AGRICULTURAL AND FOOD CHEMISTRY

From Detrimental to Beneficial Constituents in Foods: Tracking the Publication Trends in *JAFC*

James N. Seiber* and Loreen Kleinschmidt

Department of Environmental Toxicology, University of California, Davis, Davis, California 95616, United States

ABSTRACT: A large part of the research focus on food constituents in the 20th century was toward health-detrimental contaminants—pathogens, toxins, chemical residues, and some food additives. This is reflected in the publications in the *Journal of Agricultural and Food Chemistry* and other journals. This era witnessed the formation of the U.S. Food and Drug Administration (FDA) and Environmental Protection Agency (EPA) and the rise and fall of DDT and other synthetic chemicals, as well as a number of artificial sweeteners, preservatives, and coloring/flavoring agents that attracted consumer and government attention. During the past 25 years or so, the emphasis in food chemistry and biochemistry has trended more toward health-beneficial chemicals in foods, as their examination yields information on naturally occurring components—polyphenolic antioxidants, unsaturated fatty acids, soluble fibers, and many other classes of constituents that may ward off chronic diseases. This perspective addresses the changes in emphases in published research to the present and trends that indicate the directions that food chemistry/biochemistry and related sciences might follow in the future.

KEYWORDS: health benefits, food, food analysis, food safety, publications, diet, toxic chemicals, antioxidants, food chemistry, food biochemistry, organic foods, contaminants

The Journal of Agricultural and Food Chemistry, 1 of 46 peerreviewed journals published by the American Chemical Society and a leading international journal in its field, was founded in 1953. In recent years JAFC published papers in 13 categories. The number of categories is being reduced in 2012 by consolidation and renaming, while retaining the coverage that now exists. One of the categories that has grown considerably since about 1990, Bioactive Constituents, includes many of the published papers on health-beneficial chemicals in foods, but not all. Some papers addressing this subject may have fallen under Analytical Methods, Food Chemistry/ Biochemistry, Molecular Nutrition, or another category, so that the trend analysis, which is the subject of this paper, must include a look at all of the categories.

In the 1970s a number of federal laws were passed in the United States that dealt with reducing exposure to toxic chemicals to a minimum.¹ The Clean Air Act, for example, designated a listing of hazardous air pollutants and the Safe Drinking Water Act addressed minimizing or eliminating toxic contaminants from drinking water. The mindset accompanying these federal laws was that of a "chemical of the month" for public and regulatory scrutiny, as one chemical after another was detected and found to possess toxicity at some level that would suggest they be branded, monitored, and removed from use in ways that added to their environmental concentrations. DDT and other "legacy" pesticides were in that group, as were volatile organic compounds (VOCs) and semivolatile organic compounds (SVOCs), widespread contaminants in water, hazardous air pollutants (HAPs), artificial sweeteners (e.g., cyclamates), naturally occurring chemicals such as aflatoxins, nitosamines, mercury, and other heavy metals, and many others. Pesticides in particular were scrutinized, and many were removed from registration or greatly curtailed in usechlordane, toxaphene, Alar, and ethyl parathion, to name a few. Methyl bromide and atrazine presently face uncertain

futures, although some uses remain in 2012. Aflatoxins are still found in food as metabolites of the mold Aspergillus spp. and are particularly troublesome in large parts of Asia, where they are thought to significantly increase the risk of hepatocellular carcinoma among those with chronic hepatitis B virus infection.² In the United States, aflatoxin levels in foods are monitored and must be below an action level mandated by the FDA and by those countries that import food from the United States. Almonds, for example, have an FDA action level for aflatoxins of 20 ppb, and for the European Union (EU), the allowable level is only 10 ppb for direct human consumption or 15 ppb if destined for further processing. This restricts imports of almonds into the EU nations. Aspergillus infests apples, pears, corn, tree nuts, peanuts, cotton seed, and other commodities subject to insect damage, which allows the fungus to enter the nut, kernel, or seed and produce the family of aflatoxins as metabolites. The key to reducing aflatoxins is thus to control the insects that cause damage, potentially leading to use of more pesticides, including insecticides and fumigants.

