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Perspective

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Mapping the Scientific Research on Wine and Health (2001−2011)

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ABSTRACT: There have been a substantial number of studies suggesting possible health benefits from polyphenols in wine, especially red wine. These hypothetical effects, in addition to those of alcohol, are attributed by many to antioxidant and anti-inflammatory effects of the polyphenols. The aim of this paper was to map the scientific research on wine and health by using bibliographic analyses of papers published during the period 2002−2011. Papers were published in 535 different journals and in 106 different subject categories, the most productive journals being the *Journal of Agricultural and Food Chemistry*, *Food Chemistry and Molecular Nutrition*, and *Food Research*, and the most productive subject category being food science and technology. Institutions in the main network of collaboration between centers were primarily located in France, Italy, and the United State. The number of papers on the medicinal use of wine has been dramatically rising in recent years because of the increased awareness of its importance in modern society. We emphasize the large distribution of information among numerous journals and the multidisciplinary nature of the topic. In the network of co-words, we observe the central role played by the terms "resveratrol", "wine", and "polyphenols".

KEYWORDS: *wine, health, bibliometrics, social network analysis, keyword analysis, co-word analysis*

INTRODUCTION

It has been estimated that the medicinal use of wine dates back to 2200 BCE.[1] In the early 1990s, media coverage of the "French paradox" popularized the health benefits of red wine. Twenty years after the formulation of this concept, there have been a substantial number of studies suggesting possible health benefits that moderate wine consumption has on human health.[2,3] In particular, for individuals who consume a moderate amount of wine (10−20 g of alcohol per day), a reduction of 25−35% mortality was observed.[4−6] This hypothetical effect was particularly evident among wine drinkers compared to those consuming normal beer or other alcoholic beverages.[4,7,8]

In their article "Wine and Health: A Review", Guilford and Pezzuto[2] list several application products of the vine (grape juice and seed extracts) in the medical field. The same effect has been demonstrated for wine, although it is not clear if alcohol plays a complementary role[9] or if polyphenols' role is independent of alcohol.[6] The alcohol contained in wine increased the level of high-density lipoprotein (HDL) cholesterol and reduced aggregation of blood platelets. In addition, polyphenols develop their antioxidant and anti-inflammatory effects, reduce platelet aggregation, and play a role in chemoprevention, neuroprotection, and cardioprotection.[10]

Polyphenols in wines are primarily represented by flavan-3-ols.[11] Moreover, the phenolic components of wine showing positive effects on health are melatonin, lutein, catechins, ellagic acid, quercetin, and resveratrol. These molecules are active as antioxidants, reducing low-density lipoprotein (LDL) cholesterol from oxidation and aggregation of blood platelets.[2,9] In particular, resveratrol is classified as an inhibitor of oxidation of LDL and the aggregation of platelets, with cardioprotective effects. It was also observed that resveratrol is an inhibitor of certain types of tumors and that this molecule plays an important anti-inflammatory, antibacterial, antifungal, antiviral, neuroprotective, and antiangiogenic role.[12,13] In addition, these molecules are characterized by low bioavailability, and the products of their metabolism play a key role in the case of positive effects on human health.[14−17] Wine, therefore, contains several molecules (some of which are not currently known) that may have implications in the field of human health.

In general, if the beneficial effect of regular and moderate consumption of wine is clear, that is, approximately 150 mL/day for women and 300 mL/day for men,[18] we must also take into account the dietary pattern wherein wine is integrated. Indeed, the introduction of wine into a healthy diet and lifestyle increases its positive effects, which is the case for the Mediterranean diet, where wine demonstrates synergy with other foods, such as fruits, vegetables, cereals, olive oil, milk, and cheese.[4,19] There are other foods such as peanuts, walnuts, blueberries, chickpeas, and onions that are also rich in resveratrol. Additionally, resveratrol is readily synthesized chemically and can be produced and treated like a drug. Miller et al. in their studies show that there are other products such as rapamycin that are much more effective than resveratrol for survival in male or female mice.[20]

The aim of this paper was to analyze the knowledge structure of scientific research on wine and health integrating the analyses of productivity, collaboration, and scientific impact

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Table 1. Papers in Most Productive Journals, Five Year Periods, and Impact Factor

journal	2002−2006	2007−2011	total	country	IF 2010
Journal of Agricultural and Food Chemistry	42	44	86	United States	2.816
Food Chemistry	8	30	38	England	3.458
Molecular Nutrition and Food Research	2	16	18	Germany	4.713
Annals of the New York Academy of Sciences	9	5	14	United States	2.847
Food and Chemical Toxicology	3	10	13	England	2.602
Analytica Chimica Acta	6	6	12	The Netherlands	4.311
Cancer Letters	3	9	12	The Netherlands	4.864
Journal of Nutrition	7	5	12	United States	4.295
European Journal of Pharmacology	1	10	11	The Netherlands	2.737
Journal of Food Composition and Analysis	2	9	11	United States	1.948
American Journal of Physiology−Heart and Circulatory Physiology	3	7	10	United States	3.881
Atherosclerosis	3	7	10	United States	4.086
Free Radical Biology and Medicine	3	7	10	United States	5.707
International Journal of Cancer	3	7	10	Switzerland	4.926
Life Sciences	7	3	10	England	2.451
Biochemical and Biophysical Research Communications	3	6	9	United States	2.595
European Food Research and Technology	4	5	9	Germany	1.585
FASEB Journal	4	5	9	United States	6.515
Nutrition and Cancer−An International Journal	2	7	9	United States	2.553
Anticancer Research	5	3	8	Greece	1.656
Biochemical Pharmacology	5	3	8	United States	4.889
Cancer Research	2	6	8	United States	8.234
Journal of Food Science	1	7	8	United States	1.733
Journal of Nutritional Biochemistry	2	6	8	United States	4.538
Lebensmittel-Wissenschaft und-Technologie−Food Science and Technology	1	7	8	England	2.292
American Journal of Clinical Nutrition	6	1	7	United States	6.606
Drugs Under Experimental and Clinical Research	7	0	7	Switzerland	
Food Additives and Contaminants Part A−Chemistry Analysis Control Exposure and Risk Assessment	5	2	7	England	2.230
Food Research International	3	4	7	United States	2.416
International Journal of Food Science and Technology	2	5	7	England	1.223
Journal of AOAC International	4	3	7	United States	1.229

with subject category analysis, keyword analysis, social network analysis (SNA), and co-word analysis. The identification of the knowledge structure of scientific research on wine and health can help neophytes and newcomers to enter this field or to provide sufficient insight to leap forward in a new competitively advantageous research direction. Knowledge structure of scientific research identifies the sources where research is published and their impact, leading research centers, the papers that have received greater recognition through citations in subsequent studies, and specific thematic aspects addressed in the investigations and their relationships and interactions.

