Special Article

Terms and nomenclature used for plant-derived components in nutrition and related research: efforts toward harmonization

Jan Frank, Naomi K. Fukagawa, Anna R. Bilia, Elizabeth J. Johnson, Oran Kwon, Vish Prakash, Teruo Miyazawa, Michael N. Clifford, Colin D. Kay, Alan Crozier, John W. Erdman Jr, Andrew Shao, and Gary Williamson

Many terms for plant-derived food components are commonly used in the literature, but there is a notable lack of standardization and definition of nomenclature. The use of terms is often field-specific, leading to misunderstanding and problems with literature searches and systematic reviews, and results in isolated and divided research; this impacts not only publication quality but also innovation, regulatory compliance, and enforcement. To begin to address this issue, this narrative review describes the current use and definition of terms. The terms are either chemical and/or origin-based, such as phytochemical *(chemicals from plants), or function-based, such as* phytonutrient*,* bioactive*, or* nutraceutical*. The ultimate goal is to establish a common harmonized, evidence-based understanding for when to use each term, thereby providing clarity and a specific scientific basis for such nomenclature. Neither the quality nor the quantity of evidence needed to allow the use of functional terms such as phytonutrient or nutraceutical is specifically discussed here; rather, it is simply noted that evidence is needed to apply these terms. The next step would be to define the evidence necessary for a compound to have a functional descriptor. The aim in this article is to establish scientific criteria for definitions that could be applied to clearly define and differentiate commonly used terms and thus ensure their consistent application in the scientific literature.*

Affiliation: *J. Frank* is with the University of Hohenheim, Stuttgart, Germany. *N.K. Fukagawa* is with the USDA ARS Beltsville Human Nutrition Research Center, Beltsville, Maryland, USA. *A.R. Bilia* is with the University of Florence, Florence, Italy. *E.J. Johnson* is with Tufts University, Boston, Massachusetts, USA. *O. Kwon* is with Ewha Woman's University, Seoul, South Korea. *V. Prakash* is with the Institute of Chemical Technology, Mumbai, and RUAS Bangalore, India. *T. Miyazawa* is with Tohoku University, Sendai, Japan. *M.N. Clifford* is with the University of Surrey, Guildford, UK. *C. D. Kay* is with North Carolina State University, Kannapolis, North Carolina, USA. *A. Crozier* is with the University of California, Davis, California, USA, and University of Glasgow, Glasgow, UK. *J.W. Erdman Jr*. is with the University of Illinois, Urbana-Champaign, Illinois, USA. *A. Shao* is with *Chromadex Corp*., Los Angeles, California, USA. *G. Williamson* is with Monash University, Melbourne, Victoria, Australia.

Correspondence: *G. Williamson*, Department of Nutrition, Dietetics and Food, School of Clinical Sciences at Monash Health, Faculty of Medicine, Nursing and Health Sciences, Monash University, Notting Hill BASE facility. Address: 264 Ferntree Gully Road, Notting Hill, VIC 3168, Australia. Email: gary.williamson1@monash.edu.

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ISSUES WITH NOMENCLATURE AND TERMS CURRENTLY IN USE

Although vitamins have been well defined and characterized, there are a large number of compounds in the diet derived from plants which may impact health, but are not classified as vitamins. For this class, often referred to as *phytochemicals*, a variety of terms are used in the research, industry, agricultural, and regulatory communities. Terms such as *phytonutrient*, *phytochemical*, *polyphenol*, *bioactive*, and *nutraceutical* are used widely, loosely, and somewhat interchangeably in the scientific, regulatory, and popular literature (Table 1). The lack of standardization may confound literature searches, hamper scientific consensus, and prevent harmonization of results. Since most terms are neither appropriately defined nor officially recognized, use of different terminology to describe the same substances can cause confusion, particularly where ingredients or products are either notified or registered with governmental agencies. In 2004, a federal working group led by the US Department of Health and Human Services began the process by proposing a definition for bioactive food components and then soliciting public comments.[1] The proposed definition, "Bioactive food components are constituents in foods or dietary supplements, other than those needed to meet basic human nutritional needs, that are responsible for changes in health status," (Table 1) was intended to "help in guiding and encouraging future research with these components." Public comments, including proposed definitions for bioactive food components that were fairly consistent with the proposed definition, have been summarized.[2] However, while definitions of these terms do exist in the literature[3–7] and some in regulatory documents,[8] the definitions remain inconsistent between sources since the criteria upon which they are based have neither been clearly articulated nor wholly founded upon scientific consensus.

