Research Article

Critical evaluation of folate data in European and international databases: Recommendations for standardization in international nutritional studies

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Scope: The objective was to perform an inventory and critical evaluation of folate data in selected European and international databases. The ultimate aim was to establish guidelines for compiling standardized folate databases for international nutritional studies.
Methods and results: An *ad hoc* questionnaire was prepared to critically compare and evaluate folate data completeness, quantification, terminologies, and documentation of 18 European and international databases, and national fortification regulations. Selected countries participated in the European Prospective Investigation into Nutrition and Cancer project and European Food Information Resource Network (EuroFIR). Folate completeness was generally high. "Total folate" was the most common terminology and microbiological assay was the most frequently reported quantification method. There is a lack of comparability within and between databases due to a lack of value documentation, the use of generic or non-appropriate terminologies, folate value conversions, and/or lack of identification of synthetic folic acid.
Conclusion: Full value documentation and the use of EuroFIR component identifiers and/or INFOODS tagnames for total folate ("FOL") and synthetic folic acid ("FOLAC"), with the additional use of individual folates, will increase comparability between databases. For now, the standardized microbiological assay for total folate and HPLC for synthetic folic acid are the recommended quantification methods.

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1 Introduction

Folate is an essential B-group vitamin involved as a co-factor in cellular one-carbon reactions for nucleotide synthesis, methylation, and gene expression [1] and protects against neural tube defects. Research in the last 10 years has focused on the role of folate in reducing the risk of cardiovascular disease, by lowering serum homocysteine levels [2–6], certain cancers such as colorectal and colon [7–9] and dementia in the elderly [10, 11]. In particular, there has been much debate on the evaluation of evidence regarding the impact of folate status on initiation, progression, and growth of subclinical cancers and neuro-psychiatric disorders [12, 13].

Methodological issues related to nutrient measurements have implications on estimated diet–disease associations in large nutritional epidemiology studies. The issues for folate have already been discussed for food composition tables from nine European countries participating in the European Prospective Investigation into Cancer and Nutrition (EPIC, epic.iarc.fr) [14].

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Abbreviations: DFE, Dietary Folate Equivalents; **EPIC,** European Prospective Investigation into Cancer and Nutrition; **EuroFIR,** European Food Information Resource Network; **ENDB,** EPIC Nutrient Database; **MA,** microbiological assay

Because of the lack of a reference European nutrient database at the time, the EPIC Nutrient Database (ENDB) project was initiated by the International Agency for Research on Cancer to provide *ad hoc* standardized nutrient databases for the calibration of the EPIC baseline dietary data of the 10 involved European countries [15, 16]. The ENDB project was therefore considered to be an important practical experience in the development, standardization, and use of databases for nutritional research, and was used as a prototype within the EuroFIR project (European Food Information Resource Network, http://www.eurofir.eu) as a guide for database harmonization in Europe. Moreover, it provided insight into the current strengths and weaknesses of standardizing nutrient databases, and provided recommendations to the EuroFIR Network in order to anticipate and minimize limitations in the standardization of a larger set of food composition databases.

The ENDB has been completed for a first set of 26 priority nutrients, and has yet to be completed with folate data. The inventory and critical evaluation of folate data and databases across Europe was considered to be a prerequisite in the extension of the ENDB project with folate data.

Thus, the main objective of the current study was the inventory of folate data from European and international databases in order to critically evaluate the level of completeness, quality and documentation of folate data in these databases that are frequently used for nutritional epidemiological investigations into folate and cancer in Europe. Results of the inventory are presented and reference guidelines and recommendations are provided. These guidelines and recommendations will both serve to develop a standardized folate database for research purposes at IARC, as well as to improve the quality and completeness of folate data in national databases from compiler organizations in EuroFIR.

2 Materials and methods

Databases were selected from peer-reviewed, published, national databases and eligibility for inclusion was based on partner participation in the EPIC study and/or EuroFIR. Countries participating in the ENDB project were by design included in the inventory (Denmark, Sweden, Norway, Germany, the Netherlands, UK, France, Italy (ISPO database), Spain and Greece). Additional databases were selected from the EuroFIR project including those from Italy (INRAN database), Poland, Slovakia, Switzerland, and Finland. The US and New Zealand databases were also evaluated to be able to make comparisons between European and non-European databases.

An *ad hoc* folate questionnaire (available on request) was prepared by IARC and circulated to national database compiler organizations for completion during the period June 2008 and September 2009, and covered questions concerning the (i) completeness of folate data; (ii) folate quantification; (iii) folate terminologies used; (iv) folate data documentation; and (v) folic acid fortification and its national regulations. Each contact was asked to perform an assessment on the most up-to-date folate values in their databases. The questionnaire was intended to reveal the amount of work involved for the compilation of a standardized folate database, and its documentation. The completeness of each database was defined as the percentage coverage of folate across food items in the database.

3 Results and discussion

3.1 General

The main folate vitamers and entities, together with the currently used EuroFIR component identifiers (http://www.eurofir.net/eurofir_knowledge/eurofir_thesauri) and INFOODS tagnames (http://www.fao.org/infoods/tagnames_en.stm), are given in Table 1. Recent harmonization between the systems has resulted in the preferred use of "Total Folate" ("FOL"), "Folic acid, synthetic" ("FOLAC") and "Folate, food" ("FOLFD"; EuroFIR only). The use of the terms "Folate, bound" and "Folate, free" have been discontinued by EuroFIR as these terms have been considered ambiguous and dependent of the method used for deconjugation before determination by microbiological assay (MA).

The overview of selected databases is given in Table 2. Abbreviations are used to refer to these databases in this paper. The countries selected are representative of a wide cross-selection of different European geographical regions. The Slovak database SKA04 mostly contains historical data. New editions of the Dutch, New Zealand, Slovak and US databases were available online after the inventory (late 2009–2010), but were not included in this evaluation. The new Dutch database offers new analytical folate data, revised folate data, and adapted terminologies. The new online Slovak database also has adapted terminologies. The changes in terminologies are discussed in this paper. The New Zealand database contains updated information on fortified foods, differentiates fortified foods from non-fortified foods and industry data from analytical values. The US database has a new food group, updated information on fatty acids, and more vitamin C values. Moreover, the Spanish food database was not included in the inventory because the folate data had not been fully evaluated and published.