Items under study were obtained from the Science Citation Index-Expanded (SCIE) database, accessed through the Web of Science (WOS) platform from Thomson Reuters. The terms used in the search strategy were extracted from a review on wine and health by Guilford and Pezzuto,[2] published in the *American Journal of Enology and Viticulture* in 2011. These terms were as follows:

Title = (wine* OR resveratrol OR polyphenol* OR procyanidin* OR ochratoxin*) AND Title = (health OR disease* OR diabetes OR cancer OR neoplasm* OR cardiovasc* OR atheroscler* OR hypertens* OR "metabolic syndrome" OR "neurol* disorder*" OR Gastrointest* OR Immun* OR inflamat* OR coagulat* OR platelet OR endothelial OR "vascular function" OR "lipid effect*" OR antioxidant* OR coagulat* OR coronar* OR ″oxidative stress″ OR fibrinol* OR antiatherogen* OR antiinflamat*).

To achieve greater accuracy in the results, the search was conducted in the Title field because if applied in the Topic option, which includes the search fields Title, Abstract, and Keywords (KW), many records obtained were not relevant. The terms were truncated using an asterisk to obtain all documents associated with the derived words (e.g., polyphenol* allows for the recovery of items containing the terms polyphenol, polyphenols, and polyphenolic). All records obtained were reviewed to ensure their relevance. The analyzed period was limited to the decade 2002−2011. The considered interval was selected because the main aim of this research was to identify the latest research in the field rather than analyze the origin or perform a historical analysis. It was during the past decade when the greatest increase in the number of publications was produced. In the previous decade (1992−2001) 389 papers were published in SCIE, whereas only 48 were published during the period 1982−1991. In the period analyzed in this work 1266 research papers were published in the area. The study was restricted to research papers in the strict sense, taking into account original papers and review papers and excluding letters, editorials, book reviews, abstracts of conference papers, reprints, bibliographical papers, and news.

SCIENTIFIC PRODUCTIVITY, IMPACT FACTOR, AND MOST CITED PAPERS

During the decade 2002−2011, 1266 papers were published (1174 original papers (92.73%) and 92 review papers (7.27%). The number of papers has increased steadily over the decade,

Table 2. Most Cited Papers

authors	title	source	times cited
Baur, J. A.; Pearson, K. J.; Price, N. L.; Jamieson, H. A.; Lerin, C.; Kalra, A., et al.	Resveratrol Improves Health and Survival of Mice on a High-Calorie Diet	*Nature* **2006**, *444*, 337−342	1142
Aggarwal, B. B.; Bhardwaj, A.; Aggarwal, R. S.; Seeram, N. P.; Shishodia, S.; Takada, Y.	Role of Resveratrol in Prevention and Therapy of Cancer: Preclinical and Clinical Studies	*Anticancer Res.* **2004**, *24*, 2783−2840	441
Wallerath, T.; Deckert, G.; Ternes, T.; Anderson, H.; Li, H.; Witte, K.; Förstermann, U.	Resveratrol, a Polyphenolic Phytoalexin Present in Red Wine, Enhances Expression and Activity of Endothelial Nitric Oxide Synthase	*Circulation* **2002**, *106*, 1652−1658	254
Carluccio, M. A.; Siculella, L.; Ancora, M. A.; Massaro, M.; Scoditti, E.; Storelli, C., et al.	Olive Oil and Red Wine Antioxidant Polyphenols Inhibit Endothelial Activation: Antiatherogenic Properties of Mediterranean Diet Phytochemicals	*Arterioscler. Thromb. Vasc. Biol.* **2003**, *23*, 622−629	209
Marambaud, P.; Zhao, H.; Davies, P.	Resveratrol Promotes Clearance of Alzheimer'S Disease Amyloid-β Peptides	*J. Biol. Chem.* **2005**, *280*, 37377−37382	197
Boocock, D. J.; Faust, G. E.; Patel, K. R.; Schinas, A. M.; Brown, V. A.; Ducharme, M. P., et al.	Phase I Dose Escalation Pharmacokinetic Study in Healthy Volunteers of Resveratrol, A Potential Cancer Chemopreventive Agent	*Cancer Epidemiol. Biomarkers Prev.* **2007**, *16*, 1246−1252	184
Lee, K. W.; Kim, Y. J.; Lee, H. J.; Lee, C. Y.	Cocoa Has More Phenolic Phytochemicals and a Higher Antioxidant Capacity than Teas and Red Wine	*J. Agric. Food Chem.* **2003**, *51*, 7292−7295	184
Athar, M.; Back, J. H.; Tang, X.; Kim, K. H.; Kopelovich, L.; Bickers, D. R., et al.	Resveratrol: A Review of Preclinical Studies for Human Cancer Prevention	*Toxicol. Appl. Pharmacol.* **2007**, *224*, 274−283	174
Leikert, J. F.; Räthel, T. R.; Wohlfart, P.; Cheynier, V.; Vollmar, A. M.; Dirsch, V. M.	Red Wine Polyphenols Enhance Endothelial Nitric Oxide Synthase Expression and Subsequent Nitric Oxide Release from Endothelial Cells	*Circulation* **2002**, *106*, 1614−1617	168
Aziz, M. H.; Kumar, R.; Ahmad, N.	Cancer Chemoprevention by Resveratrol: In Vitro and in Vivo Studies and the Underlying Mechanisms (review)	*Int. J. Oncol.* **2003**, *23*, 17−28	147
Bhat, K. P.; Pezzuto, J. M.	Cancer Chemopreventive Activity of Resveratrol	*Ann. N. Y. Acad. Sci.* **2002**, *957*, 210−229	146
Asensi, M.; Medina, I.; Ortega, A.; Carretero, J.; Baño, M. C.; Obrador, E., et al.	Inhibition of Cancer Growth by Resveratrol Is Related to Its Low Bioavailability	*Free Radical Biol. Med.* **2002**, *33*, 387−398	144
Potter, G. A.; Patterson, L. H.; Wanogho, E.; Perry, P. J.; Butler, P. C.; Ijaz, T., et al.	The Cancer Preventative Agent Resveratrol Is Converted to the Anticancer Agent Piceatannol by the Cytochrome P450 Enzyme CYP1B1	*Br. J. Cancer* **2002**, *86*, 774−778	144
Delmas, D.; Rébé, C.; Lacour, S.; Filomenko, R.; Athias, A.; Gambert, P., et al.	Resveratrol-Induced Apoptosis Is Associated with Fas Redistribution in the Rafts and the Formation of a Death-Inducing Signaling Complex in Colon Cancer Cells	*J. Biol. Chem.* **2003**, *278*, 41482−41490	143
Murphy, K. J.; Chronopoulos, A. K.; Singh, I.; Francis, M. A.; Moriarty, H.; Pike, M. J., et al.	Dietary Flavanols and Procyanidin Oligomers from Cocoa (*Theobroma cacao*) Inhibit Platelet Function	*Am. J. Clin. Nutr.* **2003**, *77*, 1466−1473	137
Opipari, A. W., Jr.; Tan, L.; Boitano, A. E.; Sorenson, D. R.; Aurora, A.; Liu, J. R.	Resveratrol-Induced Autophagocytosis in Ovarian Cancer Cells	*Cancer Res.* **2004**, *64*, 696−703	136
Svilaas, A.; Sakhi, A. K.; Andersen, L. F.; Svilaas, T.; Ström, E. C.; Jacobs, D. R., Jr., et al.	Intakes of Antioxidants in Coffee, Wine, And Vegetables Are Correlated with Plasma Carotenoids in Humans	*J. Nutr.* **2004**, *134*, 562−567	127

