ABSTRACT Some nitrosocompounds that are formed during food preservation, as well as polycyclic aromatic hydrocarbons (PAH) and heterocyclic amines (HAs), that are not naturally present in foods but may develop during cooking, may have carcinogenic activity. An accurate assessment of dietary intake of such compounds is difficult, mainly because they are not naturally present in foods, and they are not included in standard food composition tables. Our objective was to develop a food composition database of nitrates, nitrites, nitrosamines, HA, and PAH. We conducted a literature search on the food content of these compounds using the Medline and EMBASE databases. We gathered the following information: 1) Food information: name, cooking methods, preservation methods, cooking doneness, temperature, and time; 2) compound information: type, quantity, value type, analytic method, and sampling methods; and 3) publication information: year, author, and country. We developed a table that includes 207 food items with information concerning the concentration of nitrates, nitrites, and nitrosamines, 297 food items with information about HA concentration and 313 food items with information about PAH. The database is based on 139 references from 23 different countries. It is arranged according to compounds and food groups to facilitate its practical use. The potential limitations are due to the quality of the information we could obtain through Medline and EMBASE databases. This database will allow investigators to quantify dietary exposure to several potential carcinogens, and to analyze their relation to the risk of cancer.

KEY WORDS: • nitrosamines • heterocyclic amines • polycyclic aromatic hydrocarbons • food database • cancer risk

There are 2 main classes of HAs, aminimidazol-quinolines and aminimidazol-pyridines. Among the latter, [2-amino-1-methyl-6-phenylimidazol(4,5,b)pyridine] (PhIP) accounts for most of the overall HA exposure (3). All of them were found to be carcinogenic under experimental conditions and in animal models; however, their health effects in humans have not been clearly established. The most common nitrosamines and PAHs, as well as [2-amino-3-methylimidazol(4,5,f)quinoline] (IQ), are classified by the International Agency of Research on Cancer (IARC) as 2A, whereas other nitrosamines and most HAs are classified as 2B (4). On the other hand, even though diet is the main source of exposure in the general population, these chemicals are also present in the occupational environment, tobacco smoke, and air pollution due to incomplete combustion of organic matter. Most epidemiologic studies concerning the effects of such compounds are based on selected groups that are exposed to relatively high levels of contaminants in an occupational setting or residents living near potential sources of pollution. Dietary exposure studies are usually based on indirect measures, such as consumption of preserved foods or red meat.

There is no conclusive evidence that any cooking method is causally related to cancer risk, but diets that are rich in meats cooked at high temperatures may increase the risk of colorectal and gastric cancers (5). Apart from Chinese-style...
preserved fish, which was found to cause nasopharyngeal cancer, there is no convincing evidence that other preserved foods cause cancer. In any case, foods that have a high content of nitrosamines may be associated with increases in colorectal, gastric, and esophageal cancers (5).

One of the main difficulties in assessing the effects of the dietary nitrosamines, PAHs, and HAs is the lack of information about the levels of these compounds in foods. Because they are not a natural component of foods and do not have nutritional value, they are not included in food composition databases. Furthermore, assessment of the intake of some compounds is hampered because their concentrations depend on the cooking methods used in the preparation of various foods. This information is not included in most food intake questionnaires. The purpose of this paper is to present a complete and standardized database that includes the concentrations of nitrosamines, PAHs, and HAs in foods and to estimate intakes of these 3 groups of potential dietary carcinogens.

MATERIALS AND METHODS

A literature search was conducted to identify sources of data on the concentrations of nitrosamines, PAH, and HA in foods. We searched Medline (6) and EMBASE (7) from 1980 to 2003. The search terms were “nitrates,” “nitrites,” “nitrosamines,” “heterocyclic amines,” “polycyclic aromatic hydrocarbons,” “food content,” and “dietary sources.” Papers that included the concentrations of nitrites and nitrates in foods were included because they are precursors of endogenous nitrosamines. When data were gathered from a review or compilation, the original source was identified and accessed whenever it was considered relevant. In some cases, additional data were requested from authors directly. The initial review was also used to identify experts, many of whom were contacted to obtain unpublished or missing data. We did not use data from studies that were based upon determinations made exclusively in highly contaminated areas. In most cases, the purpose of such research was to monitor environmental pollution. We did not consider these data to be representative of dietary exposure in general populations.

The following information was extracted from each publication: 1) food information: name, preservation, and cooking method, including temperature, cooking time, and degree of doneness; 2) measurement information: value and type of value (mean, median, range, other), analytical method, and sampling method; and 3) publication information: year, author, country, and type of publication (review or original data).

The selection of these variables was made according to recommendations for the development of food composition databases (8,9), and taking into account data that were considered relevant to the final concentration of each individual compound.

