How Much Folate Is in Canadian Fortified Products 10 Years after Mandated Fortification?

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ABSTRACT

Objective: In 1998, the Canadian government mandated folic acid fortification of white flour and enriched grain products to lower the prevalence of neural tube defects. There is now growing concern over the potential harmful effects of too much folic acid on some segments of the population. Given that the actual amount of folate in Canadian foods is unknown, the objective of this study was to measure the folate content in selected fortified foods.

Methods: Using data from the 2001 Food Expenditure Survey and the ACNielsen Company, 95 of the most commonly purchased folic acid-fortified foods in Canada were identified. Folate concentrations in these foods were determined using tri-enzyme digestion followed by microbiological assay. Analyzed values were compared to those in the Canadian Nutrient File (2007b, CNF) and to label values.

Results: The analyzed folate content of foods was, on average, 151% $\pm$ 63 of the CNF values. Analyzed values as a percent of CNF values ranged from 116% in the "rolls and buns" category to 188% in "ready-to-eat cereals". Analyzed values were higher than label values for "breads", "rolls and buns" and "ready-to-eat cereals" (141%, 118% and 237%, respectively [$p < 0.05$]).

Conclusions: Ten years after folic acid fortification of the food supply, neither the CNF nor label values accurately reflect actual amounts of folate in foods. Further, overage differences by food category hinder the development of future strategies designed to strike the right balance between health benefits and risks; monitoring of fortified foods for their nutrient content is required.

Key words: Folic acid; Canada; food supply; fortified foods

La traduction du résumé se trouve à la fin de l'article.

Can J Public Health 2009;100(4):281-84.

Folate, a B-vitamin, is necessary for proper neural tube development, which occurs early after conception when most women are still unaware they are pregnant.¹ In light of this, women of child-bearing age are encouraged to consume a supplement containing folic acid (a synthetic form of folate); however, Canadian data suggest only 57.7% of women report taking folic acid during the peri-conceptional period.² Therefore in 1998, the Canadian government mandated folic acid fortification of all white flour and enriched pasta to 150µg/100g and 200µg/100g, respectively, to increase daily intake by 100µg.³

Since folic acid fortification has become mandatory, the incidence of neural tube defects (NTDs) has declined in Canada by approximately 50%,⁴ with improvements in blood folate indices^{5,6} and folate intake.⁶ Given the apparent success with this intervention, there have been calls to raise the levels of folic acid fortification in Canada to further reduce the incidence of folate-dependent NTDs.^{7,8} In addition to this, suboptimal intakes of folate have been associated with other congenital defects (cleft lip and palate), vascular disease, neuropsychiatric disorders, and cancer.¹

However, a growing body of literature suggests that consuming high levels of folic acid may have several negative consequences beyond the masking and progression of vitamin B12 deficiency,¹ including cancer progression,^{9,10} and reduced natural killer cell cytotoxicity.¹¹ In one recent study, a combination of high folate levels and low vitamin B12 status has been associated with increased cognitive impairment in seniors;¹² in another recently

published study, the same combination in pregnant women was associated with increased insulin resistance and higher central adiposity in their children.¹³

When evaluating the current Canadian situation, the arguments on either side of the "how much folic acid should be added to the food supply?" debate are hampered by a lack of understanding of how much folate is actually in the foods we eat. In the early years after mandated fortification, analysis of folate in foods indicated actual levels were twice that mandated in the United States (US).¹⁴ Researchers from a subsequent study showed that the levels of fortification in the US have declined since an initial post-fortification high, and that monitoring of folic acid fortification may be necessary.¹⁵ In the 10 years following mandated folic acid fortification, there have been no Canadian studies in which foods have been directly analyzed and compared to label values or Canada's main

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Acknowledgements of sources of support: The authors acknowledge the support of the Natural Sciences and Engineering Research Council of Canada. Yaseer Shakur was supported through a studentship, in part, by the Ontario Student Opportunity Trust Fund - Hospital for Sick Children Foundation Student Scholarship Program. Carly Rogenstein was supported in part through a Canada Graduate Scholarship Masters Award from the Canadian Institutes of Health Research.

reference nutrient database, the Canadian Nutrient File (CNF). Therefore, we determined the folate content in a selection of folic acid-fortified foods in Canada.