Table 3. Papers by Main Subject Areas, Keywords, and Most Productive Journals

subject area	N	main keywords KW 1	n	KW 2	n	KW 3	n	most productive journals
food science and technology	225	antioxidant	93	polyphenols	90	wine	78	*Food Chemistry*; *Molecular Nutrition and Food Research*; *Food and Chemical Toxicology*
pharmacology and pharmacy	149	resveratrol	84	wine	28	antioxidant	23	*European Journal of Pharmacology*; *Life Sciences*; *Biochemical Pharmacology*
nutrition and dietetics	140	wine	53	polyphenols	50	antioxidant	49	*Food Chemistry*; *Journal of Nutrition*; *Nutrition and Cancer—An International Journal*
biochemistry and molecular biology	123	resveratrol	61	wine	26	antioxidant	25	*Free Radical Biology and Medicine*; *Biochemical and Biophysical Research Communications*; *FASEB Journal*
oncology	120	resveratrol	72	apoptosis	31	chemoprevention	20	*Cancer Letters*; *International Journal of Cancer*; *Nutrition and Cancer—An International Journal*
technology	90	antioxidant	42	polyphenols	38	wine	33	*Journal of Agricultural and Food Chemistry*; *Journal of the Science of Food and Agriculture*
toxicology	62	resveratrol	25	ochratoxin A	16	oxidative stress	16	*Food and Chemical Toxicology*; *Food Additives and Contaminants Part A—Chemistry Analysis Control Exposure and Risk Assessment*; *Cell Biology and Toxicology*
chemistry, applied	61	antioxidant	39	polyphenols	36	wine	27	*Food Chemistry*; *Journal of Food Composition and Analysis*; *Food Additives and Contaminants Part A—Chemistry Analysis Control Exposure and Risk Assessment*
chemistry, analytical	61	wine	23	ochratoxin A	22	antioxidant	15	*Analytica Chimica Acta*; *Journal of AOAC International*; *Analytical and Bioanalytical Chemistry*
cell biology	59	resveratrol	24	wine	7	oxidative stress	7	*FASEB Journal*; *Cell Biology and Toxicology*; *International Journal of Tissue Reactions—Experimental and Clinical Aspects*
endocrinology and metabolism	58	resveratrol	28	wine	14	cardiovascular disease	9	*Free Radical Biology and Medicine*; *Nutrition Metabolism and Cardiovascular Diseases*; *Prostate*

from 84 in 2002 to 221 in 2011. Most (65.56%) were published during the period 2007−2011. This growth is more striking for original papers than for review papers. The papers were published in 535 different journals. Table 1 lists the 31 journals that published seven or more papers distributed by five year periods, country of publication, and impact factor in 2010. The most productive journals were the *Journal of Agricultural and Food Chemistry* (n = 86), *Food Chemistry* (n = 38), and *Molecular Nutrition and Food Research* (n = 18). Most were published in the United States, although some were from the United Kingdom, The Netherlands, Germany, Greece, and Switzerland.

Journals with higher impact factors were *Cancer Research* (FI = 8.234), *American Journal of Clinical Nutrition* (FI = 6.606), *FASEB Journal* (FI = 6.515), and *Free Radical Biology and Medicine* (FI = 5.707), all of which are edited in the United States.

The 18 studies receiving more than 100 citations are presented in Table 2. The most cited article, "Resveratrol Improves Health and Survival of Mice on a High-Calorie Diet", was published in *Nature* in 2006 by Baur et al. of Harvard Medical School together with researchers from several other American and foreign institutions, including the National Institute on Aging, National Institutes of Health, Centre for Education and Research on Aging (both in the United States), University of Sydney (Australia), and University Pablo de Olavide-Spanish Research Council (Seville, Spain). This paper received 1142 citations, which exceeds the second most cited paper, "Role of Resveratrol in Prevention and Therapy of Cancer: Preclinical and Clinical Studies", by 700 citations and was published in 2004 in *Anticancer Research* by Aggarwal et al., affiliated with the Universiy of Texas and the Center for Human Nutrition at the David Geffen School of Medicine (Los Angeles, CA, USA).

In relation to the most cited papers, several aspects should be emphasized. First, a good portion of them treat the hypothetical effects of resveratrol. Second, the thematic of the journals in which the articles have been published shows the multidisciplinarity of the subject concerned. Third, the importance stirs up issues related to the prevention and treatment of diseases of great importance and impact in society, such as cardiovascular diseases and cancer.

SUBJECT CATEGORIES (SC) ANALYSIS

The papers were published in 106 different SC from WOS. Table 3 shows the most productive SC, the most common keywords (KW) assigned to the papers, and journals publishing more papers in each area. In first place stands the SC "food science and technology" (n = 225), for which the most common KW were "antioxidant" (n = 93), "polyphenols" (n = 90), and "wine" (n = 78). Journals belonging to this SC that published most papers were *Food Chemistry*, *Molecular Nutrition and Food Research*, and *Food and Chemical Toxicology*. In second place is "pharmacology and pharmacy: (n = 149); the most frequent KW were resveratrol (n = 84), wine (n = 28), and antioxidant (n = 23), with the most productive journals being the *European Journal of Pharmacology*, *Life Sciences*, and *Biochemical Pharmacology*. The other three areas published more than 100 papers: "nutrition and dietetics"; "biochemistry and molecular biology"; and "oncology". With a total of more than 50 papers, the list was completed by SC "technology, toxicology, chemistry" (applied), "chemistry" (analytical), "cell biology", and "endocrinology and metabolism". Other frequently appearing KW in addition to the above were apoptosis and chemoprevention (in the SC "oncology"), ochratoxin A and oxidative stress (in the SC "toxicology"), and cardiovascular disease (in the SC "endocrinology and metabolism").

