

ANIMAL SCIENCE

Title: Critical review on botanical extracts as alternatives production enhancers in swine production system – **NPB #04-137**

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Date Submitted: February 3, 2006

Abstract

The use of botanicals is currently recognized as an essential tool for continuous improvement of total quality animal protein products for humans. A large number of publications by various authors reflect the interest in this alternative field of organic production. Reviews of literature on botanicals have been done in the past by several authors and research groups. However, considering the contributions in the recent times, a more comprehensive review is attempted here. In this paper, the authors have reviewed botanicals literature in a way that would help researchers, academicians and practitioners to take a closer look at the growth, development and applicability of botanicals in several fields taking into account their functional properties. The authors have examined various papers applying a descriptive approach and have proposed a special scheme of classification in accordance to types of research and accountability of this research. In addition, certain gaps that would provide hints for further research in botanicals have been identified.

Keywords: Botanicals, literature, quality, classification

Introduction

Policy makers and practitioners in the field of Animal Science are constantly on the look out for alternative feed additives or supplements techniques that may have different mechanisms of action such as botanicals on their functional properties as: antioxidant, antibacterial, antiparasitic, antiviral, anti-inflammatory, etc to enable to total quality schemes would be implemented in both human society and animal production systems. Botanicals have become popular in the recent times because their positioning as alternative to traditional antibiotics or antioxidants.

These research results were submitted in fulfillment of checkoff funded research projects. This report is published directly as submitted by the project's principal investigator. This report has not been peer reviewed

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Thoughts on botanicals are not new. The plant world has been the most important source of medicinal agents for the treatment of human and animal disease, and for use as preventative agents in maintaining good human health through the history. However, the scale of the challenge may be more clearly appreciated when it is realized that there are approximately 750,000 species of flowering plants on earth, only very few of which have been scientifically studied for their potential functional values. Bioactivity of botanical materials is broadly acknowledged by the scientific and medical communities and it has now found more social actors subscribers, and occupies a prominent place, helping quality up gradation in several disciplines and as a science, herbal science.

The term "physiologically active plants" is usually used to refer to plants containing physiologically active metabolites but due to a general lack of knowledge with regard to the active principles and standardizing on the totality of the biological active compounds, that term is typically replaced by standardizing on so called "marker substances" or "markers", i.e. specific known constituents of the plant, whose relevance for the functional uses have, however, not been generally proven. Many authors have contributed to the literature on botanicals resulting in more than 443 publications as of December 2004. Considering the growth of publications, some attempts have been made in the past to review the literature. It is essential that the present attempt would be different from the earlier reviews and more broad based in coverage. In this sense, this paper, besides providing a review of literature on botanicals, covers the following objectives:

- a) Arranging the publications in an orderly manner to enable easy and quick search
- b) Classification of literature
- c) Scrutiny of outcome of publications; and
- d) Identifying gaps and providing hints for further research.

However, it is not the intention here to provide any overview or summary of botanicals. Users are suggested to search in Endnote software platform and to look into an scheme of categories the cited literature, for example general aspects or fundamentals and experimental models- review. This paper first provides a comparison among the reviews on botanicals and highlights the outcome in each case. Next, a new methodology for classifying the literature is suggested. The growth and categorization of publications are presented in a graphical form for easy understanding. The papers have been closely examined and scope for further work has been identified.

Preamble to literature review

Over the last year, the authors had several opportunities to collect and study literature pertaining to botanicals. Two main reasons are:

- (1) A critical review will go through and editing process and be compiled by the authors for submission into some peer reviews with the sponsor of National Pork Board (NPB).
- (2) One of the author pursuing doctoral studies in the field of use of oregano in swine production systems

As a part of the research it was decided to classify and analyze the literature in detail. The course of action included the following steps:

- (1) Updating the database to ensure that literature is as current as possible. The collection of literature has been reviewed till December 2004.
- (2) For literature search, both hard copy search in established libraries of the University of Minnesota and electronic search in World Wide Web were made. Search engines (conventional and scientific)

available at World Wide Web were specifically used to ferret the literature pertaining to botanicals from a wide variety of sources on the internet. While we have tried their best to include as many publications as possible, we do not claim that their listing is complete or exhaustive in nature.

(3) Developing a classification scheme was the next step. First a bibliographical list of all publications was developed and it was created in Endnote 8 software.

(4) Keeping these observations in mind we decided to approach the review process in a different way, as illustrated in the next part of the paper.

Methodology and scheme of review

The classification scheme proposed in this paper includes a simultaneous parallel categorization that highlights the growth of literature from time to time and also the coverage of botanicals specific to different groups like:

a) Botanicals: general aspects or fundamentals and experimental models

All publications under this category deal with very general and fundamental concepts of botanicals, essentially for first time readers. Fundamentals are usually covered to a large extent particularly when the thematic areas and disciplines are in the introduction, growth stage or exponential cycle of life. This can be confirmed by the number of publications, which appeared in the early time period of the time scale considered.

b) Botanicals: specific applications and case studies. People are more interested to know about applications and success research and applications. Therefore this should be a useful group. Under this categorization, all literature dealing with specific applications to Animal Science and other sectors, excluding human were included..

c) Botanicals: innovations/extensions/new approaches. When the processes and products reach a saturation stage in terms of its popularity (asintote period), novel and emerging approaches and innovations start appearing in the literature. This category is considered to recognize and appreciate the novel approaches or paradigm shifts in botanicals products in animal science and other sector including human.

d) Botanicals: applicable to swine production. This category is specially included here for academicians, practitioners and farmers and also forms a major aspect of the present peer review. Another reason is the affiliation of both the authors and sponsor (NPB) to this sector as it mentioned above.

Reviews of literature on botanicals

During the current review at least 63 literature reviews have been made in the past and all but one was studied by the authors. The different reviews in chronological order and their outcomes are shown in Tables 1, 2 and 3. The number of publications for each category in a Pareto diagram is shown in Figure 1.

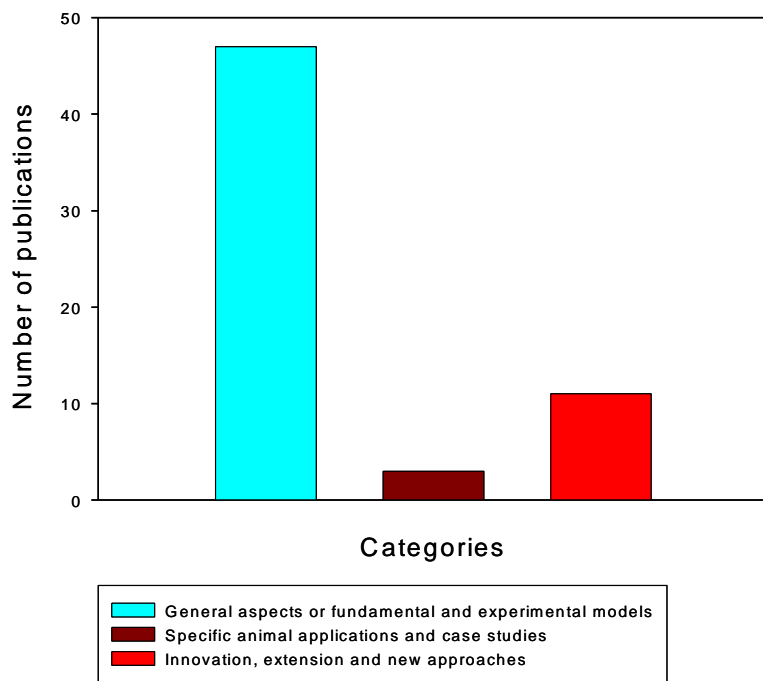


Figure 1. Pareto diagram showing the number of reviews of botanicals.

Further, a comparison among the attempts to review literature on botanicals is made using certain attributes.

The attributes considered for comparisons are:

Focus and objectives: this refers to a brief coverage of the publications in terms of the content and the applicability.

Number and type of publications covered: the number of publications listed and whether they are text books, journal papers, conference proceedings or periodicals.

Review methodology: this looks at the way in which the literature has been reviewed and classified. Apart from these distinguishing attributes, certain common parameters like, the name of publication, author(s), year of publication, journal of publication are also used. This comparison is shown in Tables 4, 5 and 6.

All reviews of literature in the categories described earlier have further been coded based on the chronological appearance of the review article. Coding had been done from 2000 onwards, since botanicals emerge as an integrative concept, recently. Also, the time interval for all categories is taken as two years. This is adopted, since the number of review papers during the last four first years are higher compared to previous years. Chronological listing of publications can be seen in the line graph form in Figure 2. All the reviews based on this coding pattern, are available as an electronic publication (i.e. PDF version) or as photocopy of the original paper. A serial number by category could be seen in an annex of bibliographical list prepared in Endnote 8 software.

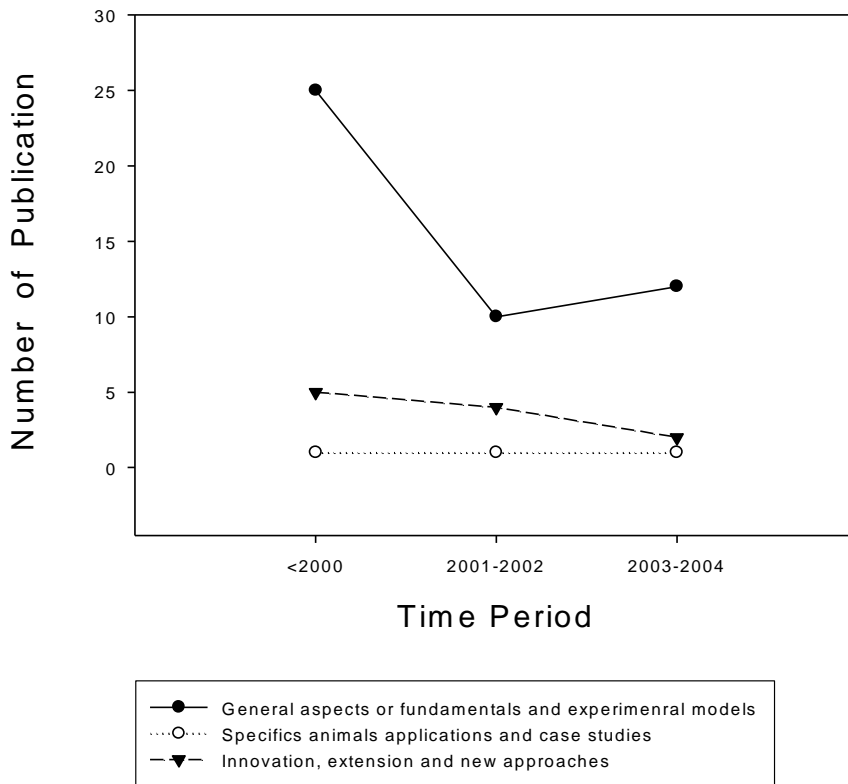


Figure 2. Graph showing chronological appearance of all reviews

General aspects or fundamentals and experimental models

The body of explicit and empirical knowledge in the category of general aspects or fundamentals and experimental models has been important during this period (<2000). Plants, herbs, and spices and their respective and collective roles in promoting an integrative approach in human have been characterized at different hierarchical levels.

Classification of individual plant, herbs and spices has been made on analytical chemistry, botanical, morphological and commercial aspects (Balentine et al., 1999; Conner, 1993; Iwu et al., 1999; Kabara, 1991; Nakatani, 2000; Salzer, 1977; Stahl-Biskup, 1991; Svoboda and Hampson, 1999). Further studies centered around novel in vivo and in vitro systems to elucidate the adaptogenic mechanism should now evolve, so that more and better drugs will be developed to benefit mankind (Farnsworth et al., 1985).

Botanicals are poorly exploited sources of alternative antimicrobials agents whose structures and modes of action may well differ from those derived from the better known. Although the functional attributes of bacterial outer membrane can be correlated well with the presence of unusual structural components and the precise molecular organization of these components, the properties of some of the mutants, as well as the alterations of permeability under certain conditions, suggest that a complete picture of the outer membrane structure has not been elucidated yet (Nikaido and Vaara, 1985). Further studies will lead us to a better understanding of this topic, but for example, the effect of phenolic compounds expanding oil/water interface which exerts a marked influence on the distribution

of long-chain free fatty acids and phenolics between the aqueous and oil phases accelerated the rate of death of Salmonella (Nychas, 1995).

Suitable candidates for the development of useful immunostimulatory drugs in the class of high molecular weight compounds, especially polyssacharides of a particular structure type are a multitude. However, this kind of compounds should be: 1) chemically defined, 2) easily degradable biologically, 3) non-(co)carcinogenic or non-mutagenic, 4) neither too strong nor too weak in its stimulatory efficacy, and 5) nontoxic and without any side or cascade effects (Wagner and Proksch, 1985).

From the large number of papers published in the time period analyzed (1976- 1986) so far it is clear that essential oils (EO) possess interesting antimicrobial properties which may be useful for practical purposes (Janssen et al., 1987a; Janssen et al., 1987b), but antimicrobial activity are difficult to compare because the tests methods differ widely. Future studies should mention the strain number of a test organism, EO composition and conditions which the oil will be obtained (Farnsworth et al., 1985; Janssen et al., 1987a; Janssen et al., 1987b). In this sense, diffusion and dilution methods have been employed to study the antimicrobial activity of medicinal plants but some factors (culture medium composition, microorganisms tested, extractive method, pH, solubility of the sample in the culture medium, etc.) can change results and it is difficult using these methods to standardize a procedure for the study of antimicrobial plants. Bioautography is mentioned as alternative method for studying antimicrobial activity (Rios et al., 1988).

Antioxidants are substances that when present in foods or in the body at low concentrations compared with that of an oxidizable substrate markedly delay or prevent the oxidation of that substrate. Antioxidants are known to act at different levels in the oxidative sequence involving lipid molecules. The process of autoxidation and development of rancidity in foods involves free radical chain mechanism proceeding via initiation, propagation and termination steps. Lipid peroxidation is a problem not only in the edible oil and the food industry (Shahidi, 1997), especially in countries that depend heavily on fresh foods and in less-developed areas (Namiki, 1990), but also in the human body (Shahidi, 1997). Over production of active oxygen radicals in human body causes oxygen stress in DNA and cell membrane, and consequently induces toxic effects and diseases. Self defense system against these oxidative damages is supported by antioxidants such as α -tocopherol and ascorbic acid (Shahidi, 2000).

The search for new chemicals which can aid in food preservation is hampered by several restrictions. First, the cost of developing a new chemical and getting it approved ranges from 100 to 200 million dollars (US); second, it may take a great deal of time (10-12 years) and effort to get the product onto the market. Such obstacles make for new opportunities in seeking alternative routes for finding new food preservatives. Whilst both antioxidants (BHA, BHT) and chelating (EDTA) substances have been used in food for antioxidant purpose. They have been demonstrated to have antimicrobial effects alone and in combination (Kabara, 1991). However, the use of natural antioxidants in crude isolated form would be more desirable also for reasons of stability, ease of use, and cost. Also desirable from a practical point of view is the combined use of such isolates with known natural antioxidants, e.g., ascorbic acid and tocopherol (Namiki, 1990). Natural antioxidants from dietary sources include phenolic and polyphenolic compounds, chelators, antioxidant vitamins and enzymes, as well as carotenoids and carnosine (Nakatani, 1997; Nakatani, 2000; Shahidi, 2000).