METHODS

Selection of foods

The choice of products for analysis was based on a comprehensive review of the most commonly purchased foods across households in Canada, combining data from the 2001 Food Expenditure Survey (FOODEX)¹⁶ with more detailed data from the ACNielsen Company (Markham, Ontario) on brands of food purchased. The 2001 FOODEX contains household level data from over 10,000 dwellings collected throughout 2001 and is representative of 98% of Canadians. Trained interviewers recorded detailed information on food expenditures for each household for 2 weeks. The FOODEX data were used to identify the number of households reporting the purchase of a given food category, considering only categories where foods were folic acid-fortified. These categories were: 1) breads; 2) buns and rolls; 3) cookies; 4) ready-to-eat cereals; 5) prepackaged desserts; 6) cooked pasta; and 7) crackers. Data purchased from the ACNielsen Company identified the top 25 food brands sold in each of the aforementioned categories. From this list, we analyzed the top 15 fortified food brands from each food category purchased by more than 20% of households, and the top 10 brands of fortified food from food categories purchased by 15-20% of households. Products were purchased from supermarkets in Toronto, Montreal, or Vancouver (depending on availability) between January and July of 2007 and analyzed prior to their expiration date.

Folic acid content based on CNF and label values

In Canada, the Nutrition Facts panel on food products reports folate content as % Daily Value.¹⁷ The Daily Value of 220µg for folate is set at the 1983 Recommended Nutrient Intakes for Canadian adult males 18 years of age and older.¹⁸ Using this value, the amount of folate claimed per serving was calculated. The CNF values were obtained directly from the most up-to-date version of the database (2007b)¹⁹ available from Health Canada's website, which, in turn, is based primarily on the USDA Nutrient Database for Standard Reference.²⁰ The CNF values are modified where needed to reflect current Canadian regulations for mandatory folic acid fortification. Three brands of pasta that were identified using the ACNielsen data were whole wheat pasta. While all three brands contained folic acid, they were not subject to mandatory fortification and thus were excluded from all subsequent analysis.

Laboratory analysis

All samples were analyzed as purchased except for pasta, which was prepared according to directions on the package. Samples were homogenized with a 50mM (millimoles per litre) CHES-HEPES buffer with 2% ascorbic acid and 0.2 M (moles per litre) 2-mercaptoethanol (pH 7.8) and stored at -80°C until analysis.^{21,22} Aliquots of the thawed homogenate were treated to liberate folates from food matrices and binding proteins and convert folates to their microbiologically assayable form using the tri-enzyme digestion method.²¹⁻²³ Total folate concentration of the resultant supernatants were assessed by microbiological assay using *Lactobacillus rhamnosus* (ATCC 7649; American Type Tissue Culture Collection, Manassas, VA).²⁴ The accuracy and reproducibility of these assays

were assessed using lyophilized liver with a certified value (13.3 mg folate/kg, Pig Liver BCR 487, IRMM, Geel, Belgium). Our analysis yielded a folate concentration of 13.4 ± 1.12 mg/kg, with an overall CV (coefficient of variation) of 8.4%.

Statistical analysis

Data are presented as means and standard deviations. All statistical analyses were performed with the SAS software (version 9.1; SAS Institute Inc., Cary, NC). Paired t-tests were conducted comparing analyzed folate results in each food category to the CNF and label values. A p-value <0.05 was considered significant.

RESULTS

Results from a total of 92 fortified food products in seven food categories are presented. For all foods, the mean analyzed folate content over the CNF values was $151\% \pm 63$. Analyzed values were higher than the CNF reported folate content for all food categories except "cooked pasta" and "crackers" ($p < 0.05$) (Table 1). "Ready-to-eat cereals", on average, contained the highest amount of folate relative to the CNF values ($188\% \pm 57$) (Table 1); 12 and 14 of the 15 cereal brands analyzed had folate contents greater than 1.5 times the CNF and label values, respectively. Folate was only reported on package labels in the "breads", "rolls and buns", and "ready-to-eat cereals" categories. A comparison of analyzed and label folate values is presented in Table 2. The analyzed values were higher than the label values for all three categories ($p < 0.05$).