The aim of this article is to capture a range of terms and nomenclature currently used globally to refer to and describe a range of plant-derived food components, to propose criteria for how these terms should be used, to describe the relationship between the different terms, and to provide some specific examples of how such terms may be applied. Another intended goal is to help eliminate inconsistency and confusion around terminology and definitions that affect interpretation of data, and ultimately, conclusions about the biological effects of the compounds. This will potentially facilitate greater dialogue on, and collaboration around, phytochemical research by providing a harmonized approach. Standardizing the nomenclature would also help streamline innovation and facilitate regulatory compliance.

IDENTIFYING- AND ORGANIZING-RELATED TERMS

A list of commonly used, but not exhaustive, terms appears in Table 1, along with definitions that have been proposed and/or used regularly from a variety of sources. In some cases, different terms appear to have nearly identical definitions. Figure 1(A and B) shows the use of these terms in publications in the PubMed and Web of Science databases; Figure 1A includes the year the term was first cited in a publication and the total number of publications citing the terms. Table 2 attempts to simplify the definitions of the terms and organize them according to the basic principles of chemistry, functionality, and intended use. Clearly, use of the prefix *phyto* (from the Greek word *phyton* [plant]) refers to substances derived from, or identical to, those occurring in plants. Phytochemicals, therefore, are compounds present in, or derived from, plants. The terms *polyphenol* and/or *phenolics* refers to a large class of compounds containing at least one phenolic ring. To avoid the need to combine terms such as *polyphenols* (multiple phenolic rings) and *phenolic* (a single phenolic ring), the use of *(poly)phenols* has been adopted by some authors[9–12] to cover both classes. The term (poly)-phenols would also include the class of "tannins" – an older term referring to higher molecular weight phenolic polymers with multiple rings and less defined structures (encompassing gallotannins, ellagitannins, complex tannins, and condensed tannins) that are typically complex mixtures but defined by their ability to tan hides and thus produce leather. The basis of these terms is chemical in nature and the context of use is similar to that for other plant-derived compounds, such as carotenoids, organosulfur compounds, and alkaloids.[13] All of these terms are chemistry-based and do not change regardless of biological activity, and use of the terms themselves does not denote biological efficacy or health benefit, unless otherwise specified.

Strictly, the term *nutrient* implies that the substance, chemical, or constituent in question is essential for growth and the maintenance of life as, by definition, when removed, its absence results in diagnosable deficiency syndromes.[14] On the other hand, the term *phytonutrient* takes on a somewhat different meaning, and, although not a nutrient in the traditional sense, it implies that the compound contributes to "wellness" or provides a health benefit beyond preventing nutritional deficiency. The "phyto" part, as in *phytochemicals*, indicates that phytonutrients are derived from plants. The term phytonutrient should not be confused with "plant

Table 1 **Non-exhaustive examples of terms and definitions currently used in the scientific and other literature to describe plant-derived compounds**