Different experimental models of botanicals have been aimed from the point of view of therapeutic research; there has not been a lot of clinical data generated on Echinacea during the era of modern medicine. The main reason for that has been the lack of a consensus relative to the total activity of the herb. In addition, considering the remarkable properties of Echinacea and its total lack of

observed toxicity (Bergner, 1997; Hobbs, 1995; Mowrey, 1990). Different reviews showed the immunostimulatory activity of Echinacea extracts, and assigned the activity to certain groups of constituents (Bauer and Wagner, 1991; Bergner, 1997; Mowrey, 1990). At empirical level, Echinacea has been categorized by Native American Indians, German's medical doctors and American herbalists as a selective herb to prevent and help different ailments.

EO of thymus taxa are revised and thymol and carvacrol are presented in each specific species due to their importance in terms of functional properties (Stahl-Biskup, 1991). A general description of garlic, its chemical composition, its history and folk use; its pharmacology: Antimicrobial, antibacterial, and antifungal activity, antihelmintic, antiviral, immune enhancing and anticancer effects; clinical applications: high cholesterol level, blood pressure-lowering activity, platelet aggregation inhibition, fibrinolytic activity, prevention of low-density lipoprotein oxidation; dosage and toxicity are addressed in other review (Murray, 1995).

Other compounds such as flavonoids in tea and anthocyanins in tart cherries were presented as examples of how to move forward in understanding active compounds (Balentine et al., 1999); as well as the chemical compositions of the EO and botanical, and aphrodisiac, medicinal, and therapeutic properties, and pharmacological applications of leaves, fruits and wood of Vitex agnus-castus (Russo and Galletti, 1996). Rosemary phenolic antioxidants are found to have a additional purpose in the food industry besides those of traditional flavoring and stabilizing agents (Offord et al., 1997).

Ten reviews were generated during the period of 2001-2002 in the category of general aspects and experimental models. Important traditional medical systems like the Traditional Chinese Medicine, the Ayurvedic Medicine as well as the European 'Humoral Medicine' consider different aspects of the sick human being, like the constitution of the patient (holistic approach), and take qualities of herbal drugs, vegetarian food, and spices into account for therapeutic purposes (Saller et al., 2001). The first database and monographs are presented representing the toxicity of individual Chinese herbs with toxicological grades based on the evidence of published studies. That information should assist in promoting the safe and effective use of Chinese herbal medicine (Bensoussan et al., 2002).

The concept of synergy was developed. Synergy is occurring when the effect of the combination of medicines is greater than the sum of its cumulative individual action; in other words, a plant extract is more than the sum of its parts (Williamson, 2001). In this context, Phytomedicine works on so many physiological systems that it is impossible to fully quantify the plethora of interactions via a single herb, let alone a combination of six or seven compounds (Sarris and Flaherty, 2002). This concept changes substantially the perception that natural medicines have something special to offer, at least a scientifically based explanation for the clinical equivalence of many plants extracts compared to synthetic drugs at the same therapeutic indications. Although synergy can be ascertained via a precise mathematical formula, it is difficult to test consistently with plant medicines as the individual constituent levels vary. The isobole method is proposed as method of choice to identify synergy; this method is independent of the mechanism of action and applies under most experimental conditions (Sarris and Flaherty, 2002).

EO production is highly integrated with the physiology of the whole plant and so depends on the metabolic state and preset developmental differentiation programmed of the synthesizing tissue. However, EO productivity is ecophysiological and environmentally friendly. These and other aspects of the modulation of EO production are presented in this period, along with a brief outline of the current concept of their relevant biosynthetic mechanisms (Bhattaram et al., 2002; Sangwan et al., 2001). From the point of view of therapeutic research, the therapy of functional gastrointestinal disorders was one of the domains of phytotherapeutic treatments reviewed (Saller et al., 2001).

The nutritive value of major spices from India, their role in health and disease, shelf, life of spices, microbiological safety of spices, quality control of spices and future perspectives were described by (Subbulakshmi and Naik, 2002). Other models analyzed during this period were garlic, onion and lavender has many health benefits and has been traditionally used worldwide over the centuries. S-allylcysteine, S-allylmercaptocysteine, Na-fructosyl arginine and others, formed during the garlic extraction process appeared to possess hepatoprotective, immune-enhancing, anticancer and chemopreventive activities (Amagase et al., 2001). However, the chemistry of garlic is complicated and the quality of garlic products is dependent on the manufacturing process. On the other hand, inconsistency in the efficacy of garlic supplements may be due to the incorrect standardization and the overlooking of other truly active compounds like allicin (Amagase et al., 2001).

Onions are rich in two chemical groups that have perceived benefits to human health. These are the flavonoids and the alk(en)yl cysteine sulphoxides (ACSOs). Compounds from onion are reported to have a range of health benefits which include anticarcinogenic properties, antiplatelet activity, antithrombotic activity, and antiasthmatic and antibiotic effects. Socialization of these findings showed that World onion production has increased making it, the second most important horticultural crop after tomatoes. Storage characteristics and durability for shipping have been also contributed to this expansion (Griffiths et al., 2002). A current state of knowledge about the effect of lavender oils on psychological and physiological parameters and its use as an antimicrobial agent are showed in detail. Those findings support the traditional uses of lavender (Cavanagh and Wilkinson, 2002).

In the last two years (2003-2004), general aspects or fundamentals and experimental models category was devoted to discuss the data required to determine the safe use of botanicals and botanical preparations, and provides advice on the development of risk assessment strategies consistent with due diligence under existing food regulations (Schilter et al., 2003). The strategy was elaborated by Natural Toxin Task Force of the European Branch of the International Life Sciences Institute (ILSI) Europe and comprises: product specifications, composition and characterization of standardized and authentic materials, documented history of use and comparison to existing products (taking into account the effect of industrial processing), description of the intended use and consequent exposure are highlighted as key background information on which to base a risk evaluation. Experimental research requires: in vitro assays, animal, and/or human studies; as well as, a decision tree to determine the extent of data requirements based on product comparison. Other research group reviewed the classical methods commonly used for the evaluation of EO antibacterial and antifungal activities. In addition, an overview is available on the susceptibility of human and food-borne bacteria and fungi towards different EO and their constituents (Kalemba and Kunicka, 2003).

The term complementary medicines describes a range of pharmaceutical-type preparations, including herbal medicines, homoeopathic remedies, EO and dietary supplements, which mainly sit outside conventional medicine (Barnes, 2003a, 2003b). This kind of Medicine is a popular healthcare approach in the UK, and there are signs that the use of such products is continuing to increase. However, evidence of efficacy (and safety) for herbal medicines should be considered to be extract specific. For instance, Pharmaco vigilance for complementary medicines is in its infancy and a new system for registration of traditional herbal medicines would ensure that marketed products meet standards for quality and safety (Barnes, 2003b). Perhaps, the increasing utilization of herbal therapy world-wide has also augmented the concern that such treatment may possibly expose the patient to unknown dangers (Magee and Loiacono, 2004).

During this period, herbal medicine has been widely used in the United States, with approximately one quarter of adults reporting use of an herb to treat a medical illness within 2003. However, to improve the safety and consistency of herbs, additional research is needed to define the pharmacology, stability, and bioavailability of these products (Bent and Ko, 2004). In this sense, the

newly announced research priorities of the National Center for Complementary and Alternative Medicine, which have placed an increased emphasis on studies of the mechanism of action of herbs and other complementary and alternative therapies would be provide new information about active ingredients, pharmacology, stability, and the bioavailability of herbs (Xue et al., 2004).

A growing body of research has demonstrated that the commonly used herbs and spices such as garlic, black cumin, cloves, cinnamon, thyme, allspices, bay leaves, mustard, and rosemary, possess antimicrobial properties that, in some cases, can be used therapeutically (Lai and Roy, 2004). A reference database on natural medicines is now available; it is a useful resource that will aid the development of modern medicines from natural sources as herbs and spices.

Garlic continues to be an experimental model to demonstrate the importance of dietary and medicinal plants leading prescription drugs in some Western countries. Reactive oxygen species (ROS) seem to be at the core of many disease processes and it is an attractive and convenient hypothesis that garlic might exert its antimicrobial activities through modulatory effects on ROS. However, the presence of more than one compounds in garlic, with apparently opposite biological effects, has added to the complexity of the subject (Banerjee et al., 2003). Oregano has a good antioxidant capacity and also presents antimicrobial activity against pathogenic microorganisms like Salmonella typhimurium, Escherichia coli, Staphylococcus aureus, Staphylococcus epidermidis, among others. The antimutagenic and anticarcinogenic effects of oregano were also analyzed, representing an alternative for the potential treatment and/or prevention of certain chronic ailments, like cancer (Arcila-Lozano et al., 2004).

An extensive literature search identified 6 randomized controlled clinical trials in which the efficiency of Chinese herbal medicine had been investigated for the treatment of allergic rhinitis (Xue et al., 2004). In addition, a number of the herbs in Chinese herbal formulae used in the trial, and/or their constituent compounds have been reported to possess anti-allergic, anti-inflammatory or immune modulation activities. Based on the evidences from animal studies, the well recognized digestive stimulant action of spices may be considered to be mediated through two possible modes (i) stimulation of the liver to secrete more bile enriched in bile acids, and (ii) stimulation of enzyme activities that participate in digestion, both of pancreatic and intestinal origin. Such stimulation of bile secretion and of the activities of digestive enzymes leads to an accelerated overall digestive process, resulting in a significant reduction in the duration of passage of food through the gastrointestinal tract (Platel and Srinivasan, 2004).

A number of EO components have been identified as effective antibacterials in vitro studies, e.g. carvacrol, thymol, eugenol, perillaldehyde, cinnamaldehyde and cinnamic acid, having minimum inhibitory concentrations but a higher concentration is needed to achieve the same effect in foods. EO comprises a large number of components and it is likely that their mode of action involves several targets in the bacterial cell. The hydrophobicity of EO enables them to partition in the lipids of the cell membrane and mitochondria, rendering them permeable and leading to leakage of cell contents. Physical conditions that improve the action of EO are low pH, low temperature and low oxygen levels. Synergism has been observed between carvacrol and its precursor p-cymene and between cinnamaldehyde and eugenol. Some EO components are legally registered flavorings in the EU and the USA (Burt, 2004).

Innovation, extension and new approaches

Before 2000, reviews of innovation, extension and new approaches claimed that the absence of strong commercial and marketing incentives to develop natural systems has been changed in recent years, in response to consumers changing needs, but those systems need to be effective and save

and fulfills a real technological requirements (Gould, 1996). On the other hand, their additivity or synergism with other factors and techniques would be evaluated in the future, particularly if more studies are undertaken in real foodstuffs as well as in laboratory media (Lewinsohn, 1996). Aromatherapy is against scientific approach as it wants to retain the mystical element of the process. However, in practice the attributes of certain individuals' EO can be applied successfully and researched further (Lis-Balchin, 1997).

During this period, and enormous efforts in instrumentation were evident. The use of supercritical fluid extraction (SFE) in the preparation and analysis of Chinese herbal medicine (CHM), replacing traditional organic solvent was justified and promising to use in the dual role of extracting useful ingredients and removing pesticide residues (Chen and Ling, 2000). HPLC coupled with various column and detection systems were analyzed in terms of techniques for the qualitative and /or quantitative evaluation of medicinal herbs. To complement gas chromatography and liquid chromatography, capillary electrophoresis was also evaluated (Tsai et al., 1997).

Economic potential of molecular biology for the generation of novel aromatic and medicinal crops is enormous, but there are many obstacles that need to be addressed such as: a better understanding of the biosynthetic pathways involved in the information of the target compounds, choosing the gene or set of genes that will have the desired effects on the target plant metabolism, with minimal effect on other metabolic processes, being biochemical knowledge of the biosynthetic pathways crucial for the identification of target genes. In addition, many legal issues concerning the regulation and marketing of genetically engineered plants and plant products need to be also addressed; as well as public acceptance of transgenic products as foods, fragrances and industrial materials (Lewinsohn, 1996).

From 2001 to 2002 reviews outline the developmental nature of instrumental approaches to EO analysis. Gas chromatography and mass spectrometry were included in a comprehensive dissertation on the field of EO analysis (Marriott et al., 2001). Practical aspects of supercritical fluid extraction (SFE) such as modifiers, sample preparation, special considerations for collection and modeling for the extraction and separation of active compounds from herbs and other plants were presented by (Huie, 2002; Lang and Wai, 2001). The basic principles of microwave-assisted extraction (MAE) and pressurized liquid extraction (PLE) are very similar to those of classic extraction techniques (Huie, 2002).

Medicinal plants may be associated with a broad variety of microbial contaminants, which are represented by bacteria, fungi and viruses. Risk assessment of the microbial load of medicinal plants has, therefore become an important subject in the establishment of modern Hazard Analysis and Critical Control Point (HACCP) schemes. This could be considered for guidelines and/or possible inclusion in the European Pharmacopoeia in a constructive way (Kneifel et al., 2002).

During 2004, two reviews were devoted to demonstrate that some herbal/dietary constituents form reactive intermediates capable of irreversibly inhibiting various cytochrome P450 products (CYPs). Those represent a novel type of chemopreventive agents with higher selectivity and lower toxicity compared to synthetic compounds. Herbal medicines often contain multiple active substances and multiple cellular molecules might be the targets of herbal medicine. The identification of these targets may provide molecular evidence for the herb's pharmacological activity and toxicity (Zhou et al., 2004). On the other hand, phenolic antioxidants from food-grade plants would be considered for designing functional foods exploiting the concept of the alternative proline-linked pentose phosphate pathway in terms of: (1) screening high phenolic antioxidant producing food-grade clonal herbs, (2) using biological, biochemical and stress elicitation to stimulate high phenolic antioxidants in several sprout systems, (3) using food-grade fungal bioprocessing to generate consistent phenolic

antioxidants from botanical substrates, (4) environmental applications of plants producing strategies for generation of high phenolic clonal systems for phytoremediation of aromatic pollutants and (5) environmental applications in plants for better environmental adaptation of transplanted seedlings from tissue culture or greenhouse systems (Shetty, 2004).

Specific applications and case studies

Reviews in the category of specific applications and case studies are scarce. Condiments used in the processed foods industry, and derived from spices and herbs include EO and oleoresins around US commercial farming. The quality of extracts is firstly dependent upon the quality of the botanical source, and in this context, horticulturist have a prominent role in developing and testing improved strains of condimental herbs and spices (Todd, 1996). Plant secondary metabolites are a natural resource that is largely unexploited in 'conventional' animal production systems. A review of the use of plants and their extracts to manipulate the rumen microbial ecosystem to improve the efficiency of rumen metabolism in pasture systems is presented (Greathead, 2003).

Plant volatile oils are composed of a complex mixture of a range of low molecular compounds, predominantly terpenes and phenylpropanoids. Despite the lack of understanding of the mode of action, the greatest potential of plant volatile oils is in the food industry, especially as their flavors are generally acceptable. Application in other fields may be limited due to their physical properties and non-specific action. Oregano could acts as antioxidant dietary supplements during pregnancy of mammals with changes of fatty acid composition of different lipid fractions of the dams and their neonates of mammals (Dorman, 1999). The antifungal activity of the volatile oils tested showed results particularly significant, as effort to control of *Fusarium* fungal infections and prevent or eliminate the presence of its mycotoxins. Interesting results in this field are presented by food components contained in coffee, strawberries, tea, pepper, grapes, turmeric, fava tonka, garlic, cabbage, and onions (Galvano et al., 2001).

Publications on botanicals

It is understandable that a very strict demarcation in the categorization showed above is not possible since there may be certain overlaps in the publication analyzed. A Pareto diagram of the number of publications in different categories is given in Figure 3. All the publications in the categories described earlier have further been coded based on the chronological appearance of the article to see a retrospective of the development of research fields in botanicals. Coding had been done from 1980 onwards, since empirical concept of botanicals in the context of this review emerged during the 1980s. Also, the time interval for all categories was taken from 1981 to 2000 as five years. Publications after 2000 have been categorized on a time interval of two years. All the publications, based on this coding chronological pattern, are shown in Figure 4. All publications are available as an electronic publication (i.e. PDF version) or as photocopy of the original paper. A serial number by category could be seen in an annex of bibliographical list prepared in Endnote 8 software .