KW most often assigned to papers (>100 times) were "resveratrol" (n = 442), "wine" (n = 342), "antioxidants" (n = 286), "polyphenols" (n = 270), and "oxidative stress" (n =117). Other KW used between 50 and 100 times were "cardiovascular

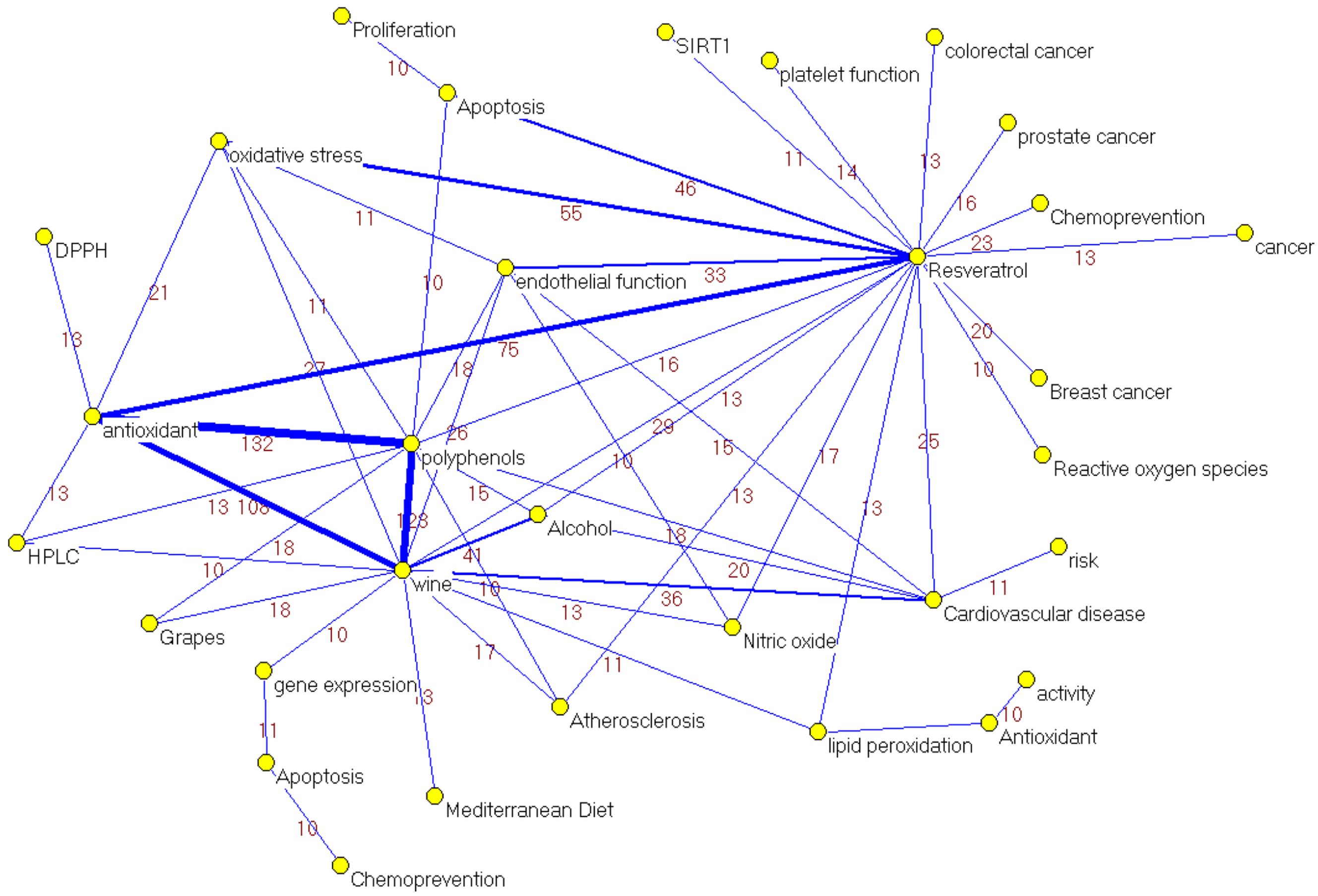

Figure 1. Network of co-words.

disease” (n = 94), “apoptosis” (n = 89), “endothelial function” (n = 86), “ochratoxin A” (n = 79), and “alcohol” (n = 70).

On the basis of the analysis of the journals and their SC, we can derive some striking deductions. The first is the large distribution, as the papers were published in 535 different journals, and the second, related to the above, is the multidisciplinary nature of the topic, which follows from the analysis of the subject category of journals. Whereas the largest numbers of papers were published in journals in the area of food science and technology, this number, in reality, accounts for only 17.8% of all items, and a large number of papers have been published in journals from other areas that exceed 10%, such as pharmacology and pharmacy (11.8%), nutrition and dietetics (11%), and chemical and other biomedical areas. The fact that the three most productive journals are devoted to food chemistry research is not surprising, given the current consideration of functional food that contains wine.[5]

The KW prioritization in wine and health-related scientific journals depends on the addressed subject area. In the food science and technology journals, the most used KW was “antioxidant”, in detriment to the words “polyphenols” and “wine”. The previous fact notes that wine’s effect on human cells is of greatest concern in this field, meaning that the property is valued as much as the compound or product itself. However, in pharmacology and pharmacy, an increased interest exists in the type of compound or molecule characterized by its antioxidant activity; therefore, the most commonly used word is “resveratrol”, in comparison to the words “wine” and “antioxidant”. In nutrition and dietetics, the greatest interest is obviously in the food containing the mentioned properties, with the word “wine” being the most used. In biochemistry and molecular biology and in oncology, “resveratrol”, the antioxidant compound present in wine, remains the most mentioned KW.

SOCIAL NETWORK ANALYSIS

Network of Co-words. The structure of knowledge can be seen graphically by analyzing co-words and their representation by SNA. Co-word analysis is a content analysis technique that quantifies the number of different co-occurrences in a set of papers revised, being effective in mapping the strength of association between KW in textual data. Co-word analysis reduces the space of descriptors (or KW) to a set of network graphs that effectively illustrate the strongest associations between descriptors. For the analysis of co-words, we assumed the assumptions presented by Law and Whittaker:[21] (a) authors of scientific papers choose their technical terms carefully; (b) when different terms are used in the same paper, it is because the author is either recognizing or postulating some nontrivial relationship between their referents; (c) if enough different authors appear to recognize the same relationship, then that relationship may be assumed to have some significance within the area of science concerned. Similar approaches have been constructed to map knowledge in other fields, such as adverse drug reactions,[22] environmental science,[23] severe acute respiratory syndrome,[24] tsunamis,[25] Parkinson’s disease,[26] ethics and dementia research,[27] and the Geographic Information Systems.[28]