The year refers to either the publishing year of the most recent (national) food composition table (DK09, FI08, FR08, DE05, GR04, ITI08, NL06, NZC06, NZF06, NO06, PL05, SE08, CH08, UK08 and US08), the year of the most recent update of the folate database (ITD08), the computerized management database (SKA04) and food label database (SKD09).

All databases are published in the official language and all, except CH08, offer an English translation. There is a trend towards providing databases online as software

Table 1. List of main folate vitamers and entities in food, IUPAC abbreviations, component identifiers[a)] (EuroFIR) and tagnames[b)] (INFOODS)

Folate vitamer or entity	IUPAC abbreviation	ID	EuroFIR Descriptor	Scope note	INFOODS tagname	Additional information[c)]
Folate, total	–	FOL	Folate, total	For total folate	FOL	Total folate is food folate (FOLFD)+folic acid (FOLAC) present. Method Indicator identifier M10453
Folate, food	–	FOLFD	Folate, food	For naturally occurring folate in food		
Folate, bound	–	FOLB	Folate, bound	Inactive descriptor[d)]	FOLB	
Folate, free	–	FOLFRE	Folate, free	Inactive descriptor[d)]	FOLFRE	
Folic acid, synthetic	PteGlu	FOLAC	Folic acid, synthetic	For synthetic folic acid added to foods	FOLAC	ChEBI 27470
10-Formylfolic acid	10-HCO-PteGlu	FOLFM10	10-Formylfolic acid	For 10-formylfolic acid		
Dihydrofolic acid	7,8-H_2-PteGlu	$FOLH_2$	Dihydrofolic acid	For 7,8-dihydrofolic acid		ChEBI 15633
Tetrahydrofolate	H_4folate	$FOLH_4$	Tetrahydrofolate	For (6S)-5,6,7,8-tetrahydrofolic acid		ChEBI 15635
5-Methyltetrahydrofolate	5-CH_3-H_4folate	$FOLH_4$ME5	5-Methyltetrahydrofolate	For (6S)-5-methyl-5,6,7,8-tetrahydrofolic acid		ChEBI 15641
5-Formyltetrahydrofolate	5-HCO-H_4folate	$FOLH_4$FM5	5-Formyltetrahydrofolate	For (6S)-5-formyl-5,6,7,8-tetrahydrofolic acid		ChEBI 15640
5-Formyldihydrofolate	5-HCO-H_2folate	$FOLH_2$FM5	5-Formyldihydrofolate	For (6S)-5-formyl-7,8-tetrahydrofolic acid		
10-Formyldihydrofolate	10-HCO-H_2folate	$FOLH_2$FM10	10-Formyldihydrofolate	For 6S-5-formyl-7,8-tetrahydrofolic acid		ChEBI 15634
10-Formyltetrahydrofolate	10-HCO-H_4folate					
5,10-Methenyltetrahydrofolate	5,10-CH^+-H_4folate					
5,10-Methylenetetrahydrofolate	5,10-CH_2-H_4folate					
5-Formiminotetrahydrofolate	5-CHNH-H_4folate					

a) See http://www.eurofir.net/eurofir_knowledge/eurofir_thesauri.
b) See http://www.fao.org/infoods/tagnames_en.stm.
c) ChEBI ID numbers are identifiers for chemical entities and refer to the freely available database at EBI (http://www.ebi.ac.uk/chebi/).
d) The use of ''Folate, bound'' and ''Folate, free'' has been discontinued.

Table 2. Overview of selected European and international databases

Name of selected database (abbreviation, year)[a]	Food items	Cooked foods	Language O = Official E = English	Availability O = online P = printed C = CD-rom D = disk	Online availability: Web address – database format(s)
Denmark					
Fødevaredatabanken version 7.01[b] (DK09, 2009)	1049	–	O+E	O[c]	www.foodcomp.dk – html, excel, ASCII, access
Finland					
Fineli Food composition database Elintarviketaulukko. Tiedot ravintokoostumuksesta[b] (FI08, 2008)	600[d]	√	O+E	O[c]+P	www.fineli.fi – html
France					
Table de composition nutritionnelle des aliments version 2008[b] (FR08, 2008)	1346	√	O+E	O[c]	www.afssa.fr/TableCIQUAL – htm
Germany					
Bundeslebensmittelschlüssel version II.3.1[b,e] (DE05, 2005)	10 654	√	O+E	O[f]	www.blsdb.de – software files
Greece					
Composition tables of foods and Greek dishes 3rd ed.[g] (GR04, 2004)	901	√	O+E	O[c,g]+P	www.hhf-greece.gr/tables – excel
Italy					
Banca dati italiana di composizione degli alimenti per studi epidemiologici version 1.2008 (ITI08, 2008)	935	√	O+E	O[c]	www.ieo.it/bda2008 – html, PDF
Database italiano del contenuto in folati degli alimenti[h] (ITD08, 2008)	165	√	O+E	O[c,i]	www.inran.it[i]
The Netherlands					
Nederlands voedingsstoffenbestand 2006[b] (NL06, 2006)	1672	√	O+E	P+C[f]	www.rivm.nl/nevo_en/online[c,j]
New Zealand					
The concise New Zealand food composition tables 7th ed.[b] (NZC06, 2006)	900[d]	√	E	P	www.crop.cri.nz[c,j] – PDF
FOODfiles (NZF06, 2006)	2759	√	E	O[f]+C[f]	www.crop.cri.nz – software FT and AP files
Norway					
Matvaretabellen 2006[b] (NO06, 2006)	1188	√	O+E	O[c]	www.norwegianfoodcomp.no – excel
Poland					
Tabele składu I wartości odżywczej żywności[b] (PL05, 2005)	932	√	O+E	P+D+C[f]	www.izz.waw.pl[j,k] – html
Slovakia					
Slovenská potravinová banka dát - Alimenta 4.3[l] (SKA04, 2004)	1547	√	O+E	O+P[m]+C+D	http://www.pbd-online.sk[c,j]
Slovenská potravinová banka dát - Daris (SKD09, 2009)	77	-	O+E	C[n]+D[n]	