Term	Definition and source
Bioactive compound	"Components in foods or dietary supplements, other than those necessary to meet the basic nutritional needs, which are responsible for changes in health status"[1]
	"A type of chemical found in small amounts in plants and certain foods (such as fruits, vegetables, nuts, oils, and whole grains). Bioactive compounds have actions in the body that may promote good health."[25]
	"Extranutritional constituents that typically occur in small quantities in foods"[26]
	"Essential and non-essential compounds (eg, vitamins, polyphenols) that occur in nature, are part of the food chain and can be shown to have an effect on human health"[27]
	"A compound which has the capability and the ability to interact with one or more component(s) of the living tissue by presenting a wide range of probable effects. The origin of these substances can be natural: terrestrial or aquatic; a plant, animal or other source (eg, microorganisms) or synthetic: partially or totally."[28]
	"Constituents in foods or dietary supplements, other than those needed to meet the basic human nutritional needs, which are responsible for changes in health status"[29]
Nutraceutical	"A foodstuff (as a fortified food or a dietary supplement) that provides health or medical benefits in addition to its basic nutritional value"[30]
	"A functional food (or part of a food) that supplements the diet and also aids in the prevention and/or treatment of a disease or disorder"[31]
	"Foods which are specially processed or formulated to satisfy particular dietary requirements which exist because of a particular physical or physiological condition or specific diseases and disorders and which are presented as such, wherein the composition of these foodstuffs must differ significantly from the composition of ordinary foods of comparable nature . . . may contain one or more of the following ingredients, namely: (i) plants or botanicals or their parts in the form of powder, concentrate or extract in water, ethyl alcohol or hydro alcoholic extract, single or in combination; (ii) minerals or vitamins or proteins or metals or their compounds or amino acids (in amounts not exceeding the Recommended Daily Allowance for Indians) or enzymes (within permissible limits); (iii) substances from animal origin; (iv) a dietary substance for use by human beings to supplement the diet by increasing the total dietary intake."[8]
	". . . a product isolated or purified from foods that is generally sold in medicinal forms not usually associated with food . . . demonstrated to have a physiological benefit or provide protection against chronic disease"[32]
	"A food (or part of a food) that provides medical or health benefits, including the prevention and/or treatment of a disease"[33]
Phytochemical	"A chemical compound (such as beta-carotene) occurring naturally in plants"[30]
	". . . bioactive non-nutrient plant compounds in fruits, vegetables, grains, and other plant foods that have been linked to reducing the risk of major chronic diseases"[13]
	"A term that refers to a variety of plant-derived compounds with therapeutic activities such as anticarcinogenic, antimutagenic, anti-inflammatory, and antioxidant properties"[34]
	"Non-nutritive plant chemicals that have protective or disease preventive properties"[35]
	"Phytochemicals are naturally occurring plant chemicals"[36]
	"Phytochemicals are chemical compounds produced by plants, generally to help them thrive or thwart competitors, predators, or pathogens."[37]
Phytonutrient	"A bioactive plant-derived compound (such as resveratrol) associated with positive health effects"[30]
	"A substance found in certain plants which is believed to be beneficial to human health and help prevent various diseases"[38]
	"(Compounds) in plant-derived foods that elicit biologic responses in mammalian systems that are consistent with reduced risk of one or more chronic diseases"[39]
	"Certain organic components of plants, and these components are thought to promote human health. Fruits, vegetables, grains, legumes, nuts and teas are rich sources of phytonutrients. Unlike the traditional nutrients (protein, fat, vitamins, minerals), phytonutrients are not 'essential' for life."[25]
Polyphenol(s)	"A polyhydroxy phenol; especially an antioxidant phytochemical"[30]
	"A compound containing more than one phenolic hydroxyl group"[38]
	"Secondary metabolites of plants and are generally involved in defense against ultraviolet radiation or aggression by pathogens"[40]
	"A substance that is found in many plants and gives some flowers, fruits, and vegetables their color. Polyphenols have antioxidant activity."[25]

nutrient," ie, chemical entities that plants require for healthy growth, survival, and propagation.

Similarly, the term *bioactive compound* suggests that the substance has a biological activity, which could in theory also include a toxic effect. Although analogous to the term phytonutrient in this sense, a bioactive compound need not be limited to plant-derived substances. In fact, the definitions for bioactive compound clearly suggest that it encompasses a broader array of substances that can be found in the diet or food supply and even encompasses a broader array of substances that can be derived from the environment (including

drugs, toxins, pollutants, and endogenous substances) (Table 2). This would include substances of plant and animal origin as well as bacterial metabolites or even synthetic compounds, but the non-plant components are outside the scope of this article.