After we compiled the database, it was reviewed by experts on both the specific chemical compounds and the food composition databases. In addition to checking the preliminary version of the table, in most cases, they recommended or directly provided additional data sources and references.

RESULTS

The food database was gathered from a total of 139 publications from 23 different countries. It includes 207 food items with information concerning the concentrations of nitrites, nitrates, and nitrosamines, 297 food items with information about HA concentration, and 313 food items with information about PAH. Table 1 is a summary of the most relevant information compiled.

The food database is divided into nitrosamine, heterocyclic amine, and polycyclic aromatic hydrocarbon sections. For each

| TABLE 1 |
| Summary of information included in the food database of potential carcinogens

<table>
<thead>
<tr>
<th>Groups of compounds</th>
<th>Compound</th>
<th>Publications</th>
<th>Country of publication</th>
<th>Food groups included</th>
<th>Food items</th>
<th>Information extracted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrates, nitrates,</td>
<td>Nitrates, nitrates, NDMA, NPIP, NPYR, NPRO, and combinations</td>
<td>54</td>
<td>CA, CN, DE, FR, GR, HK, IN, IS, JP, NL, SC, UK, US</td>
<td>Potatoes, vegetables, fruits, dairy products, cereals, meat, fish, eggs, fats, alcoholic beverages, nonalcoholic beverages</td>
<td>207</td>
<td>Name, cooking method, preservation method, value, type of value, analytic method, sampling method, year of publication, author, country, source (review or original data)</td>
</tr>
<tr>
<td>Nitrosamines</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterocyclic amines (HA)</td>
<td>PhIP, MethIQx, DimethIQx, AC, IQ, MeIQ</td>
<td>59</td>
<td>AT, CA, CH, CN, ES, FI, DE, JP, NO, NZ, SE, UK, US</td>
<td>Meat (fresh, preserved meat, meat products) and fish (fresh, seafood, canned fish)</td>
<td>297</td>
<td>Name, degree of doneness, cooking method, temperature, cooking time, preservation method, value, type of value, analytic method, sampling method, year of publication, author, country, source (review or original data)</td>
</tr>
<tr>
<td>Polycyclic Aromatic Hydrocarbons (PAH)</td>
<td>B(a)P, DB(a)A, PAH total</td>
<td>26</td>
<td>AT, BR, CA, CN, DE, ES, FI, IS, IT, KW, NL, US</td>
<td>Potatoes, vegetables, fruits, dairy products, cereals, meat, fish, fats, sweets and desserts, alcoholic beverages, nonalcoholic beverages</td>
<td>313</td>
<td>Name, cooking method, preservation method, value, type of value, analytic method, sampling method, year of publication, author, country, source (review or original data)</td>
</tr>
</tbody>
</table>

1 Food content of potential carcinogens. Nitrates, nitrites, nitrosamines, heterocyclic amines and polycyclic aromatic hydrocarbons.

2 Nitrosocompounds: NDMA (N-nitrosodimethylamine); NPIP (N-nitroso Piperidine); NPYR (N-nitrosopyrrolidine); and NPRO (N-nitrosoprololine). Heterocyclic amines: PhIP (2-amino-1-methyl-6-phenylimidazo[4,5,b]pyridine); MethIQx (2-amino-3,8dimethylimidazo[4,5,f]quinoline, 2-amino-3,4,8trimethylimidazo[4,5,f]quinoxiline (DiMeIQx); 2-amino-3-methylimidazo[4,5,f]quinoline (IQ); 2-amino-3,4 dimethylimidazo [4,5,f]quinoline (MelIQ); and AC (2-amino-9-H-pyrido[2,3,4]-indole). Polycyclic aromatic hydrocarbons: B(a)P (benzo[a]pyrene); DB(a)A (dibenzo[a]anthracene). |
group, the levels of the following chemicals are reported: nitrosocompounds: N-nitrosodimethylamine, N-nitrosopiperidine, N-nitrosopyrrolidine, and N-nitrosopropylene (NPRO). Although NPRO is not considered to be a carcinogen, it is included in most papers measuring other nitrosamines, and therefore is included in the database. Some papers reported the amount of a combination of several nitrosamines, which were not included. Taking into account the progress made 1980 as an arbitrary cutoff date; thus, papers published before completeness, we refer mainly to the degree to which all analytical methods as well as potential time trends in the literature for each compound.