Table 2. Continued

Name of selected database (abbreviation, year)[a]	Food items	Cooked foods	Language O = Official E = English	Availability O = online P = printed C = CD-rom D = disk	Online availability: Web address – database format(s)
Sweden					
The National Food Administration's food database[b] (SE08, 2008)	1898	√	O+E	O[c]	http://www7.slv.se/Naringssok/SokLivsmedel.aspx- html, excel
Switzerland					
Schweizer Nährwertdatenbank version 2.11[b] (CH08, 2008)	825	-	O	O[c]	www.swissfir.ethz.ch/datenbank – PDF, excel, ASCII
The United Kingdom					
McCance and Widdowson's composition of foods integrated dataset[b] (UK08, 2008)	3423	√	E	O[c]+P	www.food.gov.uk/science/dietarysurveys – excel, ASCII
The United States					
USDA national nutrient database for standard reference release 21[b] (US08, 2008)	7412	√	E	O[c]+C	www.ars.usda.gov/nutrientdata[j] – PDF, excel, ASCII, access

√ = cooked food items are included in the corresponding database; - = cooked food items are not included in the corresponding database.

a) Databases were selected from peer-reviewed, published, national databases (EPIC and EuroFIR). The US and New Zealand databases were selected to be compared with European databases.
b) National food composition table.
c) Free access.
d) Estimated amount.
e) The next version is planned for 2010. It will include new folate values by the SIDA method, and some MA values will be updated with HPLC values. Updated food groups include dried legumes, cereal products, bread, vegetables, fruits, milk and enriched foods. The database will also provide more documentation, as there is an upcoming co-operation with the SFK-database.
f) License agreement required.
g) Section 2 (Nutritional Composition Tables of Greek Recipes by calculation) and Section 3 (Nutritional Composition of Greek Foods and Traditional Dishes by laboratory analyses) of the database are published online. Section 1 (Composition Tables of Generally Simple Foods) is not available online, and includes folate values compiled from the McCance and Widdowson's ''*The Composition of Foods*'' 5th edition.
h) The folate database (DiFoA) will be provided as annex in the new edition of the national food composition table (Tabelle di composizione degli alimenti).
i) The folate database is planned to be published online.
j) A new edition was made available online after the inventory.
k) A fee is required to have access to all data of 932 food products and dishes.
l) Nutrition software with user database.
m) Selected packages of Alimenta 4.3e are published in eight tables (amount of food items – publishing year): (i) Fruits and Vegetables (94–1997 – does not contain cooked foods); (ii) Cereals and Legumes (117–1999); (iii) Milk and Eggs (80–2000); (iv) Fats, Oil-bearing Plants, Oils and Nuts (90–2000); (v) Fish (75–2001); (vi) Poultry and Game (72–2001); (vii) Meat (129–2002); (viii) Meals and Dishes (calculated dishes) (178–2002).
n) This is an excel spreadsheet that is used for new data collection according to EuroFIR standards. The aim is to include it in the Alimenta database.

packages, Excel-files, Access-files, ASCII-files, PDF-files, XML formats, and/or htm(l) (downloadable or not). Most of the databases are already available online. At the time of the inventory, four were only available in print, on CD-ROM and/or disk (NL06, NZC06, PL05 and SKD09). Currently, the new releases of the Dutch and New Zealand databases, as well as the Polish database, are also available online. The majority of the online databases are freely accessible. Some of the databases require a license agreement (DE05 and NZF06), or a fee (PL05).

A summary of database completeness for folate values, terminologies, quantification, unit, and mode of expression, and the sources of values, is given in Table 3. The Greek database was excluded for further analysis because its folate values are taken from the McCance and Widdowson's "The Composition of Foods" 5th edition [17].

Folate completeness is high among the majority of databases, assuming that the zero values are not missing values (80–100%). However, the Slovak databases have lower folate completeness (54% in SKA04 and 12% in SKD09). Some databases have no missing values, and therefore 100% completeness, as previously missing folate values were either assigned a zero value or estimated and/or calculated (DE05, ITI08, NZC06, NZF06, PL05, and SE08). The folate database ITD08 contains only analytical data and does not contain any missing values.

Missing values in DK09, FR08, NL06, NO06, SKA04, SKD09, and US08 were reported to be real missing values due to a lack of data, whereas missing values in FI08 and UK08 were reported to be logical zero and/or trace values. The folate data in the CH08 database have yet to be evaluated and at this stage it is not clear what missing values represent.

Zero values and trace values make up to 13 and 10%, respectively, of folate values in the databases. Zero values were defined in the questionnaire as values assigned to food items that are considered not to contain folate and/or values obtained by analytical methods indicating that no folate is present (*i.e.* below the method LOD). All databases comprise zero values, except the SKD09 database. Trace values are analyzed or calculated values below LOQ, but the ingredients of the food indicate that a small unquantifiable amount is present. Half of the databases do not identify trace values with a specific descriptor, such as "Tr" or "T" (DK09, DE05, ITD08, NO06, SKA04, SKD09, SE08, and US08). In some of these databases, traces are replaced by zero values (DE05 and NO06). However, this is not an issue when these data are used in practice in user data sets, for *e.g.* intake calculations, because traces are treated as zero values for this purpose.

3.2 Folate unit and mode of expression

All databases express folate values in µg, except the SKA04 database that expresses its values in mg. The mode of expression *per* 100 g edible portion is applied in all databases, and is substituted by *per* serving for supplements in FI08, and by 100 mL food volume for beverages in CH08, liquid products in NL06, and alcoholic beverages in ITI08 and UK08. Alternatively, ITD08 additionally reports *per* serving in all food groups, and US08 *per* common household measures.

Calculation adjustments such as recipe calculations and raw-to-cooked calculations are applied in most databases. There is no correction for raw-to-cooked conversions in ITD08 because analyses were also performed on cooked foods. Moreover, values from the McCance and Widdowson tables were subtracted by 27% in the NL06 database due to previous Dutch research that indicated that HPLC analyses yields on average 27% smaller folate values compared with MA values [18]. However, these values were converted back to their original value in the new release. In addition, some databases use DFE units (ITD08, NL06, and US08). This takes differences in bioavailability after dietary intake of naturally occurring food folates and folic acid fortificant into account, by using a 1.7 multiplier to convert natural food folates into DFE, and 0.5 for folic acid from fortified foods or supplements. Even though this may be a suitable tool to express recommended folate allowances, the use of DFE increases imprecision in food composition data because the estimation of folate bioavailability is rather crude as it is based on data on status biomarkers from a few human trials only [19]. Calculation adjustments are not used in SKD08 and could not be confirmed for CH08.