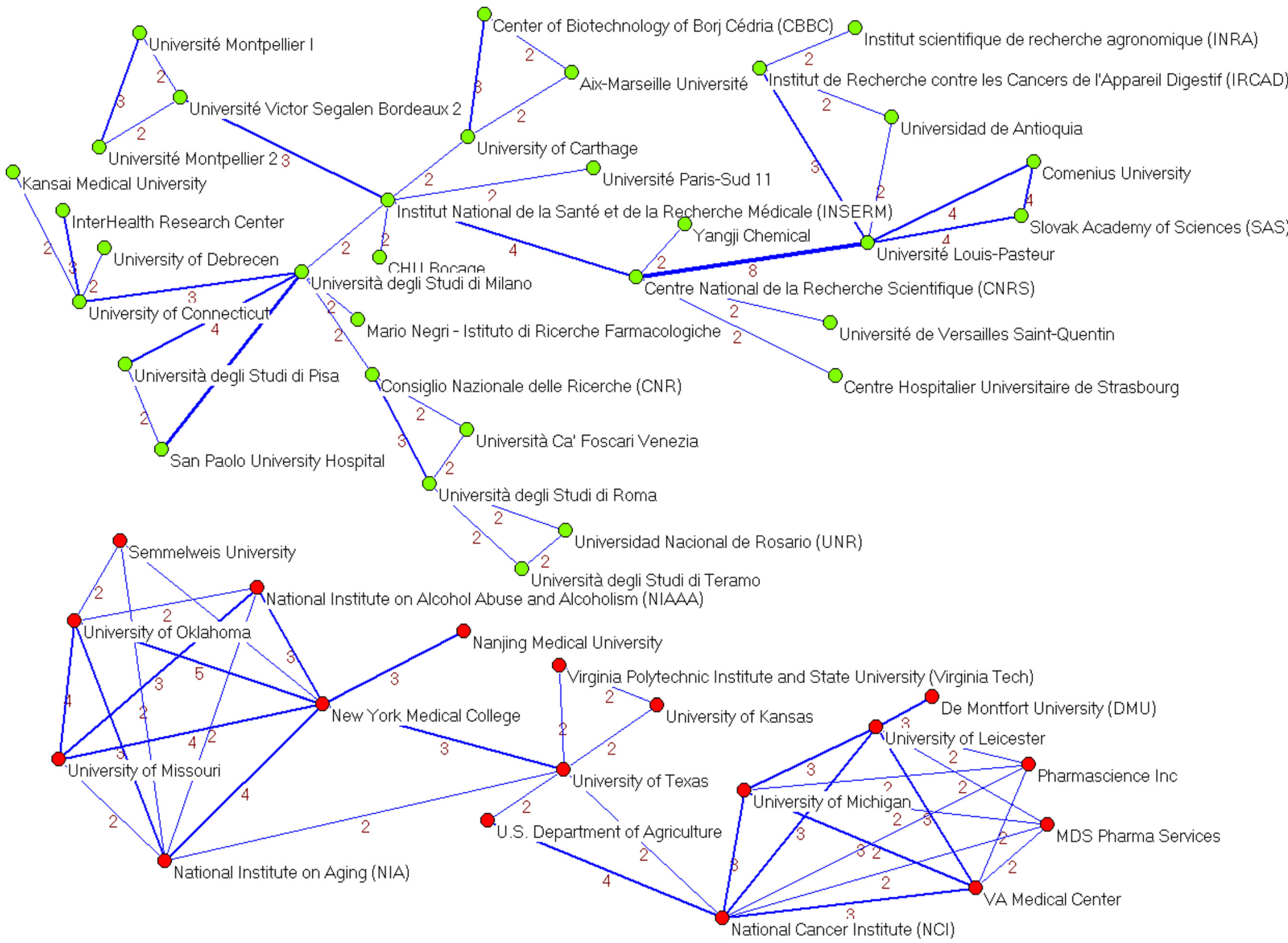

Figure 2. Main networks of institutional collaboration.

The software Pajek, designed for the analysis and visualization of networks, was used for the construction and graphical representation of the research groups[29] and VOSViewer for the construction of the density collaboration map among countries.

Figure 1 shows the network of co-words that form these KW with a frequency of at least 10 matches. The three terms with higher centrality are "resveratrol", which relates to 18 additional terms, having the largest number of co-occurrences with "antioxidant" (n = 75), "oxidative stress" (n = 55), "apoptosis" (n = 46), and "endothelial function" (n = 33); "wine", which relates to 14 terms and has the largest number of co-occurrences with "polyphenols" (n = 123), "antioxidant" (n = 108), and "cardiovascular disease" (n = 36); and "polyphenols", which has the greatest co-occurrences with "antioxidant" (n = 132) and "wine" (n = 123). The triangle with greater intensity of co-occurrences drawing the following three KW is noteworthy: "wine", "antioxidant", and "polyphenols". This network also plotted other KW and their relationships, for example, the subject association that links resveratrol with certain cancers (colorectal cancer, prostate cancer, breast cancer), diseases or pathological processes (cardiovascular diseases and atherosclerosis), and other physiological processes (e.g., platelet function, endothelial function, lipid peroxidation, and apoptosis).

In summary, in the structure obtained we can observe the central role played by three terms ("resveratrol", "wine", and "polyphenols") and the extensive network of co-words that forms with the other 29 terms. The centrality is lower in two terms: "antioxidant" and "oxidative stress". "Resveratrol" is mainly associated with terms that relate to health, mainly physiological processes (endothelial function, lipid peroxidation, apoptosis, oxidative stress, platelet function) and diseases (atherosclerosis and cardiovascular diseases), including cancer (prostate cancer, breast cancer, colorectal cancer), and chemicals such as nitric oxide and polyphenols. Among the associations of the term "wine", cardiovascular diseases (including atherosclerosis) and the Mediterranean diet are highlighted. According to this co-word analysis, these terms can be considered the conceptual nucleus of wine and health.

Networks of Research Centers and Countries. The two main networks of institutions that collaborated in the publication of the papers are presented in Figure 2. The first includes 32 institutions primarily located in France, Italy, and the United States, among which stand out for their greater centrality the Centre National de la Recherche Scientifique (CNRS) and the Institut National de la Santé et de la Recherche Medicale (INSERM), which has established collaboration with the Università degli Studi di Milano (Italy), an institution that collaborates with other Italian centers and the University of Connecticut (USA). In this network, the largest number of collaborations occurred between the Centre National de la Recherche Scientifique and the Université Louis-Pasteur (n = 8) and between the Università degli Studi di Milano and San Paolo University