Another widely used term, *nutraceutical*, which is a combination of the terms "nutrition(al)" and "pharmaceutical," has even less-defined and broader use. Both formal and informal definitions indicate that the term covers broadly dietary components with health-beneficial effects, but unlike the abovementioned terms, nutraceutical is a product-based term (as opposed to chemical- or origin-based) and reflects a targeted use in the prevention, management, and treatment of diseases. The terms *food factors*, *protective factors*, and *NOFS* (nutrients and other food substances) have also been used in the literature and by some scientific bodies. These are very general terms, and will not be dealt with further here.

Based on the above, it is recommended that the following definitions of terms are used when referring to plant-derived compounds (Table 2 and Figure 2):

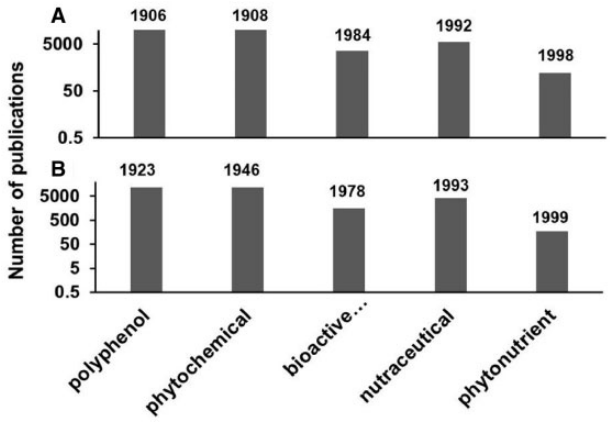

Figure 1 **Number of citations and first usage for various terms.** Number of (A) PubMed and (B) Web of Science citations identified by entering search term in quotes, eg, "phytonutrient." The first year the term appeared is shown above the bar.

Phytochemical

Phytochemical (plant metabolite) is the umbrella term and encompasses all other terms in use to describe *metabolites from plants*, but in practice includes mostly plant secondary metabolites, and can be used synonymously. Phytochemical should be used when no further subclassification is possible or required. Phytochemicals can conveniently be subdivided by chemical structure into several major groups, each with further subdivisions (and more fully discussed elsewhere)[15]: (1) phenols, polyphenols, and tannins; (2) sulfur-containing compounds (including sulforaphane); (3) terpenes; (4) alkaloids (including trigonelline, caffeine, and theobromine); (5) acetylenes and psoralens; and (6) carotenoids (including lycopene, lutein, and zeaxanthin).

Table 2 **Proposed terms, definitions, and criteria for the use of terms to refer to and describe plant-derived compounds**

Term	Proposed definition	Origin	Intrinsic implication of biological activity	Basis of term
Phytochemical	A compound present in plants (a plant metabolite)	Plant	No specific indication	Plant origin
Phenolic	A compound containing 1 phenolic ring in its chemical structure	Plant, animal, or chemical	No specific indication	Chemical structure
Polyphenol	A compound containing 2 or more phenolic rings in its chemical structure	Plant or chemical	No specific indication	Chemical structure
(Poly)phenol	A mixture containing, or combination of, phenolics and polyphenols	Plant, animal, or chemical	No specific indication	Chemical structure
Phytonutrient	A compound present in and/or derived from plants that confers a health benefit (including metabolites post consumption)	Plant	Implied beneficial effect on health	Origin and function
Bioactive	A compound present (in food) that exerts reproducible biological effects at dietary levels (including metabolites post consumption)	Plant or animal	Implied biological effect	Function
Nutraceutical	A compound or mixture of compounds present in food or food supplements intended to exert a therapeutic effect	Plant or animal	Implied beneficial effect on health or disease	Proposed use