3.3 Folate quantification and folate terminologies

Commonly, folate data in food composition databases derive from the widely accepted MA with *Lactobacillus rhamnosus* (ATCC7469) and should be presented as "total folate". The assay is based on measuring the growth of the organism, which responds similarly to all folate forms with up to three glutamate molecules, but not to folate degradation products [20]. The common calibrant in the MA is folic acid.

There is also a European (CEN) standard microbiological procedure (EN14131:2003) available that has been validated by inter-laboratory studies [21–25]. A validated method for the determination of total folate in cereals including methods for sample preparation has also been approved [26, 27].

Twelve of the 17 databases (Table 3) use MA as the folate quantification method. Compilers were therefore asked to report the amount of MA-determined folate values in the databases. It was stressed to indicate the origin of these values in order to be able to distinguish analyzed MA folate values from other MA folate values, such as estimates, calculations, values taken from literature, and borrowed values, which are not sufficiently documented. The reported percentages therefore represent minimum percentages due to the exclusion of these other MA folate values. The ITD08 database was the only database that was reported to have

Table 3. Folate completeness, terminology, quantification and sources in the selected databases

Country / Shortname database	DK / DK09	FI / FI08	FR / FR08	DE / DE05	IT / ITI08	IT / ITD08	NL / NL06	NZ / NZC06	NZ / NZF06
Food items in database	1049	600[a),b)]	1346	10654	935	165	1672	900[a)]	2759
Folate values									
Food items (%)[d)]	80	97[e)]	96	100	100	100	87	100	100
Zero values (%)[f)]	10	13	13	2[g)]	6	8[h)]	11	±5	4
Trace values (%)[i)]	n.i.	3[e)]	1[j)]	n.i.[g)]	8[j)]	n.i.	0	±10[j)]	4[j)]
Greater values (%)[k)]	90	84	86	98[a)]	86	92[h)]	89	±85	92
Unit	μg	μg	μg	μg	μg	μg	μg	μg	μg
Mode(s) of Expression									
/100 g edible portion	√	√	√	√	√	√	√	√	√
/100 ml food volume	–	–	–	–	√[l)]	–	√	–	–
/100 g total food	–	–	–	–	–	–	–	√	√
/serving	–	√[m)]	–	–	–	√	–	–	–
Folate terminology (% of food items) and definition	Folates (80%): total folate by MA, borrowed values from other tables, scientific literature, estimates and calculations Free folate[c)] (39%)	Total folate (89%)[n)]: total folate by MA Total folates (91%)[n)]: folic acid+HPLC-derived folate species Folic acid (not available for vegetables, 4.5%)[n),o)]: synthetic folic acid by HPLC 5-CH_3-H_4folate (56%), 5-HCO-H_4folate (19.5%), H_4folate (51.3%), 10-HCO-PteGlu (11.2%)[n)]: by HPLC	Total folates: total folate by MA, values by HPLC or LC MS/MS or RPBA, borrowed values from other tables, scientific literature, estimates, calculations and industry data	Total folate: free+bound folate (by MA), borrowed values from other tables, scientific literature and calculations	Total folate: folates in general and folic acid	Total folate (100%): total folate by MA Folic acid (100%): synthetic folic acid by HPLC Food folate (100%): total folate − folic acid DFE (100%): food folate (μg)+(1.7 × folic acid (μg))	Folic acid: naturally occurring folate by MA or HPLC, borrowed values from other tables, scientific literature, estimates and calculations, and synthetic folic acid from industry data[p)] DFE: μg naturally occurring folate+ (1,7 × μg synthetic folic acid)	Total folate: total folate by MA, and other values	Total folate: total folate by MA, and other values Folic acid: folic acid values from industry data
Quantification[q)]									
Method(s)	MA *Lact. rhamnosus*	MA *Lact. rhamnosus* +HPLC	MA+HPLC+ LC MS/MS +RPBA	MA+HPLC	–	MA *Lact. rhamnosus* +HPLC	MA *Lact. rhamnosus* +HPLC	MA *Lact. rhamnosus* +RPBA[r)]	MA *Lact. rhamnosus* +RPBA[r)]
MA folate values (% of values)[s)]	A: 32 B: 26	5.6[t)]	A+B: 25	A: n.k. B: n.k.	B: ±80	A: 100	A: 4 B: ±3.5	A: 19 B: n.k.	A: 19 B: n.k.
Calculation adjustments									
Recipe calculations	–	√	√	√	√	–	√	√	√
Raw-to-cooked	–	√	n.k.	√	–	–[u)]	√	√	√
Other	–	–	–	–	humidity[v)]	–	method[w)]	–	–

Table 3. Continued

Country	**DK**	**FI**	**FR**	**DE**	**IT**	**IT**	**NL**	**NZ**	**NZ**
Shortname database	DK09	FI08	FR08	DE05	ITI08	ITD08	NL06	NZC06	NZF06
Sources[q]									
Analytical values	√	√	√	√	–	√	√	√	√
Borrowed values	√ US, UK, SE, DE(SFK)	√ UK	√ UK, US, DK DE(SFK), IT	√ DE(SFK), possibly other sources	√ UK, US, DE(SFK), FR, DK, SE, FIN	–	√ UK, US, DK, FR, IT, SE	√ UK, US, possibly AUS	√ UK, US, AUS
Scientific literature	√	–	√	√	√	–	√	–	–
Estimations	√	n.k.	√	–	√	–	√	√	√
Calculations	√	√	√	√	√	–	√	√	√
Industry data	–	√	√	–	√	–	√	√	√
Country	**NO**	**PL**	**SK**	**SK**	**SE**	**CH**	**UK**	**US**	
Shortname database	NO06	PL05	SKA04	SKD09	SE08	CH08	UK08	US08	
Food items in database	1188	932	1547	77	1898	825	3423	7412	
Folate values									
Food items (%)[d]	95	100	54	12	100	90	83	86	
Zero values (%)[f]	1[g]	6	1	0	8[g]	9	3[h]	8[h]	
Trace values (%)[i]	n.i.[g]	0	n.i.	n.i.	n.i.[g]	2[j]	6[h]	n.i.	
Greater values (%)[k]	99	94	99	100	92	89	91[h]	92[h]	
Unit	μg	μg	mg	μg	μg	μg	μg	μg and μg DFE	
Mode(s) of expression									
/100 g edible portion	√	√	√	√	√	√	√	√	
/100 mL food volume	–	–	–	–	–	√	√[l]	–	
/100 g total food	–	–	–	–	–	–	–	–	
/serving	–	–	–	–	–	–	–	√[m]	
Folate terminology (% of food items) and definition	Folate: total folate by MA, borrowed values by RPBA, industry data, estimates and calculations	Folate: folates in general and synthetic folic acid	Folic acid: folates in general	Folic acid: synthetic folic acid with FOLIC ACID EuroFIR identifier	Folate: total folate by MA, folate by RPBA, and borrowed values from other tables, scientific literature, industry data, estimates and calculations	Folic acid: folates in general and possibly folic acid	Folate (83%): total folate by MA, estimates and calculations 5-CH_3-H_4folate (1%): by HPLC	Total folate (86%): total folate by MA, estimates and calculations Folic acid (81%): 15% of values by MA (without enzymes), zero values, and calculations Food folate (83%): – unfortified foods: total folate by MA, estimates and calculations – enriched cereal-grain products: analytical value before fortification	