DISCUSSION

The findings of this study indicate that 10 years after mandated folic acid fortification of the food supply in Canada, there remains a significant disjuncture between the actual folate content of fortified foods versus those reported in the CNF and on food labels, which themselves are usually derived from the CNF. The actual folate content of the foods as a percentage of the CNF reported amounts was, on average, 50% higher. As far as we are aware, this is the first direct assessment of the actual amount of folate in the Canadian food supply since folic acid fortification became mandatory. Data presented herein are consistent with that estimated in a letter to the editor by Quinlivan & Gregory in which they predicted that blood folate values post-fortification were about 1.5 times higher than anticipated.²⁵ The blood folate data used for this estimate were those from specimens sent to a large provincial laboratory in Ontario as part of clinical care.²⁶

At a national level, decisions on what nutrients should be fortified in the food supply, and at what levels, are made using a risk management approach.²⁷ First, clear evidence must exist that there is a nutritional problem of public health significance and that other strategies to address the shortfall in dietary intake will be or have been ineffective. The case for folic acid fortification in Canada clearly meets this first criterion. Beyond a doubt, folic acid fortification of the food supply has improved the folate status of women and has reduced the prevalence of NTDs in Canada by about 50%.⁴

The second consideration in deciding whether or not to fortify the food supply with a nutrient using the risk management approach is whether adding a nutrient to the food supply will do no harm. Recent evidence suggests that the upward shift in dietary folate intake, particularly synthetic folic acid intake, may cause harm to some people.²⁸ For example, it has now been confirmed that high

Table 1. Comparison of the Analyzed Food Folate Content to Values Reported in the Canadian Nutrient File (CNF)

Food Category*	n	Analyzed Values†	CNF Values†	% of CNF Value‡	
		µg/100g	µg/100g	Mean ± SD	Range
Breads	15	133 ± 29	107 ± 16§	127 ± 29	67 – 187
Rolls and buns	15	124 ± 22	106 ± 8§	116 ± 19	73 – 149
Cookies	15	94 ± 29	59 ± 14§	167 ± 56	49 – 278
Ready-to-eat cereals	15	146 ± 36	80 ± 11§	188 ± 57	113 – 280
Prepackaged desserts	15	79 ± 32	47 ± 14§	172 ± 72	53 – 362
Cooked pasta	7	102 ± 45	77 ± 0	133 ± 59	62 – 223
Crackers	10	116 ± 32	105 ± 36	137 ± 104	38 – 418

* Products were analyzed as purchased, except for pasta, which was prepared according to the directions on the package

† Mean ± standard deviation

‡ Analyzed values as a % of the CNF values

§ Significantly different from analyzed value (Student's paired t-test; $p < 0.05$)

Table 2. Comparison of the Analyzed Food Folate Content to Values Reported on the Food Labels

Food Category*	n	Analyzed Values†	Label Values†,‡	% of Label Value§	
		µg/100g	µg/100g	Mean ± SD	Range
Breads	15	133 ± 29	96 ± 16	141 ± 36	90 – 196
Rolls and buns	5	130 ± 12	112 ± 14	118 ± 12	103 – 132
Ready-to-eat cereals	15	146 ± 36	62 ± 6	237 ± 65	126 – 377

* Products were analyzed as purchased

† Mean ± standard deviation

‡ Calculated from the % Daily Value reported on the Nutrition Facts panel

§ Analyzed values as a % of the label values

|| Significantly different from analyzed value (Student's paired t-test; $p < 0.05$)

folic acid intakes in older adults can delay diagnosis of vitamin B12 deficiency, and coupled with low B12 status, may be associated with impaired cognitive function in the elderly population.¹² In addition, high levels of folic acid are associated with a reduction in the effectiveness of anti-folate drugs used against malaria, rheumatoid arthritis, psoriasis and cancer, and facilitate the progression of pre-neoplastic cells and in this way promote cancer.^{9,10,28}

Currently in Canada there are calls to increase the level of folic acid fortification of the food supply to provide a further 25% reduction in NTDs thought to be folate-related.⁸ At the same time, the Chief Medical Officer of England asked for a delay in a final decision regarding mandatory folic acid fortification in the UK until further consideration can be given to the role folic acid may have in increasing colorectal cancer risk.^{9,10} Clearly, monitoring how much folate is in the food supply would be an important first step to facilitate informed public policy decisions that strike the right balance between health benefits of folic acid fortification and potential risks.