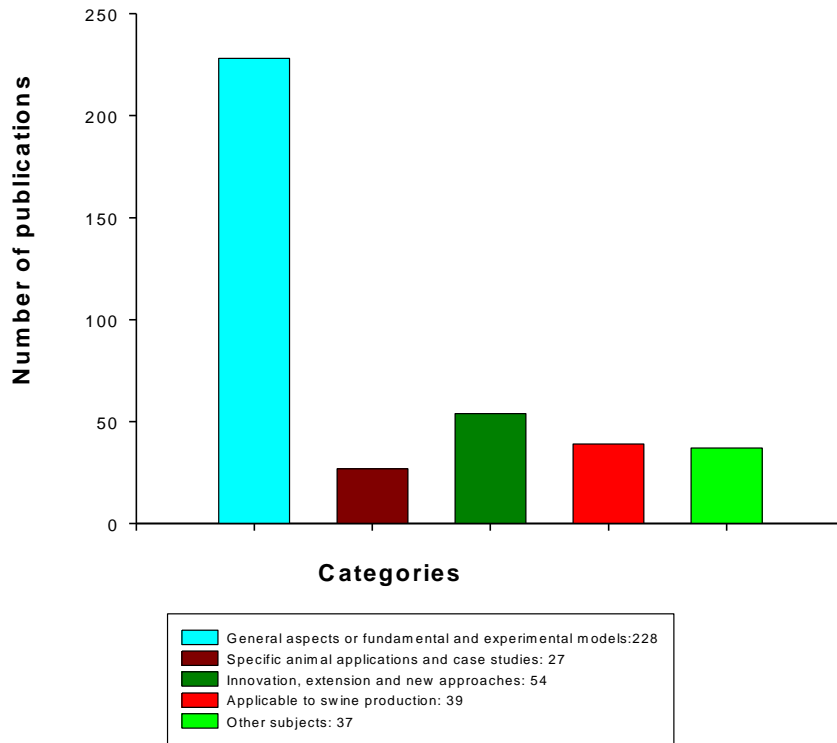


Figure 3. Pareto diagram showing the number of publications of botanicals.

Observations and comments

In this review, 445 publications in total were analyzed for the purpose of providing insights to the growth and development of botanicals around their functional properties. These publications include specific papers in national/international journals, conferences and the reviews. Other articles such as exclusive reports in newspapers and websites were presented as the authors feel that they deal with general information in a significant manner. Similarly books or chapter books written on botanicals are also included as reviews.

Further, 228 publications belong to general aspects or fundamentals and experimental models, 27 papers pertain to specific applications/case studies, 51 publications come under innovations/extensions/new approaches , 39 publications fall under the category of botanicals applicable to applicable to swine production and finally 37 publications concern other subjects. Figure 4, provides statistics of the mix of publications.

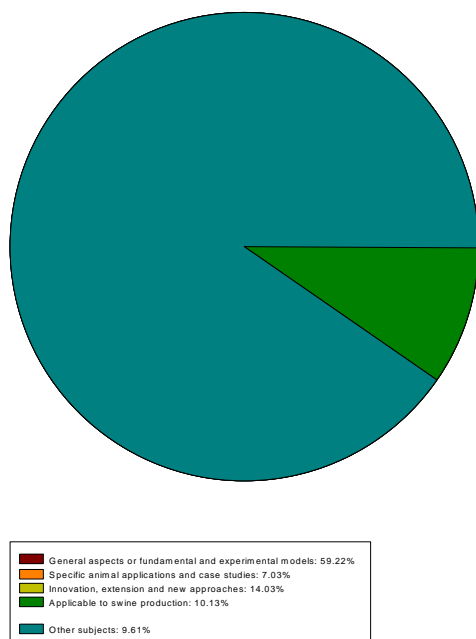


Figure 4. Mix of publications of botanicals.

As seen in Figure 4, more than a half of the publications speak about the general aspects or fundamentals and experimental models of botanicals. It is important to mention that the first article available in this review was published by (Martindale, 1910) in relation to the antiseptic properties of EO powders. Often it is also mentioned in literature cited that the antioxidant properties of natural spices were initially explored by (Chipault et al., 1952), (Chipault et al., 1956) Before 1980, literature was also devoted of antimicrobial activity of EO with 7 articles. The period 1981-1985 was characterized by using of experimental models of botanicals such as: rosemary, curcumin, artemisia and garlic. Antifungal and antiviral and anticancer properties of EO were explored during the period 1986-1990; as well as botanicals biodiversity in some countries. At this point is important to note, the paper written by (Erichsen-Brown, 1989) about medicinal and other North American Plants: a historical survey with special reference to the eastern Indian tribes. The period 1991-1995 was devoted to libiatae family and its EO in terms of several functional properties. From 1996 to 2000, this category was maximal in number of publications including 67 articles. It is relevant to mention that oregano and its EO carvacrol y thymol were analyzed in their functional properties. (Fetrow and Avila, 1999) published a professional handbook of complementary and alternative medicines and some papers (Chang, 2000; Craig, 1999; Daljit and Jasleen, 1999; Garcia et al., 2000; Shobana and Naidu, 2000) were critical in order to establish an integrative vision of botanicals.

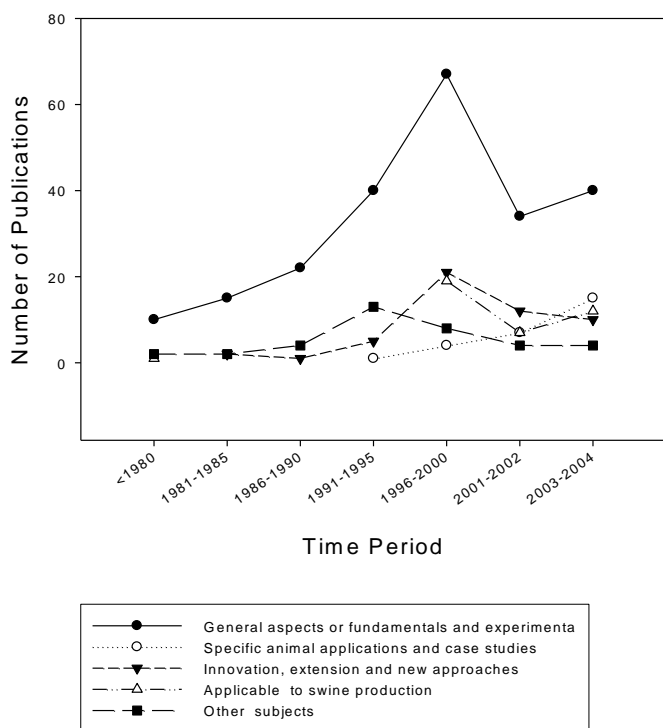


Figure 5. Graph showing chronological appearance of all publications of botanicals.

The periods 2001-2002 and 2003-2004 were devoted to EO compounds approaching different models being important to mention at general levels (Baudoux, 2002; Duke, 2002; Swanson, 2002; Yingming et al., 2004). There has been a decline in articles during these periods, but the chronological listing of publications number wise in the line graph in Figure 5 comprised two years instead of 4 years for previous periods.

In the sample of literature collected it is seen that there are 27 papers, specific to the category specific application/case studies in Animal Science. Regarding the first application that one done in antioxidant activity of oregano in mackerel oil as reported by (Tsimidou et al., 1995). There were 4 publications during 1996-2000 devoted to herb mixture and minerals and persistency of immunoglobulins in calves, preservation of sunflower oil, antimicrobial properties of oregano in beef meat and effects of dietary spices on pancreatic activity of rats. In the period 2001-2002, seven publications were generated in this category which were covered the role of oregano in lipid oxidation of poultry meat, anticoccidial effects of herbs against coccidia and environmental issue of cattle waste and plant-derived oils role. During the last two years (2003-2004), this category was maximal in the number of publications, 15. This suggests that the applications of botanicals have been increased in time. Antioxidant, antimicrobial and antiparasitic properties of EO, especially oregano have been applied successfully in poultry science (broilers and turkeys).

It can be seen in Figure 5 that under the category of innovations, extensions and new approaches, the number of publications increased from 8 before 1995 to 21 in 1996-2000. However, from 2001 onwards there appears to be a drop in the number of publications. This category includes patents registered in USA which was covered in the separate paper: a review of functional properties of botanicals extracts through innovation patents in the USA written by the authors. Here, the paper by (Kruger and Mann, 2002) is worth mentioning since the paper details safety evaluation of functional ingredients. Also, the paper by (Lambert et al., 2001) gives details about antimicrobial properties of

oregano EO, thymol and carvacrol. Modelling approach to measure the effectiveness of natural antimicrobials on *Salmonella enteritidis* was proposed by Greek researchers (Koutsoumanis et al., 1999; Koutsoumanis et al., 1998).

Among the 39 papers reviewed under the applicable to swine production category, unfortunately, it is worthwhile to mention that a lot of those were published in non-indexed journals. The first papers in this category were written by Polish research groups, which have been devoted to the use of herb mixtures in swine production (Grela, 1996; Grela et al., 1998; Kolacz et al., 1997; Soroka and Widenski, 1967). It is also worthwhile the coverage of papers generated by three research groups. First, Iowa State University group in USA, which research reports covered inclusion of botanicals (goldenseal, garlic, echinacea, peppermint) in swine diets (Holden (Holden and McKean, 2000a, 2000b, 2000c; Holden et al., 1999; Holden et al., 1998c; Holden et al., 1998b; Holden et al., 1998a; Holden et al., 1998d; Holden and McKean, 2000). The second one is USDA, meat research group devoted to the use of EO, carvacrol and thymol to reduce swine waste odor and pathogens (Varel, 2002; Varel and Miller, 2001b; Varel and Miller, 2001a) and the third one is Switzerland research which has been devoted to the use of oregano in sows and piglets, including its farm applications (Amrik and Bilkei, 2004; Kis and Bilkei, 2003; Kovac and Bilkei, 2003; Mauch and Bilkei, 2004; Park and Bilkei, 2004; Sads and Bilkei, 2003; Walter and Bilkei, 2004).

Finally, in the category other subjects, 37 papers have been reviewed. These papers deal with herbal medicine for periodontal diseases, phyto-estrogens as sources of modulation of oestrogen metabolism and hypoglycemic effect of EO extracts. Figure 5 shows the literature in this category in the order of time.

Critical view and conclusions

There is a proliferation of indexed and non-indexed literature on the topic of botanicals since ancient times, as revealed in this literature review. Considering the gamut of publications it can be said that thematic areas of botanicals are differential developments. In general botanicals could be seen in ascending growth and appears that in the near future to be heading towards exponential level. A scrutiny of the publications in the context of functional properties show that several aspects of fundamentals and experimental models exploring biodiversity with many interesting and diversified innovations and applications, have been covered in sufficient detail, especially in humans. These publications can serve a great deal towards quality improvement in weak areas such as Animal Science, particularly, swine production applications. Thus academicians, practitioners, researchers and farmers related to swine production have a good number of sources in the form of more than 450 articles, to study, discuss and debate over many aspects of botanicals in the perspective and prospective of strategic research needs and their innovations developments (processes and products) taking into account their functional properties.

The present review of literature on botanicals, carried out as a part of on-going research in their applications to swine production system, has identified certain issues which at the present have not been satisfactorily addressed or not been addressed at all. These issues can be regarded as inadequacies and they offer scope for further research and exploration in a research and transfer of technology plan. The issues identified are as follows:

- Botanicals research and transfer of technology planning are influenced by not only changes within internal but also by external operational environments. Therefore, applications and methods dealing with changes arising from the external environment would be applied in botanicals planning. SWOT the acronym standing for Strengths, Weaknesses, Opportunities

and Threats analysis is a commonly used tool for analyzing internal and external environments in order to attain a systematic approach and support for a decision situation. In this case, SWOT analysis can provide a good basis for successful strategies formulation in order to obtain an integrative approach of the use of botanicals in swine production systems. This method would be combined with the Analytic Hierarchy Process AHP, a mathematical method for analyzing complex decision problems with multiple criteria and synergism which it has been seen in this review characterized botanicals studies

- An integrative strategy to characterize biodiversity of botanicals; cost aspects of generate innovations of products require joint ventures between public and privates entities. The overall cost incurred in carrying out an integrative exercise is too expensive then exercises as realized in the past by Canadian Researchers in the case of canola is a good example in terms of cost of the models, cost of innovations and their property rights and trade offs.
- Human resources in a benchmarking approach applied to botanicals. Rationale behind formation of cross-functional benchmarking teams in relation with botanicals, identification of tasks of benchmarking teams in several components and strategies, and responsibility sharing among benchmarking teams would be considered in sufficient detail. The human role in this kind of approach needs to be clarified in complete depth to ensure better teamwork in a benchmarking plan related to the use of botanicals in swine production systems.

References

- Amagase, H., B. L. Petesch, H. Matsuura, S. Kasuga, and Y. Itakura. 2001. Intake of garlic and its bioactive components. *J Nutr* 131: 955S-962S.
- Amrik, B., and G. Bilkei. 2004. Influence of farm application of oregano on performances of sows. *Can Vet J* 45: 674-677.
- Arcila-Lozano, C. C., G. Loarca-Pina, S. Lecona-Urbe, and E. Gonzalez de Mejia. 2004. Oregano: Properties, composition and biological activity. *Arch Latinoam Nutr* 54: 100-111.
- Balentine, D. A., M. C. Albano, and M. G. Nair. 1999. Role of medicinal plants, herbs, and spices in protecting human health. *Nutr Rev* 57: S41-45.
- Banerjee, S. K., P. K. Mukherjee, and S. K. Maulik. 2003. Garlic as an antioxidant: The good, the bad and the ugly. *Phytother Res* 17: 97-106.
- Barnes, J. 2003a. Quality, efficacy and safety of complementary medicines: Fashions, facts and the future. Part i. Regulation and quality. *Brit J Clin Pharmacol* 55: 226-233.
- Barnes, J. 2003b. Quality, efficacy and safety of complementary medicines: Fashions, facts and the future. Part ii. Efficacy and safety. *Brit J Clin Pharmacol* 55: 331-340.
- Baudoux, D. 2002. Antiviral and antimicrobial properties of EO. *Positive Health. Complementary Medicine for the 21st Century*.
- Bauer, R., and H. Wagner. 1991. Echinacea species as potential immunostimulatory drugs. In: H. Wagner and N. R. Farnsworth (eds.) *Economic and medicinal plant research No. 5*. p 253-322. Academic Press Limited, London.
- Bensoussan, A., S. P. Myers, A. K. Drew, I. M. Whyte, and A. H. Dawson. 2002. Development of a chinese herbal medicine toxicology database. *Clin Toxicol* 40: 159-167.
- Bent, S., and R. Ko. 2004. Commonly used herbal medicines in the united states: A review. *Am J Med* 116: 478-485.
- Bergner, P. 1997. *Echinacea*. Prima Publishing.
- Bhattaram, V. A., U. Graefe, C. Kohlert, M. Veit, and H. Derendorf. 2002. Pharmacokinetics and bioavailability of herbal medicinal products. *Phytomedicine* 9: 1-33.
- Burt, S. 2004. EO: Their antibacterial properties and potential applications in foods: A review. *Int J Food Microbiol* 94: 223-253.
- Cavanagh, H. M. A., and J. N. Wilkinson. 2002. Biological activities of lavender essential oil. *Phytother Res* 16: 301-308.
- Chang, J. 2000. Medicinal herbs: Drugs or dietary supplements? *Biochem Pharm* 59: 211-219.
- Chen, Y. T., and Y. C. Ling. 2000. An overview of supercritical fluid extraction in chinese herbal medicine: From preparation to analysis. *J Food Drug Anal* 8: 235-247.
- Chipault, J. R., G. R. Mizuno, J. M. Hawkins, and W. O. Lundberg. 1952. The antioxidant properties of natural spices. *Food Res* 17: 46-55.