Table 3. Continued

Country Shortname database	NO NO06	PL PL05	SK SKA04	SK SKD09	SE SE08	CH CH08	UK UK08	US US08
								– some fortified foods: total folate – folic acid DFE (81%): μg DFE = μg food folate + (1.7 * μg folic acid) 5-CH_3-H_4folate (< 1%): by LC MS
Quantification[q]								
Method(s)	MA *Lact. rhamnosus*	n.k.	n.k.	n.k.	MA *Lact. rhamnosus*+ RPBA	n.k.	MA *Lact. rhamnosus*+ HPLC	MA *Lact. rhamnosus* +LC MS
MA folate values (% of values)[s]	A+B: 31	B: n.k.	A: n.k. B: n.k.	A: n.k.	A: 21[x] B: n.k.	n.k.	A+C: 93	A: 38[y]
Calculation adjustments								
Recipe calculations	√	√	√	–	√	n.k.	√	√
Raw-to-cooked	√	√	√	–	√	n.k.	√	√
Other	–	–	–	–	–	n.k.	–	solids[z]
Sources[q]								
Analytical values	√	–	√	√	√	n.k.	√	√
Borrowed values	√ SE, FIN, DK, UK, US	√ DE(SFK), UK, SE, NO, FIN	√ US, UK, DE(SFK)	–	√ NO, FIN, DK, UK, US	√ FR, IT, DK, DE(SFK), DE(BLS), US, ES, NO, SE, CAN, FIN	–	–
Scientific literature	–	√	√	√	√	√	–	√
Estimations	√	–	–	–	√	n.k.	√	√
Calculations	√	√	√	–	√	n.k.	√	√
Industry data	√	√	√	√	√	√	–	√

√ = applicable, – = not applicable, n.i. = not identified, n.k. = not known, 5-CH_3-H_4folate = 5-methyl tetrahydrofolate, 5-HCO-H_4folate = 5-formyl tetrahydrofolate, H_4folate = tetrahydrofolate, 10-HCO-PteGlu = 10-formylfolic acid, MA = microbiological assay without bacterial strain specifications, MA *Lact. rhamnosus* = microbiological assay using *Lactobacillus rhamnosus*, RPBA = radio-protein binding assay; A = analyzed values; B = borrowed values; C = calculated values.

a) The value is estimated.
b) The amount of food items refers to the online database.
c) These values are not published, but can be provided.
d) Folate completeness or the percentage of total food items in the database with one or more value(s) for folate (folate, total folate, 5-CH_3-H_4folate, food folate, folic acid, DFE, *etc*).
e) The percentage of food items with folate values refers to ''total folates'' as the sum of HPLC-derived folate vitamers (91%), and ''total folate'' as folate values analysed by MA (5.6%). Trace values also refer to HPLC and MA.
f) Zero values (''0'') are used when it has been shown analytically that folate is not present in the food sample or are used for a food item which is assumed not to contain folate. This is the proportion of zero values to available folate values.
g) The percentages of zero values include both zero values and trace values. Trace values are not identified as such in the database.
h) Values refer to the terminology ''DFE'' (ITD08), ''folate'' (UK08), or ''total folate'' (US08). Moreover, 5-CH_3-H_4folate values in US08 are referred to as ''total folate'', but they are footnoted as ''5-CH3-H4folate''.
i) Trace values (''T'' or ''tr'') signify that folate is present, but at a level that cannot be measured adequately. This is the proportion of trace values to available folate values.
j) Trace values are borrowed from other tables (ITI08), determined by MA (NZC06 and NZF06), or have insufficient documentation to determined the analytical method (CH08).
k) Greater values are values that are neither zero values nor trace values. This is the proportion of ''greater values'' compared with available folate values.

l) Applicable for alcoholic beverages.
m) The mode of expression includes ''per portion'' (in the supplements of FI08, not the online database), or several household measures (US08).
n) The online database publishes only ''folate (HPLC)'' which is the sum of folic acid and HPLC-determined folate isomers (''total folates''). The terminologies presented in this table are all the terminologies that are available.
o) The terminology in the printed table is ''folic acid'' because this is the term used for the Finnish nutrient recommendations. It is unclear whether the background of the recommendations concerns the definition by HPLC.
p) Synthetic folic acid values are available in a separate list at the back of the printed table. These values were taken from industry data and have no method description.
q) Provided according to available documentation.
r) Some historical folate data refer to RPBA.
s) Minimal percentages were calculated or taken from documentation. Estimates, calculations, scientific literature, and borrowed values from other tables (no ''total folate'' values) were excluded to make percentages comparable.
t) The MA folate values refer to a mixture of methodologies. The type of methodologies was not obtained.
u) There is no correction for raw-to-cooked conversions because analyses were performed on cooked foods as well.
v) Data are recalculated if dry matter of the food in the database differs by more than 10% from the dry matter of the food from the original source.
w) Folate values borrowed from the Mc Cance and Widdowson table are subtracted by 27% because Dutch research indicated that HPLC yields on average 27% smaller folate values compared with MA.
x) MA was the only method used before 1981 and after 1999. Between 1981 and 1997, RPBA was the only method. Between 1997 and 1999, RPBA was used to analyze folic acid fortified products. The percentage (21%) is a minimum, and refers to folate values analysed after 1997. Values analysed before 1981 have insufficient documentation and could not be included in the calculation.
y) This is the percentage analyzed ''total folate'' values among all ''total folate'' values. The remaining part comprises estimates and calculations.
z) Some estimated folate values have been taken from a similar food and were adjusted for the difference in solids.