A significant disconnect between theoretical and actual levels of folic acid fortification can influence public policy and dietary recommendations. For example, we recently reported that at “mandated” levels of folic acid fortification, 32% of a sample of well-educated lactating women are unlikely to meet their Estimated Average Requirement (EAR) for folate from dietary sources alone.²⁹ Given these findings, we concur with Health Canada's guidance that women consume a folic acid supplement during lactation,³⁰ and most certainly so if a woman is capable of becoming pregnant.³¹ However, re-modeling our dietary data in this sample of lactating women based on “actual” levels of folic acid fortification reported herein, the prevalence of inadequacy during lactation becomes less than 13%. At twice mandated levels of fortification, as was found early post-fortification in the US,¹⁴ the prevalence of inadequacy in our model becomes 0%. Clearly if the latter were the case, folic acid supplementation during lactation just for maintenance of maternal stores may be unnecessary for many women. While our work has focused on folate, there is evidence of disjuncture between the actual and mandated levels for

other nutrients.³² Using a sample of fluid milk from Ontario, Faulkner et al. reported that 44% and 69% of vitamin A and D levels, respectively, were outside the required range.³²

We acknowledge that we analyzed a limited number of folic acid-containing foods in this study. However, among the tens of thousands of food products on the market, our sampling of fortified foods was systematic using the most recent national food consumption data (FOODEX) and brand data purchased from the ACNielsen Company. Hence, we believe these data are sufficient to gauge the extent of the overage problem in Canada and the likely variation by food category.

In conclusion, the findings of this study suggest that 10 years after folic acid fortification of the food supply in Canada, the actual amount of folate in fortified foods is approximately 50% higher than what was mandated. However, the magnitude of this overage varies considerably by food category. While the success of folic acid fortification in the reduction of NTDs is undisputed, emerging evidence suggests that high levels of folic acid may be potentially harmful to some segments of the population. In order to strike the right balance between health benefits and risks, monitoring of fortified foods for their nutrient content is required.

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Received: September 27, 2008
Accepted: February 27, 2009

RÉSUMÉ

Objectifs : En 1998, le gouvernement du Canada a exigé l'ajout d'acide folique à la farine blanche et aux produits de grains enrichis afin de réduire la prévalence d'anomalies du tube neural. Une nouvelle inquiétude prend de plus en de place concernant les effets nocifs d'une dose trop forte d'acide folique dans certains segments de la population. Étant donné que l'on ignore la quantité actuelle d'acide folique ajouté aux aliments canadiens, cette étude vise à mesurer le contenu d'acide folique à une sélection d'aliments enrichis.

Méthodes : Nous avons utilisé les données de l'Enquête sur les dépenses alimentaires des familles 2001 et de la société ACNielsen afin de déterminer 95 des aliments enrichis d'acide folique les plus vendus au Canada. Nous avons établi les concertations d'acide folique de ces aliments en utilisant la digestion tri-enzymes, suivie d'une épreuve microbiologique. Nous avons ensuite comparé les valeurs analysées à celles du Fichier canadien sur les éléments nutritifs (2007b, FCEN) et aux valeurs nutritionnelles affichées sur l'étiquette.

Résultats : Le contenu d'acide folique des aliments se situe en moyenne à 151 % $\pm$ 63 des valeurs du FCEN. Les valeurs analysées en tant que pourcentage des valeurs du FCEN varient de 116 % dans la catégorie « petits pains » à 188 % dans les « céréales prêtes à manger ». Les valeurs analysées sont plus élevées que les valeurs affichées sur les étiquettes des « pains », « petits pains » et « céréales prêtes à manger » (141 %, 118 % et 237 % respectivement [$p < 0,05$]).

Conclusions : Dix ans après avoir enrichi les aliments d'acide folique, ni les valeurs du FCEN ni celles des étiquettes ne reflètent précisément les quantités réelles d'acide folique que contiennent les aliments. En outre, les différences globales par catégorie d'aliment peuvent entraver l'élaboration de stratégies futures conçues pour trouver le bon équilibre entre les avantages et les risques pour la santé; il faut donc surveiller le contenu en nutriments des aliments enrichis.

Mots clés : acide folique, Canada, approvisionnement alimentaire, aliments enrichis