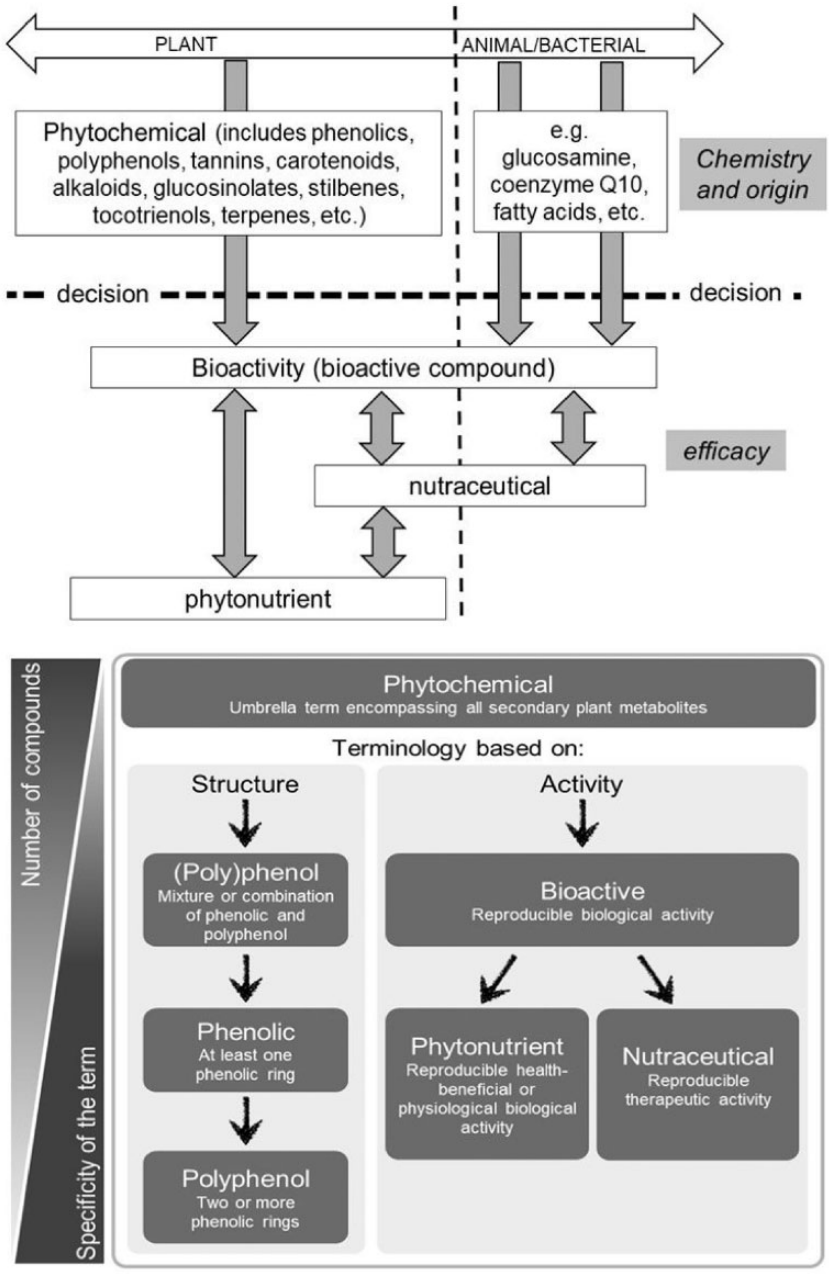

Figure 2 **Origin, chemistry, and efficacy requirement for each of the terms.** Top: Relationship between terms. Left of the vertical dashed line are compounds from plants, and to the right compounds from other sources. The horizontal line represents a decision concerning efficacy, ie, what evidence for potential health benefits is necessary to transition from phytochemical or named compound/chemical class to phytonutrient/bioactive compound/nutraceutical. Bottom: Decision tree for use of terms.

Most of the confusion and overlap occurs in the literature for the terminology of the first group (phenols, polyphenols, and tannins) and so this will be the main focus of the phytochemicals covered here.

(Poly)phenol. (Poly)phenol is a term based on a structural feature – namely, the presence of an unspecified number of phenolic rings – and can be subdivided into "phenolic" (phytochemicals with one phenolic ring) and "polyphenol" (phytochemicals with 2 or more phenolic rings, which includes the "flavonoids"). To provide as much information as possible, the term (poly)phenol should be used when referring to mixtures of phenolics and polyphenolic compounds. For example, the flavonoids (including isoflavones and the bacterial metabolite equol) and black tea theaflavins and thearubigins are polyphenols, whereas oleuropein, caffeic acid, gallic acid, and hydroxytyrosol are phenolics, but all of these compounds could be included under the umbrella term (poly)phenol. The use of the term *phenol*

alone (instead of phenolic) is discouraged, as it refers to a specific organic aromatic compound made up of a benzene ring bearing a hydroxy group.