100% (in-house) analyzed MA folate values for all food items.

The databases FI08, FR08, DE05, ITD08, NL06, UK08, and US08 report some data from chromatographic folate quantification. HPLC, LC-MS, or more specific LC-MS/MS methods allow quantification of individual folate forms, but none has yet been officially approved [25, 28–31]. HPLC methods are limited by their dependence on commercial folate standards and usually folates are quantified as monoglutamates after enzymatic deconjugation. Few methods are published for the quantification of folate polyglutamates [32, 33]. Folic acid is usually quantified using HPLC with UV or electrochemical detection [34, 35] or by LC-MS [36–38]. Procedures for the sample preparation and quantification of one of the predominant dietary folate forms (5-methyltetrahydrofolate) have been standardized in a European method intercomparison study [29]. HPLC data should be presented either as concentrations of individual folates (in particular 5-methyltetrahydrofolate) or as a ''sum of individual folates, expressed as folic acid''. For the purpose of food composition databases it is recommended to specify which individual folates are included in the sum.

For some food items in a few of the databases, FR08, NZC06, NZF06, and SE08, radioprotein-binding methods have been used. Radioprotein-binding methods have been applied with limited success for food analysis. The folate binder in these, for clinical purposes automated, competitive binding assays possesses different affinity to the individual dietary folate forms, and it was recommended to apply this method only for foods containing mainly 5-methyltetrahydrofolate [39].

Most selected databases provide one generic terminology, such as ''folate(s)'' or ''total folate(s)''. Some of those databases provide an additional terminology, corresponding to other folate entities, for a limited amount of food items. The DK09 database provides additional ''free folate'' values. The ITI08 and NZF06 databases also refer to ''folic acid'' in a separate note (ITI08) or in an Appendix (NZF06). The UK08 database refers to ''5-CH_3-H_4folate'', determined by HPLC, for 1% of food items. Moreover, the CH08, SKA04, and SKD09 databases use ''folic acid'' as the generic terminology. This terminology should only be used to represent the synthetic form of folate, but it also includes naturally occurring folate in the SKA04 and CH08 databases. However, the new online Slovak database provides ''total folate'' and ''folic acid'' terminologies.

Changes in methods and/or terminology may occur over the time period that a database is compiled and consequently the chosen generic terminology does not always correspond to the specific folate entity.

Four databases provide multiple terminologies for a larger amount of food items, either referring to folate bioavailability (''Dietary Folate Equivalents'' or ''DFE''), the type of analysis used such as MA (''total folate''), and HPLC (''total folates'' as the sum of HPLC-derived entities, such as ''5-CH_3-H_4folate'', ''5-HCO-H_4folate'', ''H_4-folate'', and

"10-HCO-PteGlu"; and the synthetic "folic acid"), and/or a calculation that subtracts synthetic folic acid from total folate ("food folate"). The FI08 database distinguishes between various folate vitamers, which were all analyzed by HPLC, and refers to the sum of individual folates as "total folates". However, it is suggested to refer to the sum as "sum of individual folates, expressed as folic acid". The ITD08 and US08 databases provide mixed terminologies including "total folate", "folic acid", "food folate", and "DFE". The food folate term in the "DFE" values in both databases was calculated using MA data. The NL06 database includes two terminologies, namely "DFE" and "folic acid". The latter terminology was used incorrectly in that it referred to naturally occurring folate and synthetic folic acid. However, the new release now provides "folate", "folic acid", and "folate equivalents", respectively, identifying naturally occurring folate, synthetic folic acid and DFE.

3.4 Documentation

One of the key aims of the EuroFIR project was to improve comparability of data within European data sets and allow users access to additional information that could help them decide whether or not values are fit for purpose. Most data sets have traditionally been published in forms that do not easily allow publication of additional information. However, online publication and advances in information management mean that it is increasingly possible to provide the end user with additional information relating to the reliability and limitations of its use.

The key starting point of the EuroFIR data documentation initiative was to provide references for all data to allow further investigation of the data if required. By 2009, compilers from 20 countries had provided references for each published food and wherever possible this was extended to providing references for each individual value.

EuroFIR compilers also agreed to provide full documentation for all newly published data based on the requirements of the EuroFIR technical annex that forms the basis of the proposed CEN standard CEN/TC387 on "Food composition data – Structure and interchange format". The standard allows documentation of information relating to areas including food description, sample, component, method specification, value, reference, and data quality. The level of detail that can be documented is very comprehensive and documentation properties are split into mandatory properties that are required as they build the core set of documented data that are needed to properly identify and describe the food composition data and optional properties that provide additional information describing the data and thereby assisting the user to assess them.

A system for assessing quality of data from laboratory analytical reports and scientific publications has been developed based on information included in the documentation standard (Oseredczuk, to be published). The EuroFIR e-search facility (http://www.eurofir.net/eurofir_aisbl/membership_benefits/eurofir_esearch_facility) allows data sets to be searched either on the basis of food name or Langual food description identifiers and currently publishes details of the component identifier, unit, mode of expression, value, number of analytical samples, method, and reference.

Details on the availability of folate value documentation are given in Table 4. Compilers reported to have documentation to varying extents for all folate values for DK09, FR08, DE05, ITI08, ITD08, NL06, PL05, SKD09, UK08, and US08. Other databases (FI08, NZC06, NZF06, NO06, and SE08) were reported to have documentation to varying extents for fewer folate values. Two databases were reported to have written documentation in another location (SKA04) or insufficient documentation (CH08) for folate values.