Analytical chemistry is a principal way in which contaminant levels in foods and other samples are monitored. Trends in improved methods coincided roughly with the passage of laws in the United States, EU, and/or individual states and nations. Gas and liquid chromatography techniques were improved immensely by coupling with mass spectrometry detection systems—giving rise to GC-MS and LC-MS in the 1970s and 1980s, continuing to the present.³ Analytical advances such as

Special Issue: Food Bioactives and the Journal of Agricultural and Food Chemistry

Received:	December 8, 2011
Revised:	February 29, 2012
Accepted:	March 6, 2012
Published:	March 26, 2012

these lower the detection limits and increase the accuracy and precision of the results. They may also increase the cost of equipping laboratories, but do not necessarily increase the per sample cost of analysis because of increased sample throughput in well-equipped laboratories. The same techniques used for chemical contaminants, particularly GC-MS and LC-MS, are now used routinely to identify and monitor the content of antioxidants and other health-beneficial constituents in foods.

The trend in food safety in the past 10–15 years has involved a much greater focus on microbial pathogens, becoming at least equivalent to that of chemical contaminants. *Escherichia coli* O157:H7, *Salmonella* enteritidis, *Listeria monocytogenes*, and other pathogens are increasingly implicated in food-poisoning outbreaks, prompting much more analytical development and certainly much more public concern. Mass spectrometry, particularly matrix-assisted laser desorption ionization (MALDI) time-of-flight, and gene-based assays are under rapid development to address this constant threat to the food supply.

As pointed out in a recent review,⁴ new techniques of mass spectrometry can be used (i) to identify/classify pathogenic bacteria via biomolecules (proteins, DNA) that are characteristic of the pathogens; (ii) for analysis of expressed proteins that may be linked to genetic identity of bacteria; (iii) for sequence-specific fragment determination; and (iv) to rapidly and unambiguously identify foodborne pathogens by comparison with MS databases via "top-down" proteomics.

For example, Fagerquist et al.⁵ applied MALDI-TOF-TOF MS and proteomics to identify *E. coli* O157:H7 in connection with pathogens in leafy green vegetables in California's vegetable-producing areas in the past decade.

Genome sequencing is another relatively new technique that can serve as a basis for genotyping via regions that vary between strains of microorganisms. Microarray technology allows for determination of which genes are present or absent in a particular isolate and to determine relationships between isolates. Parker et al.⁶ compared genotypes of *Salmonella enterica* Serovar Enteritidis phage type 30 and 9c strains isolated during three outbreaks associated with raw almonds from California that occurred between 2000 and 2006. Establishing relationships between outbreak strains helped in identifying common risk factors that could assist in managing or preventing food product contamination. Cluster analysis with comparative genomics indexing holds promise for minimizing ambiguity in identification as well as identifying pathogenic strains of the causative microorganisms.

An increased emphasis on the identification and optimization of health-beneficial constituents in foods has become evident in the published literature,⁷ and this trend is reflected in *JAFC* from about 1990 to the present. Papers on antioxidants in foods went up dramatically, as did reports on healthy foods such as red wine and olive oil (Table 1). Papers on lycopene and

Table 1. Healthy Food-Related Manuscripts Published in *JAFC*

	1997 (of 894)	2008 (of 1772)	2010 (of 2141)
antioxidants	45 (5%)	362 (20%)	391 (18%)
cholesterol or diabetes	8 (<1%)	73 (4%)	65 (3%)
olive oil	12 (1%)	56 (3%)	60 (3%)
red wine	18 (2%)	68 (4%)	64 (3%)
bioactives category	NA	285 (16%)	330 (15%)

Perspective

resveratrol (Figure 1), as well as other health-beneficial chemicals, increased to the point where papers addressing

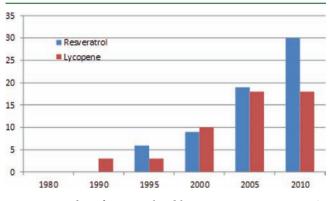


Figure 1. Number of resveratrol and lycopene manuscripts in JAFC.

health-beneficial bioactives in foods—phytonutrients, nutraceuticals, etc.—exceed those reporting on chemicals with detrimental effects.