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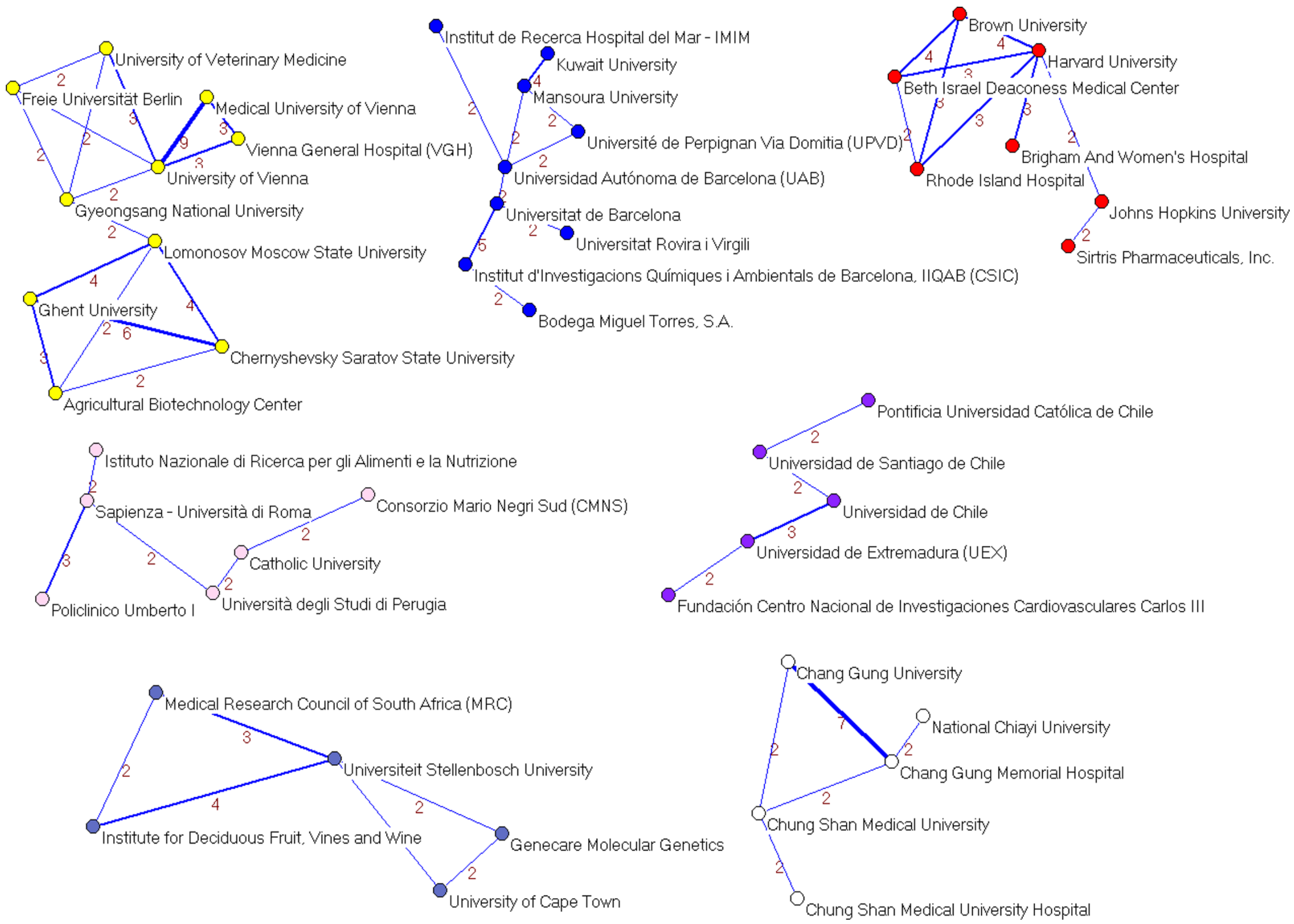

Figure 3. Other networks of institutional collaboration.

Hospital (Milan, Italy) ($n = 6$). The second network consists of centers in the United States, most notably the New York Medical College, the University of Texas, and the National Cancer Institute. In this network, the largest collaborations have occurred between the New York Medical College and the University of Oklahoma ($n = 5$).

Figure 3 shows other networks, comprising a smaller number of institutions (10, 9, 7, 6, and 5). The network of 10 institutions integrates centers from Germany (Freie Universität Berlin), Austria (University of Vienna), and Russia (Lomonosov Moscow State University). The network of nine components includes institutions mainly from Spain, among which is the centrally located Autonomous University of Barcelona. The network of seven components includes Harvard University as a central institution. Finally, the other networks correspond to centers from Italy (Università degli Studi di Perugia), Chile (Universidad de Chile), South Africa (Stellenbosch University), and China (Chang Gung Memorial Hospital).

The density collaboration map between countries is drawn in Figure 4. The names of the countries from which papers have set more relations with other ones are shown with in larger black type. The warmer colors (red) indicate a higher density, whereas lower densities are represented by the cooler colors. The map highlights the place of greatest centrality in the United States, and other relevant countries are France, Spain, and Italy.

The extensive network of relations between countries indicates a positive international collaboration in which each country finds its particular way of contributing to different knowledge. The network illustrates a country knowledge map where not all of these countries are relatively uniformly distributed and where the United States occupies a central position (along with France, Spain, and Italy), which is not surprising, as these countries are among the largest producers of wine in the world, and it is logical that research on the beneficial effects of wine on health comes from them. It is well-known that bibliometric analysis in most research fields for the purpose of performance evaluation normally shows that the United States is ranked first in both quantity and quality.[30−32] Other major producing countries are not as central in the network, such as Chile, South Africa, and New Zealand, likely because research in these countries is less developed.[33] As shown in Table 4, which provides the relative adjusted productivity of the 10 largest wine-producing countries according to wine production and population, the relative country productivity of papers per hectoliters of wine is headed by France (50.2) followed by Italy (40.3) and Spain (40.1). On the other hand, the ranking of the relative productivity of papers per million inhabitants is led by Italy (3.82), Spain (2.73), and France (1.34).