All documented databases provide documentation on the value level. Value documentation of the UK08 database is planned for the near future. Some databases also provide documentation on the food item level for some foods (DK09, FR08, ITI08 and PL05). Folate values in all databases, but DE05, SKD09, NO06, and SE08, were reported to have the main types of documentation (value type, method type, reference type, and acquisition type). Value type is a qualitative description of the value, such as mean, minimum, maximum, and average. Method type is the way a value was obtained, such as analytical result, calculated as recipe or from related food. Reference type describes the publication format, such as "article in book", "article in journal", "article in report" or "book". Acquisition type describes general categories of food composition data sources and methods of data acquisition, such as in-house or affiliated laboratory, independent laboratory, food composition table, peer-reviewed scientific paper and scientific communication (http://www.eurofir.net/eurofir_knowledge/eurofir_thesauri).

All countries, except New Zealand, can furnish bibliographic sources; however, the extent of covered folate values varies between countries. All databases, except SKA04, provide a date or year linked to the folate value, being the date the folate value was entered into the database, date of evaluation, date of analysis, publication date or year associated with an analytical report or scientific article, and/or date when the value was borrowed from another database. Databases that borrow folate data from other databases do not always provide the date when the value was borrowed. However, the publishing year or version of the original database was reported to be found in the bibliographic source for DK09, FR08, ITI08, NO06, and SE08 (not confirmed for PL05 and CH08). Around 50% of the databases offer information on number of samples, minimum and maximum values, and/or value ranges.

Details on method protocols (extraction, deconjugation procedures, specific bacterial strains (MA), analytical quantification method, detection method) and quality assessments (use of certified reference materials, ring tests, and/or

Table 4. Documentation of folate values in the selected folate documented databases

Country	**DK**	**FI**	**FR**	**DE**	**IT**	**IT**	**NL**	**NZ**	**NZ**	**NO**	**PL**	**SK**	**SK**	**SE**	**CH**	**UK**	**US**
Shortname database	DK09	FI08	FR08	DE05	ITI08	ITD08	NL06	NZC06	NZF06	NO06	PL05	SKA04	SKD09	SE08	CH08	UK08	US08
Types of documentation[a)]																	
Value type	$\surd^{S}$	$\surd^{D}$	$\surd^{S}$	$\surd^{S}$	$\surd^{S,b)}$	$\surd^{D}$	$\surd^{S,c)}$	$\surd^{S}$	$\surd^{S}$	–	$\surd^{S}$	–	$\surd^{D/S}$	$\surd^{D}$	$\surd^{S}$	$\surd^{S}$	$\surd^{D/S,d)}$
Method type	$\surd^{S}$	$\surd^{D}$	$\surd^{S}$	–	$\surd^{D/S,b)}$	$\surd^{D}$	$\surd^{S,c)}$	$\surd^{S}$	$\surd^{S}$	$\surd^{S}$	$\surd^{S}$	–	–	$\surd^{D}$	–	$\surd^{S}$	$\surd^{D/S,d)}$
Reference type	$\surd^{S}$	$\surd^{D}$	$\surd^{S}$	$\surd^{S}$	$\surd^{S,b)}$	$\surd^{S}$	$\surd^{S,c)}$	$\surd^{S}$	$\surd^{S}$	$\surd^{S}$	$\surd^{S}$	–	$\surd^{D}$	–	–	$\surd^{S}$	$\surd^{S,d)}$
Acquisition type	$\surd^{S}$	$\surd^{D}$	$\surd^{S}$	$\surd^{S}$	$\surd^{S,b)}$	$\surd^{S}$	$\surd^{S,c)}$	$\surd^{S}$	$\surd^{S}$	$\surd^{S}$	$\surd^{S}$	–	$\surd^{D}$	$\surd^{D}$	–	$\surd^{S}$	$\surd^{D/S,d),e)}$
Bibliographic source	$\surd^{D}$	$\surd^{D}$	$\surd^{D}$	$\surd^{S}$	$\surd^{D/S,b)}$	$\surd^{S}$	$\surd^{D/S,c)}$	–	–	$\surd^{D}$	$\surd^{D}$	$\surd^{S}$	$\surd^{D}$	$\surd^{D}$	$\surd^{D/S}$	$\surd^{S}$	$\surd^{D/S,d)}$
Method protocol	$\surd^{S}$	$\surd^{S}$	$\surd^{S}$	–	–	$\surd^{S}$	$\surd^{S}$	$\surd^{S}$	$\surd^{S}$	$\surd^{S}$	–	–	–	$\surd^{S}$	–	$\surd^{S}$	$\surd^{S,d)}$
Associated date																	
Folate value entry date	$\surd^{S}$	$\surd^{D}$	$\surd^{S}$	–	$\surd^{S}$	–	$\surd^{S}$	$\surd^{S}$	$\surd^{S}$	–	–	–	$\surd^{D}$	$\surd^{D}$	–	–	$\surd^{S}$
Evaluation date	–	–	$\surd^{S}$	–	$\surd^{S}$	–	$\surd^{S}$	$\surd^{S}$	$\surd^{S}$	–	–	–	–	$\surd^{D}$	–	$\surd^{S}$	$\surd^{S}$
Date of analysis	$\surd^{S,f)}$	$\surd^{D,g)}$	–	$\surd^{S,g)}$	–	–	–	$\surd^{S}$	$\surd^{S}$	$\surd^{S}$	–	–	–	$\surd^{S}$	–	–	$\surd^{S}$
Publication date report/article	$\surd^{D,h)}$	–	$\surd^{D,h)}$	$\surd^{S}$	$\surd^{D,h)}$	–	–	–	–	$\surd^{S,h)}$	$\surd^{D/S}$	–	$\surd^{D}$	$\surd^{S}$	$\surd^{S}$	$\surd^{S}$	$\surd^{D/S,h)}$
Date when value was borrowed	–	$\surd$	–	$\surd^{S}$	–	–	–	$\surd^{S}$	$\surd^{S}$	–	–	–	–	–	–	–	–
Statistical measures																	
Standard deviation	–	–	–	–	–	–	–	–	–	–	–	$\surd^{S}$	–	–	–	–	$\surd^{D/S}$
Number of samples	$\surd^{D,i)}$	$\surd^{D}$	$\surd^{D}$	–	–	$\surd^{D}$	–	$\surd^{S}$	$\surd^{S}$	–	–	–	–	–	–	–	$\surd^{D/S}$
Minimum value	$\surd^{D,i)}$	–	$\surd^{D}$	–	–	–	–	–	–	–	–	$\surd^{D,j)}$	–	–	–	–	$\surd^{D/S}$
Maximum value	$\surd^{D,i)}$	–	$\surd^{D}$	–	–	–	–	–	–	–	–	$\surd^{D,j)}$	–	–	–	–	$\surd^{D/S}$
Range	$\surd^{D,i)}$	–	–	–	–	$\surd^{D,k)}$	–	–	–	–	–	–	–	–	–	–	–
Quality																	
Quality index or indicator	–	$\surd^{D}$	$\surd^{D}$	–	–	–[l)]	–	–	–	–	–	–	–	–	–	–	–
Used as inclusion criterion	no	no	$\surd^{m)}$	no	no	no	no	no	no	no	no	no	no	no	no	no	no
Reasons for lack of documentation																	
Documentation cannot be retrieved	no	no	no	no	no	no	no	yes	yes	no	no	yes	yes	yes	yes	no	no
Available, but lack of time and resources	no	no	no	yes	yes	no	yes	no	no	yes	no	yes	no	yes	yes	no	no
Non-documented borrowed value(s)	no	no	no	no	yes	no	no	yes	yes	yes	no	yes	no	yes	yes	no	no
EuroFIR full value documentation[n)]	yes	yes	yes	yes	yes	no	yes	no	No	yes	yes	yes	yes	yes	yes	yes	no