- Chipault, J. R., G. R. Mizuno, and W. O. Lundberg. 1956. The antioxidant properties of spices in foods. *Food Technol* 10: 209-211.
- Conner, D. E. 1993. Naturally occurring compounds. In: P. M. Davidson and A. L. Branen (eds.) *Antimicrobials in foods*. p 441-468. Marcel Dekker, Inc., New York.
- Craig, W. J. 1999. Health-promoting properties of common herbs. *Am J Clin Nutr* 70: 491S-499S.
- Daljit, S. A., and K. Jasleen. 1999. Antimicrobial activity of spices. *Int J Antimicrob Agents* 12: 257-262.
- Dorman, H. J. D. 1999. *Phytochemistry and bioactive properties of plant volatile oils: Antibacterial, antifungal and antioxidant activities*, University of Strathclyde, Glasgow.
- Duke, J. A. 2002. *Handbook of medicinal herbs*. 2nd ed. CRC Press, Boca Raton, FL.
- Erichsen-Brown, C. 1989. *Medicinal and other uses of north american plants: A historical survey with special reference to the eastern indian tribes*. Dover Publications, Inc., New York.
- Farnsworth, N. R., A. D. Kinghorn, D. D. Soejarto, and D. P. Waller. 1985. Siberian ginseng (*eleutherococcus senticosus*): Current status as an adaptogen. In: H. Wagner, H. Hikino and N. R. Farnsworth (eds.) *Economic and medicinal plant research No. 1*. Academic Press Limited, London.
- Fetrow, C. W., and J. R. Avila. 1999. *Professional hand book of complementary and alternative medicines*.
- Galvano, F., A. Piva, A. Ritieni, and G. Galvano. 2001. Dietary strategies to counteract the effects of mycotoxins: A review. *J Food Protect* 64: 120-131.
- Garcia, E., C. Cabrera, M. L. Lorenzo, and M. C. Lopez. 2000. Chromium levels in spices and aromatic herbs. *Sci Total Environ* 247: 51-56.
- Gould, G. W. 1996. Industry perspectives on the use of natural antimicrobials and inhibitors for food applications. *J Food Protect suppl. S*: 82-86.
- Greathead, H. 2003. Plants and plant extracts for improving animal productivity. *Proc Nutr Soc* 62: 279-290.
- Grela, E. R. 1996. Herbs additives in pig feeding. *Trzoda chlewns* 34: 23-25.
- Grela, E. R., R. Krusinski, and J. Matras. 1998. Efficacy of diets with antibiotic and herb mixture additives in feeding of growing-finishing pigs. *J Anim Feed Sci* 7: 171-175.
- Griffiths, G., L. Trueman, T. Crowther, B. Thomas, and B. Smith. 2002. Onions: A global benefit to health. *Phytother Res* 16: 603-615.
- Hobbs, C. 1995. *Echinacea*. Botanica Press.
- Holden, P. J., and J. McKean. 2000a. *Botanicals for pigs-echinacea ii*, ISU Swine Research Report, ASL-R647, Iowa State University, Ames, IA 50011.
- Holden, P. J., and J. McKean. 2000b. *Botanicals for pigs-garlic ii*, ISU Swine Research Report, ASL-R648, Iowa State University, Ames, IA 50011.
- Holden, P. J., and J. McKean. 2000c. *Botanicals for pigs-peppermint ii*, ISU Swine Research Report, ASL-R649, Iowa State University, Ames, IA 50011.
- Holden, P. J., J. McKean, and E. Franzenberg. 1999. Inclusion of botanicals in swine diets examined. *Feedstuffs*: 11-14.

- Holden, P. J., J. McKean, and E. Franzenburg. 1998a. Botanicals for pigs-goldenseal, ISU Swine Research Report, ASL-R1558, Iowa State University, Ames, IA 50011.
- Holden, P. J., J. McKean, and E. Franzenburg. 1998b. Botanicals for pigs-garlic, ISU Swine Research Report, ASL-R1559, Iowa State University, Ames, IA 50011.
- Holden, P. J., J. McKean, and E. Franzenburg. 1998c. Botanicals for pigs-echinacea, ISU Swine Research Report, ASL-R1560, Iowa State University, Ames, IA 50011.
- Holden, P. J., J. McKean, and E. Franzenburg. 1998d. Botanicals for pigs-peppermint, ISU Swine Research Report, ASL-R1561, Iowa State University, Ames, IA 50011.
- Holden, P. J., and J. D. McKean. 2000. Botanicals for pigs. In: Alternative and Herbal Livestock Health Conference, University of Connecticut. p 47-53.
- Huie, C. W. 2002. A review of modern sample-preparation techniques for the extraction and analysis of medicinal plants. *Anal Bioanal Chem* 373: 23-30.
- Iwu, M. M., A. R. Duncan, and C. O. Okunji. 1999. New antimicrobials of plant origin. In: J. Janick (ed.) Perspectives on new crops and new uses. p 457-462. ASHS Press, Alexandria, VA.
- Janssen, A. M., J. J. Scheffer, and A. B. Svendsen. 1987a. Antimicrobial activity of EO: A 1976-1986 literature review: Aspects of test methods. *Planta Med* 53: 395-398.
- Janssen, M. A., J. J. C. Scheffer, and A. B. Svendsen. 1987b. Antimicrobial activities of EO: A 1976-86 literature review on possible applications. *Pharm Weekbl Sci* 9: 193-197.
- Kabara, J. J. 1991. Phenols and chelators. In: N. J. a. G. Russell, G.W (ed.) Food preservatives. p 200-214. Blackie, London.
- Kalemba, D., and A. Kunicka. 2003. Antibacterial and antifungal properties of EO. *Curr Med Chem* 10: 813-829.
- Kis, R. K., and G. Bilkei. 2003. Effect of a phytogetic feed additive on weaning-to-estrus interval and farrowing rate in sows. *J Swine Health Prod* 11: 296-299.
- Kneifel, W., E. Czech, and B. Kopp. 2002. Microbial contamination of medicinal plants: A review. *Planta Med* 68: 5-15.
- Kolacz, R., E. Bodak, M. Switala, and P. Gajewczyk. 1997. Herb as agents affecting the immunological status and growth of piglets weaned with body weight deficiency. *J Anim Feed Sci* 6: 269-279.
- Koutsoumanis, K., K. Lambropoulou, and G. J. E. Nychas. 1999. A predictive model for the non-thermal inactivation of salmonella enteritidis in a food model system supplemented with a natural antimicrobial. *Int J Food Microbiol* 49: 63-74.
- Koutsoumanis, K., C. C. Tassou, P. S. Taoukis, and G.-J. E. Nychas. 1998. Modelling the effectiveness of a natural antimicrobial on salmonella enteritidis as a function of concentration, temperature and ph, using conductance measurements. *J Appl Microbiol* 84: 981-987.
- Kovac, B., and G. Bilkei. 2003. Oregano (*origanum vulgare*) dietary supplementation increases thereproductive performance of sows. *Folia Veterinaria* 47: 207-209.
- Kruger, C. L., and S. W. Mann. 2002. Safety evaluation of functional ingredients. *Food Chem Toxicol* No. 41. p 793-805.

- Lai, P. K., and J. Roy. 2004. Antimicrobial and chemopreventive properties of herbs and spices. *Curr Med Chem* 11: 1451-1460.
- Lambert, R. J., P. N. Skandamis, P. J. Coote, and G. J. Nychas. 2001. A study of the minimum inhibitory concentration and mode of action of oregano essential oil, thymol and carvacrol. *J Appl Microbiol* 91: 453-462.
- Lang, Q. Y., and C. M. Wai. 2001. Supercritical fluid extraction in herbal and natural product studies - a practical review. *Talanta* 53: 771-782.
- Lewinsohn, E. 1996. Molecular biology for the improvement of medicinal and aromatic plants. *Acta Hort. (ISHS)* 426: 443-467.
- Lis-Balchin, M. 1997. EO and 'aromatherapy': Their modern role in healing. *J R Soc Health* 117: 324-329.
- Magee, K., and C. Loiacono. 2004. A review of common herbs and potential interactions. *Int J Dent Hygiene* 2: 111-121.
- Marriott, P. J., R. Shellie, and C. Cornwell. 2001. Gas chromatographic technologies for the analysis of EO. *J Chromatogr A* 936: 1-22.
- Martindale, W. H. 1910. EO in relation to their antiseptic powers as determined by their carbolic coefficients. *Perfumery and EORecord* 1: 266-296.
- Mauch, C., and G. Bilkei. 2004. Strategic application of oregano feed supplements reduces sow mortality and improves reproductive performance--a case study. *J Vet Pharmacol Ther* 27: 61-63.
- Mowrey, D. B. 1990. Echinacea for the immune system. *Guaranteed potency herbs: Next generation herbal medicine*. p 45-62. Keats Publishing Inc, New Canaan, Connecticut.
- Murray, M. T. 1995. Garlic. In: M. T. Murray (ed.) *The healing power of herbs: The enlightened person's guide to the wonders of medicinal plants*. p 121-129. Prima Publishing, Rocklin, CA.
- Nakatani, N. 1997. Antioxidants from spices and herbs. In: F. Shahidi (ed.) *Natural antioxidants chemistry; health effects and applications*. p 64-75. AOCS Press, Champaign, IL.
- Nakatani, N. 2000. Phenolic anti-oxidants from herbs and spices. *Biofactors* 13: 141-146.
- Namiki, M. 1990. Antioxidants/antimutagens in food. *Crit Rev Food Sci Nutr* 29: 273-300.
- Nikaido, H., and M. Vaara. 1985. Molecular basis of bacterial outer membrane permeability. *Microbiol Rev* 49: 1-32.
- Nychas, G. J. E. 1995. Natural antimicrobials from plants. In: G. W. Gould (ed.) *New methods of food preservation*. p 58-89. Blackie Academic Professional, London.
- Offord, E. A., F. Guillot, R. Aeschbach, J. Loliger, and A. M. A. Pfeifer. 1997. Antioxidant and biological properties of rosemary components: Implications for food and health. In: F. Shahidi (ed.) *Natural antioxidants chemistry; health effects and applications*. p 88-96. AOCS Press, Champaign, IL.
- Park, B. M. K., and G. Bilkei. 2004. Immunostimulatory effect of dietary oregano etheric oils on growing pigs' lymphocytes. *Pig J* 53: 59-68.
- Platel, K., and K. Srinivasan. 2004. Digestive stimulant action of spices: A myth or reality? *Indian J Med Res* 119: 167-179.

- Rios, J. L., M. C. Recio, and A. Villar. 1988. Screening methods for natural products with antibacterial activity: A review of the literature. *J Ethnopharmacol* 23: 127-149.
- Russo, M., and G. C. Galletti. 1996. Medicinal properties and chemical composition of *vitex egnus-castus l.*: A review. *Acta Hort. (ISHS)* 426: 105-112.
- Sads, P. R., and G. Bilkei. 2003. The effect of oregano and vaccination against glasser's disease and pathogenic *escherichia coli* on postweaning performance of pigs. *Irish Vet J* 56: 611-615.
- Saller, R., F. Iten, and J. Reichling. 2001. Dyspepsia and phytotherapy - a review of traditional and modern herbal drugs. *Forsch Komp Klas Nat* 8: 263-273.
- Salzer, U. J. 1977. The analysis of EO and extracts (oleoresins) from seasonings--a critical review. *CRC Crit Rev Food Sci Nutr* 9: 345-373.
- Sangwan, N. S., A. H. A. Farooqi, F. Shabih, and R. S. Sangwan. 2001. Regulation of EOproduction in plants. *Plant Growth Regul* 34: 3-21.
- Sarris, J., and J. Flaherty. 2002. Reviews of articles on medicinal herbs. *Aust J Med Herbalism* 14: 1-4.
- Schilter, B. et al. 2003. Guidance for the safety assessment of botanicals and botanical preparations for use in food and food supplements. *Food Chem Toxicol* 41: 1625-1649.
- Shahidi, F. 1997. Natural antioxidants: An overview. In: F. Shahidi (ed.) *Natural antioxidants chemistry; health effects and applications*. p 1-24. AOCS Press, Champaign, IL.
- Shahidi, F. 2000. Antioxidant factors in plant foods and selected oilseeds. *Biofactors* 13: 179-185.
- Shetty, K. 2004. Role of proline-linked pentose phosphate pathway in biosynthesis of plant phenolics for functional food and environmental applications: A review. *Process Biochemistry* 39: 789-803.
- Shobana, S., and K. A. Naidu. 2000. Antioxidant activity of selected indian spices. *Prostaglandins Leukot Essent Fatty Acids* 62: 107-110.
- Soroka, T., and K. Widenski. 1967. Influence of the addition of some herb mixtures on weight gain, feed utilization and quality of butchery products in fattening of swine. *Annals UMCS, Sec. E. Agriculture* 22: 257-274.
- Stahl-Biskup, E. 1991. The chemical composition of thymus oils: A review of the literature1960-1989. *J Essent Oil Res* 3: 61-82.
- Subbulakshmi, G., and M. Naik. 2002. Nutritive value and technology of spices: Current status and future perspectives. *J Food Sci Tech Mys* 39: 319-344.
- Svoboda, K., P, and J. B. Hampson. 1999. Bioactivity of EO of selected temperate aromatic plants: Antibacterial, antioxidant, antiinflammatory and other related pharmacological activities. In: *Speciality Chemicals for the 21st Century. Intermediary products, cosmetics and perfumes, medicinal applications*. p 1-17.
- Swanson, C. A. 2002. Suggested guidelines for articles about botanical dietary supplements. *Am J Clin Nutr* 75: 8-10.
- Todd, P. H. 1996. Improving foods with herbs and spices extracts. *Acta Hort. (ISHS)* 426: 259-271.
- Tsai, T. H., C. Y. Hong, and C. F. Chen. 1997. Analysis of active ingredients in medicinal herbs with high-performance liquid chromatography and related technologies: A review. *J Food Drug Anal* 5: 303-317.

- Tsimidou, M., E. Papavergou, and D. Boskou. 1995. Evaluation of oregano antioxidant activity in mackerel oil. *Food Res Internat* 28: 431-433.
- Varel, V. H. 2002. Carvacrol and thymol reduce swine waste odor and pathogens: Stability of oils. *Curr Microbiol* 44: 38-43.
- Varel, V. H., and D. N. Miller. 2001a. Plant-derived oils reduce pathogens and gaseous emissions from stored cattle waste. *Appl Environ Microbiol* 67: 1366-1370.
- Varel, V. H., and D. N. Miller. 2001b. Effect of carvacrol and thymol on odor emissions from livestock wastes. *Water Sci Technol* 44: 143-148.
- Wagner, H., and A. Proksch. 1985. Immunostimulatory drugs of fungi and higher plants. In: H. Wagner, H. Hikino and N. R. Farnsworth (eds.) *Economic and medicinal plant research* No. 1. p 113-153. Academic Press Limited, London.
- Walter, B. M., and G. Bilkei. 2004. Immunostimulatory effect of dietary oregano etheric oils on lymphocytes from growth-retarded, low-weight growing-finishing pigs and productivity. *Tijdschr Diergeneeskd* 129: 178-181.
- Williamson, E. M. 2001. Synergy and other interactions in phytomedicines. *Phytomedicine* 8: 401-409.
- Xue, C. C. L., H. M. Hugell, C. G. Li, and D. F. Story. 2004. Efficacy, chemistry and pharmacology of chinese herbal medicine for allergic rhinitis. *Curr Med Chem* 11: 1403-1421.
- Yingming, P., L. Ying, W. Hengshan, and L. Min. 2004. Antioxidant activities of several chinese medicine herbs. *Food Chemistry* 88: 347-350.
- Zhou, S., H. L. Koh, Y. Gao, Z. Y. Gong, and E. J. Lee. 2004. Herbal bioactivation: The good, the bad and the ugly. *Life Sci* 74: 935-968.