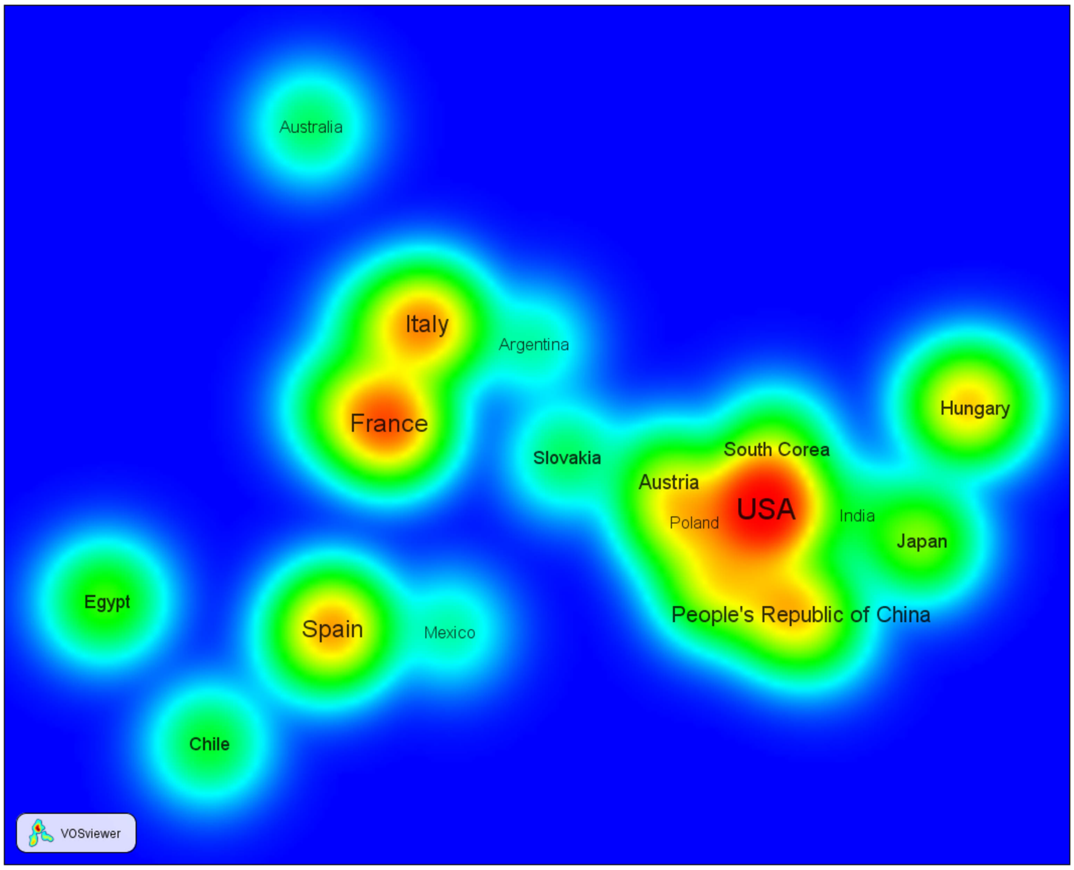

Figure 4. Density collaboration map among countries.

Table 4. Relative Productivity in Research on Wine and Health during 2002−2011 of the 10 Largest Wine-Producing Countries According to Wine Production and Population in 2011[a]

country	(*A*) articles published	(*B*) wine production[b] (million hL)	*A*/*B*	(*C*) population[c] (million inhabitants)	*A*/*C*
United States	273	18.7	14.6	313.9	0.87
Italy	133	40.3	3.3	60.92	3.82
Spain	126	40.1	3.1	46.22	2.73
People's Republic of China	115	10.3	11.16	1.351	0.08
France	88	50.2	1.75	65.70	1.34
Germany	54	9.4	5.74	81.89	0.67
Australia	29	10.5	2.76	22.68	1.28
Chile	21	10.4	2.02	17.46	1.2
Argentina	13	14.6	0.89	41.09	0.56
South Africa	12	10.2	1.18	51.19	0.23

[a]*A*, articles published within the period 2002−2011; *B*, wine production in 2011; *C*, population in 2011; *A*/*B*, articles per million hL; *A*/*C*, articles per million inhabitants. [b]Source: Bulletin O.I.V. (avalaible at www.oiv.int/oiv/info/frbulletin). [c]Source: World Bank (available at http://data.worldbank.org/country).

FINAL REMARKS AND CONCLUSIONS

The number of papers about the medicinal use of wine has been dramatically increasing because of the increased awareness of wine's importance in modern society. This increase has taken place in recent years, exceeding 100 original papers and 10 review papers published per year, so the topic of wine and health has become an emerging research field that requires a systematic analysis of its knowledge structure. Papers published in biomedical and chemical journals should achieve the greatest impact. Most cited papers emphasize the role of the beneficial effects of resveratrol and issues related to the prevention and treatment of diseases, such as cardiovascular diseases and cancer.

This study integrates SC analysis, KW analysis, SNA, and co-word analysis to investigate the knowledge structure created by scientific research published on wine and health in the 2002−2011 period. Using co-word analysis, we have highlighted features such as the heterogeneity of the scientific field concerned. The co-word approach, by summarizing papers in terms of forceful words and counting co-occurrences, has made it possible to uncover the terms in the central position and the links that exist between them. Co-word analysis can also be useful for funding agencies when deciding how to allocate resources. It may be beneficial to spend R&D resources on a research project featured by a set of keywords co-occurring in two existing separate "islands" because this newly funded research project will serve as interdisciplinary research to bridge the two islands.

It must be understood that some research limitations or biases are inevitable, and more efforts are needed to maximize this approach to knowledge structure. For example, (1) The purpose of this study is to characterize knowledge structures created by journal papers on wine and health integrating several methods: SC, KW, SNA and co-word analysis. However, any method is only an approach and will never be perfect because a real complete "knowledge structure" requires additional methods. (2) Although most of the scientific production in the studied area was published in the past decade, the scope of our work would be limited because the selected time interval could miss some key concepts. However, the aim of our study was not to perform a historical review, it was to provide a conceptual view of the recent knowledge using a combination of techniques applied to publications. (3) The quality of results from co-word analysis and the validity of maps depend on a variety of factors, such as the quality of KW, that is, how the authors or indexers chose keywords to conceptualize the scientific papers. (4) It was observed that 404 (32%) papers have received some type of funding, although the information in the records did not allow us to accurately discern the source (public or private), the amount, or the length of the grant. There was a general agreement that funding decisions should never rely on bibliometrics alone but could be used in combination with expert and qualitative review. Bibliometrics can provide measures to what extent there are outcomes from funded research (including identifying and structuring emerging fields) by looking at results (papers, patents, citations) of funded projects. Science maps based on bibliometrics provide information on the concentration of different topics in scientific fields or look at gaps on the scientific landscape that are yet to be addressed. A continuous monitoring process of the publications may provide information on the role of funded projects by following researchers and their publications long after their grant has ended and looking back to see if funded research has became a "core document" in terms of citations, has many strong links to other papers, has become a key reference to a research field, or has originated an emerging research field. For these reasons, the U.K. government is considering using bibliometrics as a possible auxiliary tool to assess the quality of the research output of U.K. universities and. on the basis of the assessment results, allocate research funding.[34,35]

Future research must focus on process and more professional journals from other bibliographic databases that enable a wider analysis.

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Notes

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■ REFERENCES

(1) Robinson, J. *The Oxford Companion to Wine*; Oxford Univertsity Press: New York, 2006.

(2) Guilford, J. M.; Pezzuto, J. M. Wine and health: a review. *Am. J. Enol. Vitic.* **2011**, *62*, 471−486.

(3) Giacosa, A.; Adam-Blondon, A. F.; Baer-Sinnott, S.; Barale, R.; Bavaresco, L.; Di Gaspero, G.; Dugo, L.; Curtis Ellison, R.; Gerbi, V.; Gifford, D.; Janssens, J.; La Vecchia, C.; Negri, E.; Pezzotti, M.; Santi, L.; Rondanelli, M. Alcohol and wine in relation to cancer and other diseases. *Eur. J. Cancer Prev.* **2012**, *21*, 103−108.

(4) Klatsky, A. L.; Armstrong, M. A.; Kipp, H. Correlates of alcoholic beverage preference: traits of persons who choose wine, liquor or beer. *Br. J. Addict.* **1990**, *85*, 1279−1289.

(5) German, J. B.; Walzem, R. L. The health benefits of wine. *Annu. Rev. Nutr.* **2000**, *20*, 561−593.

(6) Ruf, J. C. Overview of epidemiological studies on wine, health and mortality. *Drugs Exp. Clin. Res.* **2003**, *29*, 173−179.

