy are advised to control their health by consuming a balanced diet rich in folate sources, for instance, whole grains, green leafy vegetables, citrus fruits, legumes, and nuts. If it is not possible to obtain adequate folic acid through diet alone, it is recommended to consult a doctor about folic acid supplements to help ensure fetal safety and support the mother's health throughout pregnancy.

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