It is interesting that over the same period—1990 to the present—papers published in *JAFC* on pesticide synthesis, mode of action, and residues declined as a percent of all papers published (Figure 2). This can partly be explained by the

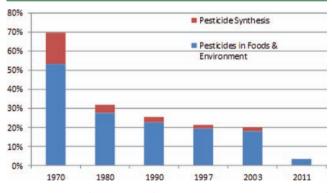


Figure 2. Pesticide paper trends over time in *JAFC*: comparison of papers published in the first issue of each listed year.

contraction in the pesticide industry worldwide as well as the impetus for pesticide chemists to patent their discoveries rather than publish them. However, this trend may well be more a reflection of public interest in healthy, local, and sustainable foods and means of growing and processing foods with minimal input of synthetic chemicals, as well as a general lowering of the environmental impacts of farming. Terms such as phytonutrients, nutraceuticals, and functional foods are no longer limited to the domain of scientists as the public catches on, looks for these terms, and uses them as part of their shopping vocabulary and daily lives. Work published in JAFC, or other scientific outlets, is often picked up rapidly and further disseminated by the news media-the New York Times, National Public Radio, U.S. News & World Report, etc. Now those papers are increasingly "good news" on the benefits of consuming foods perceived or proven to be good for one's health.

The interest in diet and health has focused on populations that seem to be thriving—living longer, with lower incidence of cancer and cardiovascular disease—and how their diets may be a major contributor to this. The Mediterranean diet has stimulated scientific interest in the constituents of olive oil, red wine, fish, whole grains, and other "healthy" foods that are mainstays in this diet. Gorinstein et al.⁸ found that red grapefruit positively influenced the serum triglyceride levels in patients suffering from coronary atherosclerosis, and that news was picked up by media worldwide, sparking a consumer demand for red grapefruits.

JAFC recently assembled a "virtual issue" on food traits that promote good health consisting of 24 of the papers published in JAFC over a recent 18 month period (late 2009–early 2011) reproduced in a web "virtual" issue.⁹ Several of the papers were on the health-beneficial properties of berries—blueberries, cranberries, raspberries, etc. Blueberries particularly have stimulated consumer interest, now appearing in some form on many breakfast, lunch, and dinner plates. Extracts of blueberries are now available in tablet form, provided by TruNature, and distributed by mainstream retailers such as Costco in the United States. Interestingly, the Costco advertisement of the TruNature product contains references to the work of USDA scientists Ron Prior and Hong Wang, published in JAFC!^{10,11}

Petkewich¹² described in lay terms the steps that lead to identifying the constituents in foods that promote good health. This may start with an observation or even folklore on the good health of people who consume a particular fruit, berry, grain, or other food. Then nutritionists confirm the perceived bioactivity with clinical trials with animals or human subjects. Chemists are involved in identifying the bioactive component(s). Plant breeders/geneticists can enhance the bioactivity by breeding. Further animal or human trials are conducted to confirm the bioactivity and that the active constituent in the food is bioavailable. The mechanism of action may be studied at this point as well. Then a health claim is pursued from the World Health Organization, FDA, or some other authoritative body, or a purified supplement is made from the bioactive ingredient.

The field is open to many new discoveries, scientific development, and commercialization. Milk, for example, has been somewhat overlooked from a scientific viewpoint. We all have heard that mother's milk is good for the neonate—for humans as well as other mammals. But what is it in milk that is the basis? German, Mills, and LeBrilla^{13–15} lead a team of researchers who are focused on oligosaccharide bioactives in milk. Less than half of the hundreds of oligosaccharides in milk had been identified, prompting intense analytical development using mass spectrometry and other advanced techniques. The effect of these compounds on promoting a healthy gut microflora has been studied. The findings with mother's milk may stimulate improvements in bovine milk so that the health benefits can be delivered more widely, to all age groups.