Within each group of compounds, the list of food items is grouped according to a standard classification (10), including the following subgroups or individual foods: potatoes: potatoes and tubers; vegetables: leafy vegetables, root vegetables, cruciferous, other vegetables; fruits: fresh fruits, dried fruits; milk and dairy products: milk, cheese, yogurt; cereals and cereal products: bread, pasta, rice, flour; meat and meat products: fresh beef, pork, chicken, sausage, hamburgers; fish: fresh fish, canned fish, seafood; eggs: fats: butter, margarine, oils; sweets: biscuits, cake, chocolate, sugar; alcoholic beverages: wine, whisky, beer; nonalcoholic beverages: coffee, tea, cacao.

The cooking methods used are reported using standard definitions as well (10,11). When relevant and available, characteristics of cooking (time, temperature), and degree of doneness of foods were provided. Most analytical methods were based on chromatographic techniques, mainly HPLC or GC. Given the diversity of sampling methods used by different authors we simply reported whether the information on number and origin of samples was complete, incomplete, or not available. In most papers, the amount of each chemical compound in a food item was given as a crude or weighted mean. Finally, the author, country, and year of the publication and the reference are reported. The complete database, in both English and Spanish, is available in printed (12) and electronic versions(13).

**DISCUSSION**

We compiled an extensive database on the food composition of several potential dietary carcinogens. We did not directly measure any of the compounds. All of the values reported were gathered from the literature, or provided directly by contributors. Two major limitations of any literature review are quality and completeness of the information included. By completeness, we refer mainly to the degree to which all information relevant to the aim of the study was included, or in other words, relevant data were not excluded. We chose 1980 as an arbitrary cutoff date; thus, papers published before that were not included. Taking into account the progress made on analytical methods as well as potential time trends in dietary habits, it seemed a reasonable choice. On the other hand, although we attempted to obtain unpublished as well as published data, it is possible that we, the contributors and the reviewers, may not be aware of some important data that may have been reported in publications that were not included in Medline or EMBASE.

A related issue concerns the quality of information collected. We did not specify a priori criteria of exclusion, except that the data reported were not to be aimed at monitoring environmental pollution in a specific area. In any case, publications that were included varied in quality; however, it was important that the analytic methods used were described. Most of these were based on chromatography, the most widely accepted method to measure food components.

The database will be useful for estimating dietary intakes of nitrosamines, PAHs, and HA in epidemiologic and nutritional studies. This will provide a basis for investigating potential relations between such compounds and the risk of different cancers, particularly those of the digestive tract, such as colorectal, gastric, and esophageal cancers. Assessments of the relations between dietary factors and such tumors have been based mainly on time, intake of foods in which these compounds are found. However, these foods may be sources of many other components that may play a role in cancer risk. For instance, PAHs and HAs are related to meat intake, but meat consumption may be correlated with a diet rich in energy and SFA, which may in turn be associated with cancer risk.

Another potential application of the table is the assessment of dietary biomarkers. Most of the compounds included in our database or their metabolites may damage the structural integrity of DNA; this occurs primarily as covalent carcinogen binding, and is referred to as carcinogen-DNA adduct formation. DNA binding appears to be linear over a wide dose range for many compounds, suggesting the usefulness of measuring adducts in the assessment of exposure. DNA adducts likely reflect the cumulative exposure to carcinogens after the action of metabolizing enzymes and despite the action of repair enzymes. They are, therefore, markers of cumulative, unrepair DNA damage (14). Intake of the compounds of interest themselves, rather than the intake of foods that contain these compounds, is a better estimate to use when investigating correlations between adduct levels and exposure. These comparisons should take into account other potential sources such as tobacco smoke and occupational exposures.

In some cases, different sources provided information concerning the same food item. We did not group these values; instead, we present all of them with the relevant information. It allows the reader to select the most appropriate value for a particular study, taking into consideration the origin of the data, giving preference to values coming from the same country, or measured by a technique thought to be more reliable. The year of publication is also important, mainly for nitrosamines, because curing and preservation practices have changed over time, resulting in a marked decrease in the concentration of nitrosocompounds in foods, particularly in Western countries (15).

The availability of a food composition database will never overcome the limitations of the dietary assessment instrument used. Thus, even high-quality food composition tables will produce poor estimates when combined with low-quality data due to of the lack of validity and/or reliability of a dietary questionnaire. Particular attention must be paid to the influence of cooking methods, especially for compounds such as HAs, which are highly affected by factors related to the method and degree of cooking.

In conclusion, we present a food composition database of potential dietary carcinogens based on data gathered from several sources. This database will allow many nutritional researchers to go one step further in the assessment of dietary

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4 The complete database of levels of nitrosamines, heterocyclic amines, and polycyclic aromatic hydrocarbons in foods is available with the online posting of this paper at www.nutrition.org.
exposure to some food components, and to be able to analyze their potential associations with cancer risk.

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LITERATURE CITED