Annex

Table 1. Chronologically outcome of earlier literature reviews on botanicals: General aspects or fundamentals and experimental models.

Attribute	Title	Outcome
1	The analysis of EO and extracts (oleoresins) from seasonings: A critical review	The most important of seasoning extracts are discussed and summarized together with the analytical criteria. Classification of individual seasonings is made on analytical chemistry and not on botanical, morphological or commercial aspects. The fatty acid composition of lipids in seasoning analyzed is also discussed.
2	Immunostimulatory Drugs of Fungi and Higher Plants	This review reveals that there is a multitude of nonmicrobial compounds with potential immunostimulating activity. As far as the class of low molecular weight compounds is concerned, no structure-activity relationships can be recognized at present. However, there appear to be suitable candidates for the development of useful immunostimulatory drugs in the class of high molecular weight compounds, especially polysaccharides of a particular structure type. A suitable immunostimulatory compound should be: 1) chemically defined, 2) easily degradable biologically, 3) non(cocarcinogenic or non-mutagenic, 4) neither too strong nor too weak in its stimulatory efficacy, and 5) nontoxic and without any side or cascade effects.
3	Molecular basis of bacterial outer membrane permeability	Bacterial outer membrane shows unusual functional properties, i.e., very low permeability toward lipophilic solutes and high permeability toward hydrophilic solutes. These functional attributes can be correlated well with the presence of unusual structural components and the precise molecular organization of these components. By using them, the gram-negative bacteria are able to produce a layer that acts as a very effective permeation barrier and at the same time still allows the efficient diffusion of nutrients. Our current understanding of the molecular organization and functions of bacterial outer membrane was made possible by the availability of mutants and of conditions, such as EDTA or polycation treatment, that alter outer membrane permeability. Yet the properties of some of the mutants, as well as the alterations of permeability under certain conditions, suggest that we do not yet have a complete picture of the outer membrane structure. It is hoped that further studies will lead us to a better understanding of this topic.
4	Siberian Ginseng (<i>Eleutherococcus senticosus</i>): Current status as an Adaptogen	The analysis of research in the area of adaptogens showed that it has only just begun. The extensive studies on ES species have contributed much to a beginning of an understanding of the adaptogenic response. Further studies centered around novel <i>in vivo</i> and <i>in vitro</i> systems to elucidate the adaptogenic mechanism should now evolve, so that more and better drugs will be developed to benefit mankind.
5	Antimicrobial Activity of EO: A 1976-1986 Literature Review: Aspects of Test Methods	The resources given in the literature with regard to testing the EO for antimicrobial activity are difficult to compare because the tests methods differ widely. These factors are influencing the results thus conclusions drawn in many papers are not based on reproducible experiments. Future studies should be mention the strain number of a test organism, EO composition and conditions which the oil will be obtained.
6	Antimicrobial activities of EO: a 1976-86 literature review on possible applications	From the large number of papers published in the time period analyzed (1976- 1986) so far it is clear that EO possess interesting antimicrobial properties which may be useful for practical purposes. Furthermore EO may play a role in some biological interactions. However, the test methods differ widely and are often inadequate. As a rule one can state that the more a test method resembles the practical situation, the more relevant the result will be. In future studies one should pay more attention to the possible use of EO as antimicrobial agents for specific purposes. Such an approach would eliminate many ambiguities that exist as to the antimicrobial properties of EO.
7	Screening methods for natural products with antibacterial activity: a review of the literature	Diffusion and dilution methods have been employed to study the antimicrobial activity of medicinal plants. Since some factors (culture medium composition, microorganisms tested, extractive method, pH, solubility of the sample in the culture medium, etc.) can change results, it is difficult using these methods to standardize a procedure for the study of antimicrobial plants. Bioautography is another method for studying antimicrobial activity. With it, previously chromatographed principles are diffused to the agar. The results can also change according to the method employed. All the various techniques are reviewed in this paper, in order to unify the different criteria and parameters, standard methods to study the antimicrobial activity of medicinal plants.
8	Antioxidants/antimutagens in food	The social need for safe and available food antioxidants continues to exist, despite technological advancement in food processing and distribution, especially in countries that depend heavily on fresh foods and in less-developed areas. The use of natural antioxidants in crude isolated form would be more desirable also for reasons of stability, ease of use, and cost. Also desirable from a practical point of view is the combined use of such isolates with known sage antioxidants, e.g., ascorbic acid and tocopherol.
9	Echinacea For the immune system	Summarizing the properties of Echinacea relative to the immune system, the following general statements pertain. On the most simple level, Echinacea prevents and cures various kinds of bacterial and viral infections. On a little more complex level, Echinacea activates macrophages (and perhaps, T-cells) that destroy cancerous cells and foreign intracellular invaders. Perhaps the most complicated mechanism under study are those involving the stimulation of infection and/or interferon-like activity. From the point of view of therapeutic research, there has not been a lot of clinical data generated on Echinacea during the era of modern medicine. The main reason for that has been the lack of a consensus relative to the total activity of the herb. In addition, considering the remarkable properties of Echinacea and its total lack of observed toxicity, the reluctance to proceed with clinical studies is, in this case, difficult to understand.
10	The Chemical Composition of Thymus Oils: A review of the literature 1960-1989	From 1960 to 1989 the EO of 84 thymus taxa from the total distribution area of the genus have been analyzed and the different countries and the number of species investigated are listed. The botanical nomenclature is taken from the original publications and complete when necessary using reputable taxonomic information. The main components of EO are listed in the order of their concentration in the oils to approximately describe the oil type of each taxon. Thymol and carvacrol are presented in each specific species due to their importance in terms of functional properties.
11	Phenols and chelators	The search for new chemicals which can aid in food preservation is hampered by several restrictions. First, the cost of developing a new chemical and getting it approved ranges from 100 to 200 million dollars (US); second, it may a great deal of time (10-12 years) and effort to get the product onto the market. Such obstacles make for new opportunities in seeking alternative routes for finding new foods preservatives. Whilst both antioxidants (BHA, BTH) and chelating (EDTA) substances have been used in foods for purpose other than antimicrobial affects, this review demonstrated that alone and in combination, they also have a useful future in helping to extend the self-life of foods.
12	Echinacea Species as Potential Immunostimulatory Drugs	This paper analyzed the literature of Echinacea species from 1985-1991 in the following aspects: its history, botany, chemical constituents, pharmacology (non-immunological and immunological properties) and therapeutic experience, studies on probands and patients in the USA and Germany. The review demonstrated the immunostimulatory activity of Echinacea extracts, and assigned the activity to certain groups of constituents. Moreover, the botanical identity of the plant materials could be determined unambiguously, and chemical standardization of Echinacea preparations, a requirement for clinical studies, can be achieved.
13	Naturally occurring compounds	The recent increased demand for minimally processed, extends shelf-life foods have renewed interest in exploitation of natural antimicrobials for food preservation uses. This review focuses primarily on those extracts that are reported to have a greatest antimicrobial activity. The discussion covers the antimicrobial activity and modes of actions of natural antimicrobials in foods based on their primary sources.
14	Natural antimicrobials from plants	Plants are poorly exploited sources of alternative antimicrobials agents whose structures and modes of action may well differ from those derived from the better known source. Therefore, as the food industry searches for naturally occurring antimicrobial compounds, further investigations into the effect of phenolic compounds such as oleuropein should be carried out; as well as the existence naturally of other phenolics compounds in various food system. The expanded oil/water interface which exerts a marked influence on the distribution of long-chain free fatty acids and phenolics between the aqueous and oil phases accelerated the rate of death of Salmonella. In addition, pharmaceutical workers considered the possible medical use of phenolics due to the increasing problems posed by bacterial resistance to current antibiotics.

Table 1. Chronologically outcome of earlier literature reviews on botanicals: General aspects or fundamentals and experimental models. Cont...

Attribute	Title	Outcome
15	Garlic	A general description of garlic, its chemical composition, its history and folk use; its pharmacology: Antimicrobial, antibacterial, and antifungal activity, anthelmintic, antiviral, immune enhancing and anticancer effects; clinical applications: high cholesterol level, blood pressure-lowering activity, platelet aggregation inhibition, fibrinolytic activity, prevention of low-density lipoprotein oxidation; dosage and toxicity are addressed in this review.
16	Echinacea: The Immune Herb	This booklet gives practical information about how to use Echinacea for everyday health problems. Echinacea has been categorized by Native American Indians, German's medical doctors and American herbalists as a selective herb to prevent and help heal colds, flu, respiratory ailments and urinary tract infections, mainly.
17	Medicinal properties and chemical composition of Vitex Egnus-Castus L.: A review	The chemical compositions of the EO and of other chemical classes present in the leaves, fruits and wood of Vitex agnus-castus are summarized. In addition, botanical, and aphrodisiac, medicinal, and therapeutic properties, and pharmacological applications are addressed.
18	Natural antioxidants: An overview	Antioxidants are substances that when present in foods or in the body at low concentrations compared with that of an oxidizable substrate markedly delay or prevent the oxidation of that substrate. Antioxidants are known to act at different levels in the oxidative sequence involving lipid molecules. Natural antioxidants from dietary sources include phenolic and polyphenolic compounds, chelators, antioxidant vitamins and enzymes, as well as carotenoids and carnosine. The process of autoxidation and development of rancidity in foods involves free radical chain mechanism proceeding via initiation, propagation and termination steps. Lipid peroxidation is a problem not only in the edible oil and the food industry, but also in the human body.
19	Antioxidant and biological properties of Rosemary components: Implications for food and health	Results analyzed in this review suggest that phenolic antioxidants, such as those found in rosemary, may have a further application in the food industry besides those of traditional flavoring and stabilizing agents because their chemopreventive properties may lead to beneficial effects on human health.
20	Antioxidants from spices and herbs	Many new antioxidants have been isolated from natural sources and their structures determined. Spices and herbs, among foods eaten daily, are one of the most promising sources, which area reviewed in this paper. Results obtained from biochemical studies on antioxidants in edible plants may lead to chemoprevention of lipid peroxidation, inflammation, cancer and aging in human organs.
21	Echinacea	Scientists agree that certain constituents in all three of the major commercial species of Echinacea have some level of immune-system-stimulating properties, but only a handful of human clinical trials using real-life situations have been undertaken until 1997. Therefore, it was very little information from scientific trials about how to use Echinacea, what species or plant parts are most effective and what form or forms are most useful.
22	Bioactivity of EO of selected temperate aromatic plants: antibacterial, antioxidant, antiinflammatory and other related pharmacological activities	The main plant species and microorganisms investigated are covered in comprehensive tables and references. The brine shrimp bioassay used for the oil toxicity testing is described in detail. The complexity of the final product in terms of pharmaceutical applications through synthetic or semi-synthetic compounds is shown. Research headlights in the discovery of active chemical structures from which they can develop and prepare synthetic analogues are analyzed. The review shows how individual components of EO are at present under specific investigation to elucidate their particular activity and the necessities for more controllable issues from the point of reproducibility, patentability, safety, and are more economically viable applications.
23	New Antimicrobials of Plant Origin	Plants have forever been a catalyst for human healing. In order to halt the trend of increased emerging and resistant infectious disease, it will require a multi-pronged approach that includes the development of new drugs. Using plants as the inspiration for new drugs provides an infusion of novel compounds or substances for healing disease. The authors showed how evaluating plants from the traditional African system of medicine provides us with clues as to how these plants can be used in the treatment of disease. Many of these plants show very promising activity in the area of antimicrobial agents, warranting further investigation.
24	Role of medicinal plants, herbs, and spices in protecting human health	The body of knowledge about plants, herbs, and spices and their respective and collective roles in promoting human health has been modest. Flavonoids in tea and anthocyanins in tart cherries were presented as examples of how to move forward in understanding active compounds. Dietary compounds, their roles in maintaining human health, and their interactions with established nutrients were determined to be short-term research priorities.
25	Antioxidant factors in plant foods and selected oilseeds	Over production of active oxygen radicals in human body causes oxygen stress in DNA and cell membrane, and consequently induces toxic effects and diseases. Self defense system against these oxidative damages is supported by antioxidants such as α -tocopherol and ascorbic acid. It is well known that catechins, antioxidant from green tea, have a wide range of biological activities that contribute to chemopreventive effects on tumor initiation and promotion. Many new antioxidants have been isolated and determined from herbs and spices. The daily intake of these foods might be one of the most promising sources against major disease leading to a healthier life. It is strongly expected that biochemical results on antioxidants in edible plants may lead to hemoprevention of lipid peroxidation, inflammation, cancer and aging in human organs.
26	Phenolic anti-oxidants from herbs and spices	Oilseeds contain a variety of phenolic compounds with varying antioxidant activity. The type of antioxidant present in each seed is different. The antioxidative effect of source materials, their extracts or fractions thereof, depended on the seed type, the content and chemical nature of their active components as nutraceuticals and functional food ingredients. However, these antioxidative compounds may be present in a cocktail or soup which includes their precursors as well as their reaction products. The protective effect of oilseed phenolics may justify the use of the seeds or their defatted meals as a source of protein as it has become the case for soybean. Thus, absorption, metabolism and beneficial health effects of oilseeds warrant further investigation.
27	Synergy and other interactions in phytochemicals	The concept of synergy is developed. In this context, a plant extract is more than the sum of its parts, which substantiate the perception that natural medicines have something special to offer, at least a scientifically based explanation for the clinical equivalence of many plants extracts with synthetic drugs at the same therapeutic indications. The review shows that it is an opportunity through further testing to prove that it is a true phenomenon
28	Regulation of EOproduction in plants	This review provides a summary of the physiological dynamics and regulation of EOproduction, from the literature and available information on diverse volatile oil crops. EOproduction is highly integrated with the physiology of the whole plant and so depends on the metabolic state and preset developmental differentiation programme of the synthesising tissue. However, EOproductivity is ecophysiological and environmentally friendly. These and other aspects of the modulation of EOproduction are presented, along with a brief outline of the current concept of their relevant biosynthetic mechanisms.
29	Dyspepsia and phytotherapy: A review of traditional and modern herbal drugs	The therapy of functional gastrointestinal disorders is one of the domains of phytotherapeutic treatments reviewed. Although, the mechanisms of action of the bitters are not completely understood, they sensorially stimulate at even very small concentrations sensorially the secretion of the stomach as well as the digestive glands and strengthen the smooth musculature of the digestive tract ,leading to a general tonification. At higher dosages bitters probably directly affect the mucous membranes of the stomach and the bowel. Bitters often are combined with EO (some volatile oils as aromatic bitters, drug combinations of a volatile oil with a bitter). EO act primarily as spasmolytics, carminatives and local anesthetics. Important traditional medical systems like the Traditional Chinese Medicine, the Ayurvedic Medicine as well as the European 'Humoral Medicine' consider different aspects of the sick human being, like the constitution of the patient (holistic approach), and take qualities of herbal drugs, vegetarian food, and spices into account for therapeutic purposes.