$\surd^{D}$ = documentation for all or fewer folate values is available in the database; $\surd^{S}$ = documentation for all or fewer folate values is available separately, not in the database; $\surd^{D/S}$ = documentation is available in database and/or separately; $\surd$ = applicable; - = the corresponding documentation of folate values cannot be provided.

a) Value type: a qualitative description of the value (mean, minimum, maximum, average, central value, weighted, trace, *etc*); method type: describes how a value was obtained (analytical result, calculated as recipe, calculated from related food, *etc*); reference type: describes the way food composition data are published (article in book, article in journal, article in report, book, *etc*); acquisition type: describes general categories of food composition data sources and methods of data acquisition (in-house or affiliated laboratory, independent laboratory, food composition table, peer reviewed scientific paper, scientific communication, *etc*)

b) Approximately 45% of folate values have full documentation, as prepared for the ENDB project. The remaining 55% has bibliographic references with corresponding publication year.

c) Documentation is available, but is a combination of the different types of documentation listed in the table.

d) Food items that have been processed since 2001 have documentation in the USDA National Nutrient Database for Standard Reference, but items that date to earlier releases have the documentation in the internal Nutrient Data Bank System or on paper.

e) Acquisition type is available within the bibliographic source or can be inferred from the bibliographic source.

f) Date of sampling of food is also available.

g) Date of analysis can be obtained only if analytical report is available. When initial data are received without analytical report, the date when data were received is reported.

h) Publication date is available within the bibliographic source.

i) These types of data are available in the downloadable formats which are available online.

j) These statistical measures are available for half of the folate data.

k)The amount of folic acid in fortified foods is presented as a value range.

l) Method performance and scheme of sampling will probably be available in the database, but not an index.

m) The quality index, named confidence code in the database, is used when choosing folate values from initial data during the aggregation process.

n) Participation in the full value documentation initiative as a EuroFIR partner.

accredited laboratories) were not always provided, yet, are essential to evaluate data comparability and reliability. Particularly, MA responds to all folate mono- and diglutamates, while HPLC only quantifies individual folate vitamers for which standards are available and the method was validated for. Moreover, there are no algorithms or other calculations that can be used to convert folate values for another method (*e.g.* applied in NL06 but not kept in its new release).

Only two databases make use of a quality index or indicator (FI08 and FR08). It is used as a criterion in the aggregation process of folate values for FR08.

3.5 Folic acid-fortified foods in the databases and folic acid fortification status

Results from the inventory show that voluntary fortification is accepted in all countries. The US mandates folic acid to be added to enriched grain products. New Zealand currently authorizes folic acid to be added to bread, except organic breads, but as of 31 May 2012 compliance will be mandatory.

In general, most databases list folic acid-fortified foods. Yet only four databases identify them by means of a symbol or a note (ITD08, NL06, NZC06, and US08); all of which, except NZC06, listing a separate folic acid value. Breakfast cereals are most commonly fortified across countries. Other fortified foods are cereal products, beverages, some dairy products, dietetic foods, clinical and infant formulas, fortified biscuits and bars.

A few national compilers could not confirm the presence of folic acid-fortified foods in their database. The German compiler reported to have no folic acid-fortified foods in their current database. The next update will provide folic acid-fortified foods, only specifically identified as being folic acid fortified when less than 2 vitamins have been added, and without a separate folic acid value.

4 Concluding remarks

Although the coverage of folate values in European food composition databases is quite high, there are a number of problems with the data and generally there is lack of comparability between countries. In terms of methods used, only data obtained using the standardized MA for total folate – fully validated by inter-laboratory studies – and folic acid by HPLC can be considered as an acceptable quality level for now. A range of suitable food Certified Reference Materials are also available for both these folate parameters that can be used by laboratories to check the accuracy of the data obtained.

The more recent use of HPLC, LC-MS and/or LC-MS/MS offers the potential for measuring individual folate monoglutamates with accuracy and precision, but these methods have not been adequately validated for food and should be used with caution. The frequent use of obtaining the sum of individual folates as total folate should be avoided unless the methods have been well-validated and adequate documentation is provided to indicate that the summation of individual folates (obtained by HPLC or LC-MS/MS) has been used in compilation. Although there are no reference procedures solely for folic acid determinations in food, both microbiological and HPLC methods have been routinely used for its quantification. However, there has been no inter-laboratory validation to date for these methods for folic acid.

The use of EuroFIR component identifiers and/or INFOODS tagnames for total folate (''FOL'') or folic acid (''FOLAC'') should become the standard with the additional use of individual folates. The adoption of DFE might also be a useful term in the future provided that both total folate and folic acid values are available. The conversion of folate values obtained by MA to ''HPLC corrected values'', and *vice versa*, should be avoided.

The ongoing compilation of an end-user folate database for the purpose of the international EPIC study will benefit from this in-depth inventory.

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