Bioactive

A *bioactive* compound is a descriptor based on a biological activity and refers to phytochemicals or animal-derived components with demonstrated activity in biological systems, usually animals and/or humans, without specifying whether the activity is beneficial or harmful.

Phytonutrient

Phytonutrient is another term based on biological activity, and as such, could also be classified as a bioactive compound. But this term goes beyond *bioactive* in that the biological activity is "deemed" health-beneficial and so should only be used for phytochemicals that exert reproducible health-beneficial effects or affect physiological functions in randomized and controlled animal or human trials. Neither doses nor the extent of the evidence are specified here, but observations solely from in vitro studies should not be sufficient to allow the use of the term phytonutrient. Strictly, *phytonutrient* also applies to essential nutrients from plants, such as vitamin C. This meaning does not seem to be in general use, but has the potential to lead to some ambiguity.

Nutraceutical

Nutraceutical is another activity-based term that also belongs to the category of "bioactive compounds." It should only be used to refer to bioactive compounds (plant, animal, fungal, or bacterial) that exert reproducible therapeutic effects in randomized and controlled animal or human trials. The current literature does not indicate whether a minimum effective dose should be specified, and some efficacy data, safety data, possible side effects, an analytical protocol to confirm identity, precise composition, and precise content of the active ingredients (and for pharmaceuticals, which specific ingredients) may also be needed. With regard to safety assessment, some guidelines in the form of a decision tree have been published.[16]

CRITERIA FOR USE AND APPLICATION OF TERMS

A key question for all stakeholders is when to use which terms, and under what circumstances. The criteria that should be met for a substance to transition, for example, from being classified as a phytochemical to being classified as a phytonutrient, have not been clearly established or communicated. It is therefore proposed that a decision tool could be used to clearly assign a substance to the respective term based on its chemical structure and efficacy (Figure 2). However, the terms are not mutually exclusive; for example, a phytonutrient will always also be a phytochemical, but many phytochemicals will not qualify as phytonutrients.

The issue of whether recommended intakes, such as dietary reference intakes, could and should be established for phytonutrients has been debated widely.[3,17,18] If dietary reference intake values are deemed appropriate, the question is how this might be achieved.[19–21] Indeed, authoritative bodies have proposed or established reference intakes for selected phytonutrients or bioactives in China,[22] South Korea,[23] and Russia.[24] Several reports have separately described the components or criteria that should be considered when establishing reference intakes for bioactive substances.[20,21] Among the key criteria needed for a bioactive or phytonutrient to be considered for reference intakes are availability of analytical methods, role as a biomarker of exposure or status, presence in food composition databases or equivalent, intake or status assessment, pharmacokinetic data, observational and prospective randomized trials on relevant health outcomes, and biologic plausibility. Which of these, or perhaps others, might be necessary to distinguish between a phytochemical, phytonutrient, and nutraceutical remains to be established. Phytonutrients exist as complex mixtures in foods or as isolated extracts, but the absolute need for a substance to be an isolated, purified compound in order to be considered as a phytonutrient has not been specifically addressed. One complication is that these substances may exert a modest effect that becomes obvious only after a long period of exposure. In addition, some mixtures of phytonutrients may have synergistic health impacts that are lost or diminished when single components of the mixture are tested.

CURRENT RELATIONSHIPS BETWEEN TERMS AND FUTURE DIRECTIONS

The information presented in this article could serve as the basis for future discussions to determine which term(s) to use and under what circumstances. In some cases, terms are synonymous and can be used interchangeably, but in other cases there should be clear distinctions.