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Attribute	Title	Outcome
30	Intake of garlic and its bioactive components	Garlic has many health benefits and has been traditionally used worldwide over the centuries. Garlic and garlic supplements are consumed in many cultures for their hypolipidemic, antiplatelet and procirculatory effects. In addition to these proclaimed beneficial effects, some garlic preparations also appear to possess hepatoprotective, immune-enhancing, anticancer and chemopreventive activities. Some preparations appear to be antioxidative, whereas others may stimulate oxidation. These additional biological effects attributed may be due to compounds, such as S-allylcysteine, S-allylmercaptocysteine, Na-fructosyl arginine and others, formed during the extraction process. However, the chemistry of garlic is complicated and the quality of garlic products is dependent on the manufacturing process and although allicin has been thought to be an active component of garlic, allicin does not account for the proposed health benefits of garlic. On the other hand, inconsistency in the efficacy of garlic supplements may be due to the incorrect standardization and the overlooking of other truly active compounds.
31	Nutritive value and technology of spices: Current status and future perspectives	This review describes the nutritive value of major spices from India, their role in health and disease, shelf, life of spices, microbiological safety of spices, quality control of spices and future perspectives. Although India asserted to be the oldest and largest producer of spices, its approach towards diversification has been very traditional. In fact, newer and better techniques in processing of spices right from farm to market are imperative for noteworthy substance in the international spice market.
32	Reviews of articles on medicinal herbs	Although synergy can be ascertained via a precise mathematical formula in this review, it is difficult to test consistently with plant medicines as the individual constituent levels vary. The isobole method is the method of choice to identify synergy; the method is independent of the mechanism of action and applies under most conditions. Synergy is defined as occurring when the effect of the combination of medicines is greater than the sum of its cumulative individual action. Its activity can be quantified as less of the substance can be administered to achieve the same effect. One of the fundamental contrasts between phytotherapy and modern pharmacy is that allopathic medicine is based on the 'single bullet' theory in which the drug usually aims to interact directly and precisely with a specific enzyme in order to bring about a specific physiological alteration. Phytomedicine conversely, works on so many physiological systems that it is impossible to fully quantify the plethora of interactions via a single herb, let alone a combination of six or seven compounds.
33	Onions: A global benefit to health	World onion production has increased by at least 25% over the past 10 years with current production being around 44 million tones making it, the second most important horticultural crop after tomatoes. Because of their storage characteristics and durability for shipping, onions have always been traded more widely than most vegetables. Onions are rich in two chemical groups that have perceived benefits to human health. These are the flavonoids and the alk(en)yl cysteine sulphoxides (ACSOs). Compounds from onion are reported to have a range of health benefits which include anticarcinogenic properties, antiplatelet activity, antithrombotic activity, and antiasthmatic and antibiotic effects.
34	Biological activities of lavender essential oil	A current state of knowledge about the effect of lavender oils on psychological and physiological parameters and its use as an antimicrobial agent are showed in detail. Although the data are still inconclusive and often controversial, there does seem to be both scientific and clinical data that support the traditional uses of lavender.
35	Pharmacokinetics and bioavailability of herbal medicinal products	The review showed that assessment of bioavailability, determination of pharmacokinetic characteristics and use of pharmacokinetic/pharmacodynamic modeling can aid in more rational use of HMPs. In this sense, much more work is needed to characterize the bioavailability and pharmacokinetics of herbal products in order to fully take advantage of their therapeutic potential.
36	Development of a Chinese herbal medicine toxicology database	Good quality studies on the toxicity of Chinese herbs are lacking. In some cases there is insufficient scientific evidence to create an evidence-based grading of the toxicity of individual herbs. Available data have been summarized in this review into detailed monographs. Twelve herb monographs (with a full toxicity profile and grading) have been completed and summary data for all adequate quality papers used in the grading are linked to the monographs. The resultant database and monographs represent the first reviews specifically on the toxicity of individual Chinese herbs with toxicological grades based on the evidence of published studies. The database and monographs should assist in promoting the safe and effective use of Chinese herbal medicine.
37	Guidance for the safety assessment of botanicals and botanical preparations for use in food and food supplements	The present paper discusses the data required to determine the safe use of botanicals and botanical preparations, and provides advice on the development of risk assessment strategies consistent with due diligence under existing food regulations. Product specifications, composition and characterisation of standardised and authentic materials, documented history of use and comparison to existing products (taking into account the effect of industrial processing), description of the intended use and consequent exposure are highlighted as key background information on which to base a risk evaluation. The extent of experimental investigation required, such as in vitro, animal, and/or human studies, depends on the adequacy of this information. A decision tree is presented as an aid to determine the extent of data requirements based on product comparison. This guidance document was elaborated by an expert group of the Natural Toxin Task Force of the European Branch of the International Life Sciences Institute—ILSI Europe and discussed with a wider audience of scientists at a workshop held on 13–15 May 2002 in Marseille, France.
38	Antibacterial and Antifungal Properties of EO	In recent years there has been an increasing interest in the use of natural substances, and some questions concerning the safety of synthetic compounds have encouraged more detailed studies of plant resources. This paper reviews the classical methods commonly used for the evaluation of EO antibacterial and antifungal activities. The agar diffusion method and the dilution method as well as turbidimetric and impedimetric monitoring of microorganism growth in the presence of tested EO are described. Factors influencing the in vitro antimicrobial activity of EO and the mechanisms of EO action on microorganisms are reported. This paper gives an overview on the susceptibility of human and food-borne bacteria and fungi towards different EO and their constituents. EO of spices and herbs (thyme, organum, mint, cinnamon, salvia and clove) were found to possess the strongest antimicrobial properties among many tested.
39	Quality, efficacy and safety of complementary medicines: fashions, facts and the future. Part I. Regulation and quality	This paper extends the use of complementary medicines, and issues related to the regulation and pharmaceutical quality of these products. The term complementary medicines describes a range of pharmaceutical-type preparations, including herbal medicines, homeopathic remedies, EO and dietary supplements, which mainly sit outside conventional medicine. The regulatory framework for herbal medicines and dietary supplements is scope of this review. A new system for registration of traditional herbal medicines would ensure that marketed products meet standards for quality and safety. At present, the pharmaceutical quality of many complementary medicines is a cause for concern.
40	Quality, efficacy and safety of complementary medicines: fashions, facts and the future. Part II. Efficacy and safety	Complementary medicines is a popular healthcare approach in the UK, and there are signs that the use of such products is continuing to increase. There is a growing body of evidence from randomized controlled trials and systematic reviews to support the efficacy of certain herbal extracts and dietary supplements in particular conditions. However, many other preparations remain untested. Strictly speaking, evidence of efficacy (and safety) for herbal medicines should be considered to be extract specific. Pharmacovigilance for complementary medicines is in its infancy. Data are lacking in several areas relevant to safety. Standard pharmacovigilance tools have additional limitations when applied to investigating safety concerns with complementary medicines.
41	Garlic as an antioxidant: the good, the bad and the ugly	Garlic has played an important dietary and medicinal role throughout the history of mankind. In some Western countries, the sale of garlic preparations ranks with those of leading prescription drugs. The therapeutic efficacy of garlic encompasses a wide variety of ailments, including cardiovascular, cancer, hepatic and microbial infections to name but a few. However, the elucidation of its mechanism for therapeutic action has proved to be more elusive and a unifying theory, which could account for its reported multifarious activities, is yet to emerge. Reactive oxygen species (ROS) seem to be at the core of many disease processes and it is an attractive and convenient hypothesis that garlic might exert its activities through modulatory effects on ROS. A literature search on garlic and its antioxidant potential churned up a surprisingly large amount of data, some of it good, some bad and some of it definitely ugly. Various preparations of garlic, mainly aged garlic extract (AGE), have been shown to have promising antioxidant potential.

Table 1. Chronologically outcome of earlier literature reviews on botanicals: General aspects or fundamentals and experimental models. Cont...

Attribute	Title	Outcome
42	Efficacy, chemistry and pharmacology of Chinese herbal medicine for allergic rhinitis	An extensive literature search identified 6 randomized controlled clinical trials in which the efficiency of Chinese herbal medicine had been investigated for the treatment of allergic rhinitis. Although 4 of these trials had methodological flaws, the therapeutic outcomes out come of all 6 have been reviewed. One of 2 trials considered to be of high quality was concerned with the treatment of seasonal allergic rhinitis and the other with perennial allergic rhinitis. It is considered that all 6 studies demonstrated various degrees of alleviation of the symptoms of allergic rhinitis. No serious side effects were reported in any of the trials. A number of the herbs in Chinese herbal formulae used in the trial, and/or their constituent compounds have been reported to possess anti-allergic, anti-inflammatory or immune modulation activity.
43	Digestive stimulant action of spices : A myth or reality?	Based on the evidences from animal studies, the well recognized digestive stimulant action of spices may be considered to be mediated through two possible modes (i) stimulation of the liver to secrete more bile enriched in bile acids, and (ii) stimulation of enzyme activities that participate in digestion, both of pancreatic and intestinal origin. Such stimulation of bile secretion and of the activities of digestive enzymes leads to an accelerated overall digestive process, resulting in a significant reduction in the duration of passage of food through the gastrointestinal tract. The animal studies on the influence of spices on bile secretion and digestive enzymes have employed spice concentrations roughly 5-times the average levels found normally in Indian diets. The age-old empirical dictum that 'Spices are digestive stimulants' stands today verified by experimental evidences at least in laboratory animals, and is exerted by stimulating bile secretion and activities of digestive enzymes.
44	A review of common herbs and potential interactions	The increasing utilization of herbal therapy world-wide has augmented the concern that such treatment may possibly expose the patient to unknown dangers. Therefore, it is significant that dental professionals, for example become knowledgeable about the common herbs that patients may be using. Interaction of these herbs with biomedical medications and the impact that herbal therapy can have on a person's systemic and oral health is mandatory
45	Antimicrobial and chemopreventive properties of herbs and spices	A growing body of research has demonstrated that the commonly used herbs and spices such as garlic, black cumin, cloves, cinnamon, thyme, allspices, bay leaves, mustard, and rosemary, possess antimicrobial properties that, in some cases, can be used therapeutically. Other spices, such as saffron, a food colorant; turmeric, a yellow colored spice; tea, either green or black, and flaxseed do contain potent phytochemicals, including carotenoids, curcumins, catechins, lignan respectively, which provide significant protection against cancer. The area of natural medicines is vast, and sometimes it is very difficult to look for authentic information. A reference database on natural medicines is now available, then it is a useful resource that will aid the development of modern medicines from natural sources as herbs and spices.
46	EO: their antibacterial properties and potential applications in foods: A review	In vitro studies have demonstrated antibacterial activity of EO (EOs) against <i>Listeria monocytogenes</i> , <i>Salmonella typhimurium</i> , <i>Escherichia coli</i> O157:H7, <i>Shigella dysenteriae</i> , <i>Bacillus cereus</i> and <i>Staphylococcus aureus</i> . A number of EO components has been identified as effective antibacterials, e.g. carvacrol, thymol, eugenol, perillaldehyde, cinnamaldehyde and cinnamic acid, having minimum inhibitory concentrations but a higher concentration is needed to achieve the same effect in foods. EOs comprise a large number of components and it is likely that their mode of action involves several targets in the bacterial cell. The hydrophobicity of EOs enables them to partition in the lipids of the cell membrane and mitochondria, rendering them permeable and leading to leakage of cell contents. Physical conditions that improve the action of EOs are low pH, low temperature and low oxygen levels. Synergism has been observed between carvacrol and its precursor p-cymene and between cinnamaldehyde and eugenol. Some EO components are legally registered flavourings in the EU and the USA.
47	Commonly used herbal medicines in the United States: A review	Herbal medicines are widely used in the United States, with approximately one quarter of adults reporting use of an herb to treat a medical illness within the past year. Herbs contain complicated mixtures of organic chemicals, the levels of which may vary substantially depending upon many factors related to the growth, production, and processing of the herbal product. Of the ten most commonly used herbs in the United States, systematic reviews have concluded that only four are likely to be effective, and there is very limited evidence to evaluate the efficacy of the approximately 20,000 other available herbal products. To improve the safety and consistency of herbs, additional research is needed to define the pharmacology, stability, and bioavailability of these products. The authors also agree with the newly announced research priorities of the National Center for Complementary and Alternative Medicine, which have placed an increased emphasis on studies of the mechanism of action of herbs and other complementary and alternative therapies. These studies will provide new information about active ingredients, pharmacology, stability, and the bioavailability of herbs.
48	Oregano: Properties, composition and biological activity	This paper critically showed that oregano has a good antioxidant capacity and also presents antimicrobial activity against pathogenic microorganisms like <i>Salmonella typhimurium</i> , <i>Escherichia coli</i> , <i>Staphylococcus aureus</i> , <i>Staphylococcus epidermidis</i> , among others. These are all characteristics of interest for the food industry because they may enhance the safety and stability of foods. It also analyzed some reports regarding the antimutagenic and anticarcinogenic effect of oregano; representing an alternative for the potential treatment and/or prevention of certain chronic ailments, like cancer.

Table 2. Chronologically outcome of earlier literature reviews on botanicals: Innovation, extension and new approaches.