Another group of foods ripe for scientific exploration are those grown under "organic" conditions. Many believe that organically grown produce is healthier (i.e., has a higher content of health-promoting bioactives) than conventionally grown produce of the same type. Papers are being published that explore this constituent hypothesis, but the data are highly variable. The number of papers that postulate a health benefit of organic food is about equal to the number that shows no difference in benefit or composition between organic and conventional food (Table 2). In many cases this is due to a lack of control of variables—weather conditions, stage of ripeness or maturity of the produce, irrigation, mineral content of the soil, etc. In one of the studies that paid closer attention to these details, Stracke et al.¹⁶ found that the polyphenol and antioxidant content (measured by FRAP, ORAC, and TEAC)

Table 2. Survey of Peer-Reviewed Papers (All Journals)
Published 2005–2009 Comparing Health-Beneficial
Phytonutrients in Conventional versus Organic Produce

commodity	conventional > organic	organic > conventional	variable or no difference
fruits	3	11	6
vegetables	0	8	13
grains	0	0	4
total	3	19	23

of golden delicious apples was significantly higher in organically grown apples, and this effect was consistent over a multiyear period. More studies of this type are needed to underpin a better understanding of how production methods influence the phytonutrient content of food crops.¹⁷

We continue to face the issues of toxic chemicals, contaminants, and pesticide and related residues in foods. Current examples are for plasticizers and other estrogenically active contaminants that migrate from packaging into foods,^{18,19} the formation of acrylamide^{20,21} and other mutagens during high-temperature preparation of foods, adulterants exemplified by the recent melamine episodes,²² and natural toxicants such as aflatoxins in foods. Accidents such as the Gulf Horizon disaster (petroleum hydrocarbon contamination) in the Gulf of Mexico and the Daiichi nuclear plant in Japan threaten the safety of our food supply as well as other components of our environment.²³ There also remains the challenge of finding the underlying causes of obesity and related inflammation diseases such as diabetes, which are so prevalent in western nations such as the United States.²⁴ These areas will continue to find a ready home for publication of good supporting science in the scientific literature for many years to come, along with the "good news" research on the healthbeneficial components of foods.

AUTHOR INFORMATION

Corresponding Author

*E-mail: jnseiber@ucdavis.edu.

Notes

The authors declare no competing financial interest.

REFERENCES

(1) Corn, M. The progression of industrial hygiene. *Appl. Ind. Hyg.* **1989**, *4*, 153–157.

(2) Kensler, T. W.; et al. Chemoprevention of hepatocellular carcinoma in aflatoxin endemic areas. *Gastroenterology* **2004**, *127*, S310–S318.

(3) Seiber, J. N.; Kleinschmidt, L. A. Contributions of pesticide residue chemistry to improving food and environmental safety: past and present accomplishments and future challenges. *J. Agric. Food Chem.* **2011**, *59*, 7536–7543.

(4) Seiber, J. N. New analytical acvances for addressing healthful constituents in foods. *J. Food Drug Anal.* **2012**, in press.

(5) Fagerquist, C. K.; Garbus, B. R.; Miller, W. G.; Williams, K. E.; Yee, E.; Bates, A. H.; Boyle, S.; Harden, L. A.; Cooley, M. B.; Mandrell, R. E. Rapid identification of protein biomarkers of *Escherichia coli* O157:H7 by matrix-assisted laser desorption ionization-time-of-flight time-of-flight mass spectrometry and top-down proteomics. *Anal. Chem.* **2010**, *82*, 2717–2725.

(6) Parker, C. T.; Huynh, S.; Quiñones, B.; Harris, L. J.; Mandrell, R. E. Comparison of genotypes of *Salmonella enterica* serovar enteritidis phage type 30 and 9c strains isolated during three outbreaks associated with raw almonds. *App. Environ. Microbiol.* **2010**, *76*, 3723–3731.

(7) Nicoli, M. C.; Anese, M.; Parpinel, M. Influence of processing on the antioxidant properties of fruit and vegetables. *Trends Food Sci. Technol.* **1999**, *10*, 94–100.