In summary, terms can generally be organized according to several basic categories, including origin (eg, plant, animal, bacterial, or synthetic), chemical structure (eg, phenolic acid or polyphenol), functional capacity (eg, confer a health benefit), or intended use (eg, as a product intended to treat or manage a

condition or disease) (Table 2). Additional criteria are needed to determine whether, and when, a given substance falls into one or more of these categories. For example, the term *polyphenol* is based on a chemical structure, and thus compounds that meet this definition (multiple phenolic rings) are polyphenols irrespective of origin, whether they provide a health benefit or have an intended use. In contrast, a *phytochemical* may or may not be a polyphenol, but must be derived from, or be present in, a plant. As the wording implies, "bioactive" and "phytonutrient" are functional terms. A bioactive may be of plant, animal, or bacterial origin, while a phytonutrient must be derived from, or be present in, a plant.

A biological or health benefit represents a key criterion for determining whether a substance can be referred to as a phytochemical rather than a phytonutrient or a bioactive, ie, transitioning from a chemical basis to a functional basis, but these criteria are not defined here. However, the transition could be based, for example, on published in vivo data demonstrating efficacy of oral consumption of the substance on a relevant health outcome together with a mechanistic understanding. On this basis, carotenoids, (poly)-phenols, glucosinolates, stilbenes, tannins, and terpenes are all phytochemicals. However, whether these families of compounds or individual compounds can be considered phytonutrients would depend on the existence of published data adequately demonstrating a health benefit, taking into consideration bioavailability and the biomarkers used to assess efficacy.

Use of the term *nutraceutical* could be limited to a product in a regulatory context, since its basis is not origin, chemical structure, or functional capacity, but rather proposed use. In other words, any or all of the terms cited in this perspective could be considered a nutraceutical, irrespective of origin, chemical structure, or functional capacity, but would still require efficacy data.

When using the above terms, authors, reviewers, editors, and dictionary compilers should consider the proposed definitions of the terms and the need for precise and specific language in scientific reports. The more coherent and specific the use of these terms, the more information can be conveyed in a single word. It should be noted that the structure-based terms (eg, phenol → polyphenol) and the activity-based terms *bioactive* and *nutraceutical* can also refer to compounds of bacterial or animal origin (or even synthetic), whereas *phytochemical* and *phytonutrient* exclusively refer to plant-derived substances (Table 2; Figure 3). The non-plant–derived components are outside of the scope of this review.

Standardizing the use of terms – or at least achieving alignment on how to classify different substances – should help to promote research reproducibility and collaboration, reduce confusion, and improve clarity. Importantly, further discussion is needed on the type and amount of evidence necessary to classify a substance as a phytonutrient or nutraceutical, rather than adopting more straightforward chemical definitions for such substances.

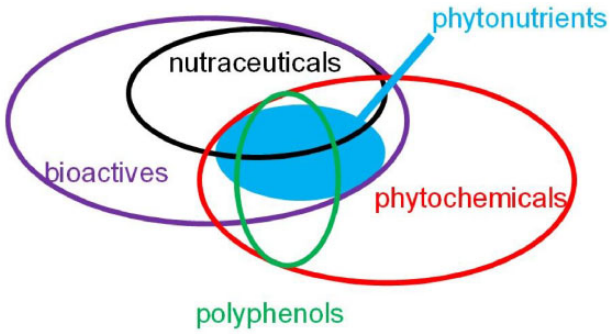

Figure 3 **Overlap of terms used to describe plant-derived minor compounds.** The set of compounds described by each term are defined by different types of criteria, such that a given compound or natural product may belong to none of them, all of them, or any number in between. For example, phytochemicals are described by their source, polyphenols by chemical structure, and bioactives and phytonutrients at least in part by their biological activities. The figure provides a conceptual diagram on the overlap of the various terms. Polyphenols can only be phytochemicals and hence are only within the phytochemical box; nutraceuticals and bioactives include phytochemicals, but also include other sources; phytonutrients are always phytochemicals, even if essential nutrients, and some phytonutrients are polyphenols, but all phytonutrients, by definition, are bioactives even if they are essential. Note that the area of the ellipses do not indicate the size of the compound class.

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the authors and do not necessarily reflect those of their affiliated institutions, including the U.S. Department of Agriculture.

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