Attribute	Title	Outcome
1	Molecular biology for the improvement of medicinal and aromatic plants	Economic potential of metabolic engineering for the generation of novel aromatic and medicinal crops is enormous, but there are many obstacles that need to be addressed before the full potential of these novel technologies can be implemented. Most of the obstacles are related to research aimed at solving specific problems such as: a better understanding of the biosynthetic pathways involved in the information of the target compounds, choosing the gene or set of genes that will have the desired effects on the target plant metabolism, with minimal effect on other metabolic processes, being biochemical knowledge of the biosynthetic pathways crucial for the identification of target genes. Many legal issues concerning the regulation and marketing of genetically engineered plants and plant products need to be also addressed, and ultimately, public acceptance of transgenic products as foods, fragrances and industrial materials will determine their availability.
2	Industry perspectives on the use of natural antimicrobials and inhibitors for food applications	An enormous number of very effective antimicrobial systems are analyzed from the perspective of the food industry. The absence of strong commercial and marketing incentives to develop their use has been changed in recent years, in response to consumers changing needs. Natural systems need to be effective and save and fulfills a real technological requirements then potential application should be explored whatever its origin just like any other technique. Natural systems will be additive or synergistic with other factors and techniques in the future, particularly if more studies are undertaken in real foodstuffs as well as in laboratory media.
3	Analysis of active ingredients in medicinal herbs with high-performance liquid chromatography and related technologies: A review	HPLC coupled with various column and detection systems are analyzed in terms of techniques for the qualitative and/or quantitative evaluation of medicinal herbs. To complement gas chromatography and liquid chromatography, capillary electrophoresis is also evaluated.
4	EO and 'aromatherapy': their modern role in healing	Aromatherapy is one of the most actively growing forms of alternative medicine in Great British, especially in nursing, and yet has had very little scientific evaluation. Studies using case notes of clients will be helping in assessing the efficacy of using of certain EO for different clinical conditions. Aromatherapy is against scientific influence as it wants to retain the mystical element of the process. However, in practice the attributes of certain individuals EO can be applied successfully and researched further.
5	An overview of supercritical fluid extraction in Chinese herbal medicine: From preparation to analysis	This review was concerning the use of supercritical fluid extraction (SFE) in the preparation and analysis of Chinese herbal medicine (CHM). The literature review foresees the trend of increasing use of SFE in CHM preparation. The application examples in the preparation of useful ingredients and analysis of pesticide residues are discussed. The use of SFE CO ₂ to replace traditional organic solvent is justified and promising. Consideration is given to the coupling of sub-critical H ₂ O and supercritical CO ₂ to extract more compounds and to use the dual role of extracting useful ingredients and removing pesticide residues. Careful integration of laboratory SFE results into the design and implementation of factory production is beneficial in ensuring the successful use of SFE in CHM.
6	Gas chromatographic technologies for the analysis of EO	This present review outlines the developmental nature of instrumental approaches to EOanalysis, using gas chromatography. Mass spectrometry was included to the extent that it represents the hyphenation of choice for most analysts when analyzing EO. Thus single-column and multidimensional analysis were covered, also sample handling or introduction techniques prior to the analysis step, where these techniques provide some measure of separation. The recent demonstration of comprehensive gas chromatography was discussed as the potentially most powerful separation method for EO. This is a comprehensive dissertation on the field of EOanalysis but it would require sufficient space to occupy a book in its own right. Rather, this review will outline selected considerations and developments, to help explain where new technology has been applied to advantage in the field of analysis of EO.
7	Supercritical fluid extraction in herbal and natural product studies: A practical review	This review article presents the practical aspects of SFE such as modifiers, sample preparation, special considerations for collection, modeling, and as well as recent developments in Supercritical Fluid Extraction (SFE) technology for the extraction and separation of active compounds from herbs and other plants. Rapid developments in SFE techniques for herbal and natural product studies are anticipated in the future. This review may provide a convenient basis for the general readers who are interested in understanding and involving in this new research area, taking into account that SFE may become a standard extraction technique for studying herbal, food and agricultural samples.
8	Microbial contamination of medicinal plants: A review	Medicinal plants may be associated with a broad variety of microbial contaminants, which are represented by bacteria, fungi and viruses. Inevitably, this microbiological background depends on several environmental factors and exerts an important impact on the overall quality of herbal products and preparations. Risk assessment of the microbial load of medicinal plants has, therefore become an important subject in the establishment of modern Hazard Analysis and Critical Control Point (HACCP) schemes. This study intends to contribute to this knowledge by giving survey of published data regarding the microbial contamination of herbal plants, by dealing with methodological aspects and by considering the influence of different commonly used pharmaceutical preparation techniques on the microbiological status of the products. Finally, quality standards are discussed, which could be considered for guidelines and/or possible inclusion in the European Pharmacopoeia in a constructive way.
9	A review of modern sample-preparation techniques for the extraction and analysis of medicinal plants	Among the modern sampling techniques described in this review, Supercritical Fluid Extraction (SFE) seems to offer unique advantages in the extraction of medicinal plants– high selectivity, minimum degradation of thermally labile analytes, and elimination of the use of hazardous organic solvents (e.g. use of pure CO ₂ as the extractant). The main drawbacks of SFE, on the other hand, such as difficulties in extracting polar compounds and high susceptibility to matrix effects, are problematic in the extraction of herbal materials. As plant matrices are highly complex, factors such as the water content and particle size of the matrix and strong analyte-matrix interactions, etc., can severely limit the capacity of SFE to effect high extraction efficiency and rapid kinetics, especially for polar analytes. The basic principles of microwave-assisted extraction (MAE) and pressurized liquid extraction (PLE) are very similar to those of classic extraction techniques.
10	Herbal bioactivation: the good, the bad and the ugly	Bioactivation of herbal constituents appears a critical step for the toxicity induction of some herbs. The resultant reactive intermediates bind covalently to DNA and proteins, leading to organ toxicity and even carcinogenicity. On the other hand, some herbal/dietary constituents were shown to form reactive intermediates capable of irreversibly inhibiting various cytochrome P450 products(CYPs). The resultant metabolites lead to CYP inactivation by chemical modification of the heme, the apoprotein, or both as a result of covalent binding of modified heme to the apoprotein. The mechanism-based inhibition of CYPs may provide an explanation for some reported herb-drug interactions. Naturally occurring compounds that inactivate CYPs may represent a novel type of chemopreventive agents with higher selectivity and lower toxicity compared to synthetic compounds. Herbal medicines often contain multiple active substances and multiple cellular molecules might be the targets of herbal medicine. The identification of these targets may provide molecular evidence for the herb's pharmacological activity and toxicity.
11	Role of proline-linked pentose phosphate pathway in biosynthesis of plant phenolics for functional food and environmental applications: a review	The empirical insights into the alternative pathway to consistent phenolic antioxidants from food-grade plants for design of functional foods has already been exploited for many applications in many plant species for: (1) screening high phenolic antioxidant producing food-grade clonal herbs, (2) using biological, biochemical and stress elicitation to stimulate high phenolic antioxidants in several sprout systems, (3) using food-grade fungal bioprocessing to generate consistent phenolic antioxidants from botanical substrates, (4) environmental applications of plants producing strategies for generation of high phenolic clonal systems for phytoremediation of aromatic pollutants and (5) environmental applications in plants using proline-linked pentose phosphate pathway for better environmental adaptation of transplanted seedlings from tissue culture or greenhouse systems. The further evolution of this concept of the alternative proline-linked pentose phosphate pathway and its implications are shown in this review.

Table 3. Chronologically outcome of earlier literature reviews on botanicals: Specific application and case studies.

Attribute	Title	Outcome
1	Improving foods with herbs and spices extracts	Condiments used in the processed foods industry, and derived from spices and herbs include EO and oleoresins around US commercial farming. Some of these are produced in a large scale and employs capital intensive methods of bringing crops to the form from which the extract is derived. The parent plant material, as well as the extracts, provide substantially more than flavor and color to foods. The quality of extracts is firstly dependent upon the quality of the botanical source, and in this context, horticulturist have a prominent role in developing and testing improved strains of condimental herbs and spices.
2	Phytochemistry and bioactive properties of plant volatile oils: antibacterial, antifungal and antioxidant activities	Plant volatile oils are composed of a complex mixture of a range of low molecular compounds, predominantly terpenes and phenylpropanoids. Variation in the spatial arrangement of the compounds was often noted. EO are effective at inhibiting the growth of tested microorganisms (i.e. E. coli, Clostridium sporogenes, Salmonella pullorum and Staphylococcus aureus). Oils of oregano and thyme were particularly active. Despite the lack of understanding of the mode of action, the greatest potential of plant volatile oils is in the food industry, especially as their flavors are generally acceptable. Application in other fields may be limited due to their physical properties and non-specific action. The antifungal activity of the volatile oils tested showed results particularly significant, as effort to control of Fusarium fungal infections and prevent or eliminate the presence of its mycotoxins. Oregano could acts as antioxidant dietary supplements during pregnancy of mammals with changes of fatty acid composition of different lipid fractions of the dams and their neonates.
3	Dietary strategies to counteract the effects of mycotoxins: a review	The authors reviewed various dietary strategies to contain the toxic effects of mycotoxins using antioxidant compounds (selenium, vitamins, provitamins), food components (phenolic compounds, coumarin, chlorophyll and its derivatives, fructose, aspartame), medicinal herbs and plant extracts, and mineral and biological binding agents (hydrated sodium calcium aluminosilicate, bentonites, zeolites, activated carbons, bacteria, and yeast). Interesting results are presented by food components contained in coffee, strawberries, tea, pepper, grapes, turmeric, Fava tonka, garlic ,cabbage, and onions.
4	Plants and plant extracts for improving animal productivity	Plant secondary metabolites are a natural resource that is largely unexploited in 'conventional' animal production systems. The present paper reviews the use of plants and their extracts to manipulate the rumen microbial ecosystem to improve the efficiency of rumen metabolism. The bioavailability of secondary metabolites and their actions on peripheral metabolism is considered with a view to improving animal performance. The challenge of delivering plants and their extracts to animals outdoors in a controlled manner are discussed.

Table 4. Chronologically summary of previous literature reviews on botanicals: General aspects or fundamentals and experimental models

Attribute	Title	Author(s)	Year of publication	Publish in	Focus and objectives	Number of publications	Type of publications	Methodology
1	The analysis of EO and extracts (oleoresins) from seasonings: A critical review	Salzer, U.J.	1977	CRC Crit Rev Food Sci Nutr	This paper presents a critical review of the analytical methods employed for the determination of the relevant components of seasonings. Particular emphasis has been placed on those methods of analysis that provide a rapid and sufficiently accurate appraisal of seasoning extracts and EO from seasonings under routine control laboratory conditions.	57	Journal articles, books	The author describes: general comments concerning seasoning extracts, general comments concerning analytical methods. Individual seasonings (cardamoms and laurel leaves, cloves, origanum and thyme, sage, dill, coriander, caraway, mace and nutmeg, pimento (allspice), celery, capsicum, ginger, pepper, turmeric (curcuma), papikra, garlic and onion, cinamon, coumarin).
2	Immunostimulatory Drugs of Fungi and Higher Plants	Wagner, H., Proksch, A.	1985	Economic and Medicinal Plant Research	The object of this review is to demonstrate that in the future, apart from microbial preparations (Gram-positive and Gram negative bacteria) such as vaccines, plant drugs and polyalcohol polymers isolated from fungi. Higher plants may play a role in enhancing immunological host resistance against infections. Although very few of the compounds or preparations described have reached the state of the clinical study, it is suggested that they may be considered as prototypes, and the development of which may lead to novel promising compounds.	87	Journal articles, books	Stimulatory drugs of fungi and higher plants are critically reviewed considering the following aspects: historical aspects, scope and aims of immunostimulation, definition of immunostimulants, mechanism of immunostimulations, screening methods for the detection of immunostimulating compounds, and classification and characterization of immunostimulating compounds.
3	Molecular basis of bacterial outer membrane permeability	Nikaido, H., Vaara, M.	1985	Microbiol Rev	The bacterial outer membrane has been an object of intensive research during the last decade, and a number of reviews have appeared previously. Because of this, this review does not try to give an exhaustive account in this field, but rather to present a critical review on the organization of the outer membrane and its role in the modulation of permeability. The paper excludes the following areas, which are covered in the recent reviews cited: "cell surface" functions, especially in interaction with the environment, including host cells; interaction with colicins and phages; and assembly of the outer membrane.	344	Journal articles, books	Even in the areas covered, the review establishes a selective in citing references to limit its length. Because most extensive studies have been carried out with <i>Escherichia coli</i> and <i>Salmonella typhimurium</i> , authors usually begin each section of this review by describing these results, sometimes without specifically mentioning the names of these species. This is followed by the description of results obtained with other bacteria, when such results are available and pertinent. In those terms, the review comprises: component, nonspecific protein channel: porins, specific diffusion channels, lipid bilayer as a diffusion barrier and fusion sites between outer and inner membranes.
4	Siberian Ginseng (<i>Eleutherococcus senticosus</i>): Current status as an Adaptogen	Farnsworth, N. R., Kinghorn, A. D., Soejarto, D. D., Waller, D. P.	1985	Economic and Medicinal Plant Research	Adaptogen is defined as a substance that: 1) must be innocuous and cause minimal disorders in the physiological functions of an organism, 2) must have a nonspecific action (i.e., it should increase resistance to adverse influences by a wide range of physical, chemical, and biochemical factors), and 3) usually has a normalizing action irrespective of the direction of the pathogenic state. In this review, Siberian ginseng is analyzed as an adaptogen. Almost all scientific information on the biological evaluation of extracts of Siberian ginseng (<i>Eleutherococcus senticosus</i>) has been published in the Russian language, and a great deal of difficulty was encountered in obtaining copies of the reports cited in this review.	92	Journal articles, books	Siberian ginseng (<i>Eleutherococcus senticosus</i>) (ES) is said to be an "adaptogen". This kind of substance is defined as having three characteristics. The first aspect an adaptogen relates to its lack of toxicity. The second aspect is its nonspecific action. In this aspect, numerous animal models have been utilized to evaluate ES action on the performance of animals under various conditions of stress, such as heat and cold, excessive exercise, swimming to exhaustion, restricted movements and others. The third characteristic is its normalization action irrespective of the direction of the changes from physiological norms caused by the presence of a pathological condition. All of those toxicity studies and biological assessments of Siberian ginseng are considered in this review.
5	Antimicrobial Activity of EO: A 1976-1986 Literature Review: Aspects of Test Methods	Janssen, A. M., Scheffer, J.J., Svendsen, A. B.	1987	Planta Med	In this paper, the data given in the literature review published during 1976-1986 concerning antimicrobial activities of EO are treated from an experimental point of view and with regard to a possible practical application. Attention is paid to four factors which are important when testing EO: assay technique, growth medium, microorganism, and essential oil.	48	Journal articles, books	The authors discuss in separate sections the four factors considered important when testing EO: assay technique, growth medium, microorganism, and essential oil.

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Attribute	Title	Author(s)	Year of publication	Publish in	Focus and objectives	Number of publications	Type of publications	Methodology
6	Antimicrobial activities of EO: a 1976-86 literature review on possible applications	Janssen, A. M., Scheffer, J.J., Svemdsen, A. B.	1987	Pharm Weekbl Sci	EO have been tested in this review from 1976 to 1986 for the following purposes: 1) to screen for antimicrobially active oils or constituents, 2) to screen for disinfecting or antiseptic activities, 3) to screen for food conserving properties, 4) to study the possible role of EO in biological interactions, 5) to study the possible use of EO as therapeutic agents.	56	Journal articles, books	The testing of EO for antimicrobial activities is reviewed with respect to various possible applications. Consideration is given to the screening for antimicrobially active oils or constituents, for disinfecting or antiseptic properties and for food conserving properties. The role of EO in biological interactions and their potential as therapeutic agents are also discussed.
7	Screening methods for natural products with antibacterial activity: a review of the literature	Rios, J. L., Recio, M.C., Villar, A.	1988	J Ethnopharmacol	The authors prepared a bibliography on the different techniques and methods employed in the antimicrobial study of medicinal plants and the principles obtained from them. The methods are classified into only three groups: diffusion, dilution and bioautographic. After reviewing the different methods used in the study of antimicrobial activity, and drawing from their own work, the authors proposed the best methods for the different extracts or compounds described.	108	Journal articles, books	Diffusion and dilution methods have been revised in the context of the study of antimicrobial activity of medicinal plants. In retrospective, a number of modifications have been made in the technique in order to obtain better results. Bioautography is another method for studying antimicrobial activity showed by authors.
8	Antioxidants/antimutagens in food	Namiki, M.	1990	Crit Rev Food Sci Nutr	The relationship between food and oxygen is very complex. From this viewpoint, antioxidants in food are in themselves indispensable constituents of food, comparable in importance with other nutritive constituent for survival. Recent advances in the search for natural antioxidants, their chemistry and their biological function at the cellular and body level are reviewed, including studies on anti- mutagenicity of antioxidative food constituents and natural substances. Because they have been thoroughly reviewed elsewhere by other authors for their biological functions and other features, tocopherol, ascorbic acid and their related compounds are for the most part excluded from this paper.	203	Journal articles, books	The relationship between food and oxygen is very complex. Recent advances in the development of natural antioxidants, their chemistry and their biological function at the cellular and body level are critically reviewed. This paper includes studies on anti-mutagenicity of antioxidative food constituents and natural substances.
9	Echinacea for the immune system	Mowrey, D.B.	1990	Guaranteed Potency Herbs: Next Generation Herbal Medicine	The primary emphasis of this review is on mechanisms of action of Echinacea. The therapeutic research section contains what little clinical work is available, and therapeutic action section is attempt to extrapolate from data how Echinacea should be used in daily life. It should be remember that most, may be all, of the properties of Echinacea discussed in this section, in one way or another, contribute to improved immune system functioning.	39	Journal articles, books	Most of what is scientifically known about Echinacea has been learned in basic laboratory research. Good clinical studies are few and far between. All of the properties of Echinacea discussed in this review contribute to improved immune system functioning.
10	The Chemical Composition of Thymus Oils: A review of the literature 1960-1989	Stahl-Biskup, E.	1991	J Essent Oil Res	This paper reviews the literature from 1960 to 1989 concerning the chemical composition of thymus oils. 84 Thymus taxa from 27 different countries all over the world have been investigated for the composition of their EO. About 200 different compounds, mostly terpenes have been identified. The terpene phenols thymol and carvacrol represent the most important compounds in the genus, followed by linalool, cymene, terpinene, borneol, terpinen-4-ol and 1,8-cineole.	137	Journal articles, books	The author gives a critical evaluation of the chemistry of the EO from 1960 to 1989. He lists the main components of EO of all taxa, seasonal variation of the thymus oils, and EO polymorphism within the genus thymus.