(8) Gorinstein, S.; Caspi, A.; Libman, I.; Lerner, H. T.; Huang, D.; Leontowicz, H.; Leontowicz, M.; Tashma, Z.; Katrich, E.; Feng, S.; Trakhtenberg, S. Red grapefruit positively influences serum triglyceride level in patients suffering from coronary atherosclerosis: studies in vitro and in humans. *J. Agric. Food Chem.* **2006**, *54*, 1887– 1892.

(9) Seiber, J. N. Food quality traits for sustaining agriculture. J. Agric. Food Chem. 2011, 59, 2127–2130.

(10) Wang, H.; Cao, G.; Prior, R.L.. Total antioxidant capacity of fruits. J. Agric. Food Chem. **1996**, 44, 701-705.

(11) Prior, R. L.; Cao, G.; Martin, A.; Sofic, E.; McEwen, J.; O'Brien, C.; Lischner, N.; Ehlenfeldt, M.; Kalt, W.; Krewer, G.; Mainland, C. M. Antioxidant capacity as influenced by total phenolic and anthocyanin content, maturity, and variety of *Vaccinium* species. *J. Agric. Food Chem.* **1998**, *46*, 2686–2693.

(12) Petkewich, R. A healthy diet starts in the field. *Chem. Eng. News* 2008, 86 (25), 12–16.

(13) Marcobal, A.; Barboza, M.; Froehlich, J. W.; Block, D. E.; German, J. B.; Lebrilla, C. B.; Mills, D. A. Consumption of human milk oligosaccharides by gut-related microbes. *J. Agric. Food Chem.* **2010**, *58*, 5334–5340.

(14) Froehlich, J. W.; Dodds, E. D.; Barboza, M.; McJimpsey, E. L.; Siepert, R. R.; Francis, J.; An, H. J.; Freeman, S.; German, J. B.; Lebrilla, C. B. Glycoprotein expression in human milk during lactation. *J. Agric. Food Chem.* **2010**, *58*, 6440–6448.

(15) Argov-Argaman, N.; Smilowitz, J. T.; Bricarello, D. A.; Barboza, M.; Lerno, L.; Froehlich, J. W.; Lee, H.; Zivkovic, A. M.; Lemay, D. G.; Freeman, S.; Lebrilla, C. B.; Parikh, A. N.; German, J. B. Lactosomes: structural and compositional classification of unique nanometer-sized protein lipid particles of human milk. *J. Agric. Food Chem.* **2010**, *58*, 11234–11242.

(16) Stracke, B. A.; Rüfert, C. E.; Weibel, F. P.; Bub, A.; Watzl, B. Three-Year comparison of the polyphenol contents and antioxidant capacities in organically and conventionally produced apples (*Malus domestica* Bork. cultivar 'Golden Delicious'). J. Agric. Food Chem. 2009, 57, 4598–4605.

(17) Seiber, J. N. Editor's comment. J. Agric. Food Chem. 2004, 52, 146.

(18) Everts, S. Chemicals leach from packaging: food and drugs just can't leave their wrappings behind. *Chem. Eng. News* **2009**, *87* (35), 11–15.

(19) Kluger, J. Little women. *Time* 2011, *187* (17, Oct 31), 46–56. (20) Tareke, E.; Rydberg, P.; Karlsson, P.; Eriksson, S.; Törnqvist, M. Analysis of acrylamide, a carcinogen formed in heated foodstuffs. *J. Agric. Food Chem.* 2002, *50*, 4998–5006.

(21) Gorman, C. Do French fries cause cancer? *Time* **2002**, *159* (18, May 6), 73.

(22) Filagenzi, M. S.; Puschner, B.; Aston, L. S.; Poppenga, R. H. Diagnostic determination of melamine and related compounds in kidney tissue by liquid chromatography/tandem mass spectrometry. *J. Agric. Food Chem.* **2008**, *56*, 7593–7599.

(23) Park, A. Feeding on fallout. Time 2011, 177 (13, April 4), 24.

(24) U.S. Department of Agriculture and U.S. Department of Health and Human Services. *Dietary Guidelines for Americans*, 7th ed.; U.S. Government Printing Office: Washington, DC, Dec 2010.