(7) Gronbaek, M.; Becker, U.; Johansen, D.; Gottschau, A.; Schnohr, P.; Hein, H. O.; Jensen, G.; Sorensen, T. I. A. Type of alcohol consumed and mortality from all causes, coronary heart disease, and cancer. *Ann. Intern. Med.* **2000**, *133*, 411−419.

(8) Jensen, M. K.; Andersen, A. T.; Sorensen, T. I.; Becker, U.; Thorsen, T.; Grønbæk, M. Alcoholic beverage preference and risk of becoming a heavy drinker. *Epidemiology* **2002**, *13*, 127−133.

(9) Lindberg, M. L.; Amsterdam, E. A. Alcohol, wine, and cardiovascular health. *Clin. Cardiol.* **2008**, *31*, 347−351.

(10) Natella, F.; Maconem, A.; Ramberti, A.; Forte, M.; Mattivi, F.; Matarese, R. M.; Scaccini, C. Red wine prevents the postprandial increase in plasma cholesterol oxidation products: a pilot study. *Br. J. Nutr.* **2011**, *105*, 1718−1723.

(11) Ribéreau-Gayon, P.; Glories, Y.; Maujean, A.; Dubourdieu, D. *Traité d'oenologie. Tome II: Chimie du vin, Stabilisation et traitements*; Dunod: Paris, France, 1998.

(12) Guerrero, R. F.; Garcia-Parrilla, M. C.; Puertas, B.; Cantos-Villar, E. Wine, resveratrol and health: a review. *Nat. Prod. Commun.* **2009**, *4*, 635−658.

(13) Nassiri-Asl, M.; Hosseinzadeh, H. Review of the pharmacological effects of *Vitis vinifera* (grape) and its bioactive compounds. *Phytother. Res.* **2009**, *23*, 1197−1204.

(14) Donovan, J. L.; Bell, J. R.; Kasim-Karakas, S.; German, J. B.; Walzern, R. L.; Hansen, R. J.; Waterhouse, A. L. Catechin is present as metabolites in human plasma after consumption of red wine. *J. Nutr.* **1999**, *129*, 1662−1668.

(15) Bub, A.; Watzl, B.; Heeb, D.; Rechkemmer, G.; Briviba, K. Malvidin-3-glucoside bioavailability in humans after ingestion of red wine, dealcoholized red wine and red grape juice. *Eur. J. Nutr.* **2001**, *40*, 113−120.

(16) Frank, T.; Netzel, M.; Strass, G.; Bitsch, R.; Bitsch, I. Bioavailability of anthocyanidin-3-glucosides following consumption of red wine and red grape juice. *Can. J. Physiol. Pharmacol.* **2003**, *81*, 423−435.

(17) Liu, J. Y.; Zhong, J. Y. Study on protective effect of grape procyanidins in radiation injury in radiation-contacted persons. *Chi. J. Prev. Med.* **2008**, *42*, 264−267.

(18) Walzem, R. L. Wine and health: state of proofs and research needs. *Inflammopharmacology* **2008**, *16*, 265−271.

(19) Caimi, G.; Carollo, C.; Lo Presti, R. Wine and endothelial function. *Drugs Exp. Clin. Res.* **2003**, *29*, 235−242.

(20) Miller, R. A.; Harrison, D. E.; Astle, C. M.; Baur, J. A.; Rodriguez Boyd, A.; de Cabo, R.; Fernandez, E.; Flurkey, K.; Javors, M. A.; Nelson, J. F.; Orihuela, C. J.; Pletcher, S.; Sharp, Z. D.; Sinclair, D.; Starnes, J. W.; Wilkinson, J. E.; Nadon, N. L.; Strong, R. Rapamycin, but not resveratrol or simvastatin, extends life span of genetically heterogeneous mice. *J. Gerontol. A: Biol. Sci. Med. Sci.* **2011**, *66A* (2), 191−201.

(21) Law, J.; Whittaker, J. Mapping acidification research: a test of the co-word method. *Scientometrics* **1992**, *23*, 417−461.

(22) Clarke, A.; Gatineau, M.; Thorogood, M.; Wyn-Roberts, N. Health promotion research literature in Europe 1995−2005. *Eur. J. Pub. Health* **2007**, *17*, 24−28.

(23) Ho, Y. S. Bibliometric analysis of adsorption technology in environmental science. *J. Environ. Prot. Sci.* **2007**, *1*, 1−11.

(24) Chiu, W. T.; Ho, Y. S. Bibliometric analysis of tsunami research. *Scientometrics* **2007**, *73*, 3−17.

(25) Chiu, W. T.; Huang, J. S.; Ho, Y. S. Bibliometric analysis of severe acute respiratory syndrome related research in the beginning stage. *Scientometrics* **2004**, *61*, 69−77.

(26) Li, T.; Ho, Y. S.; Li, C. Y. Bibliometric analysis on global Parkinson's disease research trends during 1991−2006. *Neurosci. Lett.* **2008**, *441*, 248−252.
(27) Baldwin, C.; Hughes, J.; Hope, T.; Jacoby, R.; Ziebland, S. Ethics and dementia: mapping the literature by bibliometric analysis. *Int. J. Geriatr. Psychiatry* **2003**, *18*, 41−54.
(28) Tian, Y.; Wen, C.; Hong, S. Global scientific production on GIS research by bibliometric analysis from 1997 to 2006. *J. Informetr.* **2008**, *2*, 65−74.
(29) Batagelj, V.; Mrvar, A. P. Analysis and visualization of large networks. *Lect. Notes Comput. Sci.* **2002**, *2265*, 477−478.
(30) Falagas, M. E.; Michalopoulos, A. S.; Bliziotis, I. A.; Soteriades, E. S. A bibliometric analysis by geographic area of published research in several biomedical fields, 1995−2003. *CMAJ* **2003**, *21*, 1389−1390.
(31) Glanville, J.; Kendrick, T.; McNally, R.; Campbell, J.; Hobbs, F. D. Research output on primary care in Australia, Canada, Germany, the Netherlands, the United Kingdom, and the United States: bibliometric analysis. *BMJ* **2011**, *8*, 342:d1028.
(32) Soteriades, E. S.; Falagas, M. E. Comparison of amount of biomedical research originating from the European Union and the United States. *BMJ* **2005**, *331*, 192−194.
(33) Aleixandre-Benavent, R.; Aleixandre-Tudó, J. L.; González Alcaide, G.; Ferrer Sapena, A.; Aleixandre, J. L.; du Toit, W. Bibliometric analysis of publications by South African viticulture and oenology research centers. *S. Afr. J. Sci.* **2012**, *108* (5/6), 661.
(34) European Research Council. Identification of "frontier research" and "emerging research areas" in research proposals: a bibliometric approach; available at http://erc.europa.eu/sites/default/files/content/events/Workshop_report_and_conclusions.pdf (accessed Sept 23, 2013).
(35) Higher Education Funding Council for England. http://www.hefce.ac.uk/Research/ref/ (accessed Sept 23, 2013).