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Attribute	Title	Author(s)	Year of publication	Publish in	Focus and objectives	Number of publications	Type of publications	Methodology
11	Phenols and chelators	Kabara, J.J.	1991	Food Preservatives	The approach taken in this review was to examine synthetic chemicals, which has been used in the food industry for a number of years, and which has been found to be safe and to have potential preservation action, in terms of their antimicrobial properties.	69	Journal articles, books	Two categories of food-grade chemicals antioxidants were examined as antimicrobial products: phenols (butylated hydroxytoluene, BHT and butylated hydroxyanisole(BHA)) and chelating agents (ETDA).
12	Echinacea Species as Potential Immunostimulatory Drugs	Bauer, R., Wagner, H.	1991	Economic and Medicinal Plant Research	Relevant immunological in vitro and in vivo assays have been developed in relation to Echinacea species. Therefore, in this review, it has been possible to demonstrate the immunostimulatory activity of Echinacea extracts, and to assign the activity to certain groups of constituents.	109	Journal articles, books	This paper critically reviewed Echinacea species as potential immunostimulatory drugs in terms of its history, botany, chemical constituents, pharmacology (non-immunological and immunological properties) and therapeutic experience: though studies on probands and patients from 1895 to 1991.
13	Naturally occurring compounds	Conner, D. E.	1993	Antimicrobials in Foods	The recent increased demand for minimally processed, extends shelf-life foods have renewed interest in exploitation of natural components of some foods. The purpose of this review is to present an overview of some of the most highly recognized natural antimicrobials occurring in or added to food.	140	Journal articles, books	This paper critically reviewed natural occurring compounds in terms of: plants extracts; species, EO and other oleoresins; garlic, onion, and other Allium spp.; other plants extracts; eggs, milk and others.
14	Natural antimicrobials from plants	Nychas, G.J.E.	1995	New Methods of Food Preservation	It has been reported that over 1389 plants are potential source of antimicrobial agents. Food microbiologists have investigated the antimicrobial properties of many herbs, spices and food plants, but in many cases they have ignored a number of potentially useful plants listed. For this reason, this paper should keep abreast of current advances in pharmacognosy and related sciences where an increasing interest is being taken in the potential use of plant constituents as drug or antimicrobials in general.	170	Journal articles, books	Natural antimicrobials from plants have been reviewed. Phytoalexins, organic acids, EO, phenolics, pigments and related compounds, modes of action and health and legislative aspects are addressed in this review.
15	Garlic	Murray, M.T.	1995	The Healing Power of Herbs: The Enlightened Person's Guide to the Wonders of Medicinal Plants	This paper covers an overview of garlic research and applications.	18	Journal articles, books	The review comprises a general description of garlic, its chemical composition, its history and folk use; pharmacology and clinical applications, dosage and toxicity.
16	Echinacea: The Immune Herb	Hobbs, C.	1995	Echinacea: The Immune Herb	This is a booklet: It presents up to date (1999) practical information on the use of Echinacea an important herb for infections, colds, flu, and a host of other major and minor ailments. Specific issues are including as follow: which ailments Echinacea works for, choosing the best Echinacea products, how much to take and for how long and children's dosages. All of those are supported with scientific evidences.	260	Journal articles, books	The table of contents contains Echinacea's history, modern verification of traditional uses, what conditions is Echinacea best for? How to use Echinacea. Is Echinacea safe? What is best kind of Echinacea preparation? Growing Echinacea. A few comments by herbalists who use Echinacea. The booklet has an appendix contains a comprehensive literature review of Echinacea. While the first part is supported by 39 references, the appendix has 221 cited references covering the oldest literature about Echinacea.
17	Medicinal properties and chemical composition of Vitex Egnus-Castus L.: A review	Russo, M., Galletti, G. C.	1996	Acta Hort. (ISHS)	This paper reviews the pharmacological properties and chemical composition of the Mediterranean species Vitex agnus-castus L. The botanical characteristics of V. agnus-castus are described. The uses of the drug by ancient monastic communities as an aphrodisiac and its present potential uses as a traditional medicine for the treatment of diseases connected with the female hormone system are briefly discussed.	23	Journal articles, books	The author describes the botanical classification, antique medicine, drug, therapeutic properties and pharmacological applications, and chemical composition of Vitex Angus-Castus L.

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Attribute	Title	Author(s)	Year of publication	Publish in	Focus and objectives	Number of publications	Type of publications	Methodology
18	Natural antioxidants: An overview	Shahidi, F.	1997	Natural Antioxidants Chemistry; Health Effects and Applications	Plants provide a rich source of natural antioxidants. These include tocopherols, vitamin C, carotenoids, and phenolic compounds. Plant phenolics are thought to protect the plants against tissue injuries as they oxidize and combine with proteins and other components. In addition, phenolic compounds in plants may serve as defense systems against herbivory. By-products of photosynthesis may also produce high levels of oxygen, free radicals, and reactive oxygen species in profusion. All of these aspects of natural antioxidants are addressed.	52	Journal articles, books	Natural antioxidants are over viewing in terms of plant-based antioxidants, amino acids, peptides and protein hydrolyzates as antioxidants, antioxidants activity of pyhtates, phospholipids as antioxidants and vitamins and enzyme antioxidants. This review also covers some methodologies for assessing lipid oxidation and antioxidant activity.
19	Antioxidant and biological properties of Rosemary components: Implications for food and health	Offord, E. A., Guillot, F., Aeschbach, R., Loliger, J., Pfeifer, A. M. A.	1997	Natural Antioxidants Chemistry; Health Effects and Applications	This review focuses on natural polyphenolic compounds extracted from leaves of the plant <i>Rosmarinus officinalis</i> L. First, it describes the antioxidant properties of rosemary and its application to food stabilization and then goes on to show its biological effects in cell model systems, with some interesting implications for human health.	31	Journal articles, books	This review covers the following aspects of rosemary plant: purification and characterization of its antioxidants, antioxidant activity of rosemary components in food, antioxidant activity of rosemary components in lipid and non-lipid systems, antimutagenicity in bacteria, antigeotoxicity in human bronchial cells and antitumor-promoting activity in murine JB6 cells.
20	Antioxidants from spices and herbs	Nakatani, N.	1997	Natural Antioxidants Chemistry; Health Effects and Applications	This review covers the worldwide interest in finding new and safe antioxidants from natural sources. This review has been focused on edible plants, especially spices and herbs.	51	Journal articles, books	The antioxidants obtained from spices and herbs are described in the following aspects: antioxidants from the Labiatae and Zingiber families, antioxidants from other spices and other properties of antioxidants.
21	Echinacea	Bergner, P.	1997	The Healing Power of Echinacea & Goldenseal	By the end of 1930sm, the Madaus pharmaceutical company began growing and marketing Echinacea products, and they have remained popular ever since, both among physicians and consumers in Germany. Review of scientific research about Echinacea, introduces readers, firstly to the wonders of the immune system and secondly it shows an overview of its components in order to understand the significance of the findings.	NA	Journal articles, books	Echinacea is one of them most popular herbs in the US today. This review covers Echinacea's history, traditional uses, professional medical uses, and modern scientific research. Through this review, it is possible to learn how to use this plant in various forms and for many conditions other than de common cold.
22	Bioactivity of EO of selected temperate aromatic plants: antibacterial, antioxidant, antiinflammatory and other related pharmacological activities	Svoboda, K. P., Hampson, J. B.	1999	Speciality Chemicals for the 21st Century. Intermediary products, cosmetics and perfumes, medicinal applications	This review describes the potential uses of EO from temperate aromatic plants. The constituents of the oils are mainly monoterpene and sesquiterpene hydrocarbons with the general formulae (C ₅ H ₈) _n . Oxygenated compounds derived from these hydrocarbons include: alcohols, aldehydes, esters, ethers, ketones, phenols and oxides. It is estimated that there are more than 1000 monoterpene and 3000 sesquiterpene structures. The biological activity of the oils is compared with the activity of synthetically produced pharmacological preparations.	52	Journal articles, books	The author describes the mode of action of EO, the potential suggested uses of naturally occurring compounds as human medicants, the importance of EO as potential antioxidants, and the volatile oils as plant protection agents and their antimicrobial activity. The main plant species and microorganisms investigated are covered in comprehensive tables and references. The brine shrimp bioassay used for the oil toxicity testing is described in detail.
23	New Antimicrobials of Plant Origin	Iwu, M. M., Duncan, A. R., Okunji, C. O.	1999	Reprinted from: Perspectives on new crops and new uses. 1999. J. Janick (ed.), ASHS Press, Alexandria, VA.	The review briefly point out the historic use of plants as antimicrobials and the development of Phytomedicine and Ethnomedicinal approach. It also describes the therapeutic and economic benefits of the present use of plants as antimicrobials.	24	Journal articles, books	The authors analyzed new antimicrobials of plant origin from the point of view of the historic of use of plants as antimicrobials, development of Phytomedicines and Ethnomedicinal approach against infectious disease. Therapeutic and economic benefits for using plants as antimicrobials, and plants with promising antiinfective activity are also discussed.

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24	Role of medicinal plants, herbs, and spices in protecting human health	Balentine, D. A., Albano, M. C., Nair, M. G.	1999	Nutr Rev	A panel of food scientist epidemiologists and toxicologists, natural products chemists and nutritionists addressed five questions about current knowledge priorities and obstacles regarding phytonutrients. Consumption of two types of phytonutrients; proposed benefits of tea beverages consumption, citing the demonstrated antioxidant activity of flavonoids in tea beverages and the active components from aqueous, ethyl acetate and methanol extract of tart cherries and their apparent anticancer, antioxidant and antiinflammatory activities are also addressed.	26	Journal articles, books	Current knowledge priorities and obstacles regarding phytonutrients are reviewed through the following five questions: what additional knowledge is needed to move the field forward?, What are the technical barriers to obtain this additional information?, What are the immediate priority research topics?, What are the priority research topics long-term?, What is the role of the government in phytonutrient research and How does it complement privately sponsored research?
25	Antioxidant factors in plant foods and selected oilseeds	Shahidi, F.	2000	Biofactors	This review is devoted to isolate new antioxidants and elucidate their chemistry and functionality for further study concerning chemoprevention of inflammation, tumor, atherosclerosis and aging. Its major target for effective antioxidants has been focused on edible plants, particularly spices and herbs.	17	Journal articles, books	Spices and herbs are recognized as sources of natural antioxidants and thus play an important role in the chemoprevention of diseases resulting from lipid peroxidation. Studies of this research group showed that spices and herbs have given them over a hundred compounds, known and new, having high antioxidant activity. A summary of those compounds becoming from the Labiatae family (<i>Rosmarinus officinalis</i> , <i>Thymus vulgaris</i> , <i>Origanum vulgare</i> and <i>O. majorana</i>), Zingiber family (<i>Zingiber officinale</i> , <i>Curcuma domestica</i> and <i>Z. cassumunar</i>) and Myrtaceae family (berries of <i>Pimenta dioica</i>).
26	Phenolic anti-oxidants from herbs and spices	Nakatani, N.	2000	Biofactors	The effect of dietary factors on health promotion and disease prevention has been an issue of interest since antiquity and has become a subject of renewed research activity in recent years. Many of the components involved are antioxidative in nature and include phenolic compounds. These phenolics exist in the free, esterified, glycosylated and polymeric forms. Scrutiny of the source materials, their subsequent extraction under optimized conditions and evaluation of activity, followed by fractionation and structure elucidation of active components is generally necessary. An overview of those aspects is intended in this critical paper.	20	Journal articles, books	This overview intends to provide information about the extraction, identification, properties and application of plant phenolics, including those of oilseeds. However, it should be noted that not all biological effects of plant phenolics are related to their antioxidant activities. Other properties are related to their estrogenic action and how many plant phenolics are known to inhibit certain cytochromes P450 and upregulate the expression of genes encoding enzymes that detoxify xenobiotics. Several flavonoids have also been reported to inhibit protein kinases and genistein may block the growth of new blood vessels; however, these factors and effects are not discussed in this review.
27	Synergy and other interactions in phytomedicines	Williamson, E.M.	2001	Phytomedicine	This review focused on the beginning of a new research field, Phytomedicine. It shows how these remedies work and ultimately results in reduced side effects and better therapeutic success. In this sense, synergistic interactions are of vital importance to explain difficulties in always isolating a single active ingredient, and explain the efficacy of apparently low doses of active constituents in a herbal product. Evidence to support the occurrence of this synergy is now accumulating and is reviewed.	31	Journal articles, books	Synergistic interactions are documented by the analysis of the following aspects: positive and negative effects of herbal interaction, differences in the approach to treatment, defining and proving synergy, and in vitro and other experimental evidences when herbs discussed including: <i>Ginkgo biloba</i> , <i>Piper methysticum</i> (Kava-Kava), <i>Glycyrrhiza glabra</i> , <i>Hypericum perforatum</i> , <i>Valeriana officinalis</i> , <i>Cannabis sativa</i> , <i>Salix alba</i> and others.

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28	Regulation of EOproduction in plants	Sangwan, N.S., Farooqi, A.H.A., Shabih, F., Sangwan, R.S.	2001	Plant Growth Regul	A comprehensive synthesis of the physiological dynamics and regulation of EOproduction from the literature and available information on diverse volatile oil crops are addressed. The production of EO not only depends upon the metabolic state and preset developmental differentiation programme of the synthesising tissue, but also is highly integrated with the physiology of the whole plant. Besides, the oil productivity is friendly to ecophysiological, environmental and other factors. All these aspects of the modulation of essential oil production are presented, after a brief outline of the current concept of its relevant biosynthetic mechanisms.	126	Journal articles, books	The current concept of relevant biosynthetic mechanisms of EO (terpenoids, phenylpropanoids), physiology of EOproduction (plant ontogeny, site of oil production, photosynthesis, photoperiod modulation, effect of light quality, seasonal and climatic variations, nutritional relationships, plant growth regulators) and impact of antibiotics stresses (moisture, salinity, temperature) are presented.
29	Dyspepsia and phytotherapy: A review of traditional and modern herbal drugs	Saller, R., Iten, F., Reichling, J.	2001	Forsch Komp Klas Nat	This review is written in German language. This analyses why gastrointestinal complaints rank among the most frequently reasons people asking for medical advice. The therapy of functional gastrointestinal disorders is one of the domains of phytotherapeutic treatments since bitter herbal drugs have been played a very important role in the therapy of patients with dyspeptic symptoms from ancient times. The mechanisms of action of the bitters are addressed.	72	Journal articles, books	This review comprises the following components: phytotherapeutic and dyspepsia, traditional phytotherapeutic in dyspeptic conditions, Germany's phytotherapeutics against dyspepsia and traditional Chinese, and Germany and Humoral Medicines approaches.
30	Intake of garlic and its bioactive components	Amagase, H., Petesch, B.L., Matsuura, H., Kasuga, S., Itakura, Y.	2001	J Nutr	Garlic is considered to be one of the best disease-preventive foods because of its potent and widespread effects. Although some studies have cast doubt on the benefits of garlic extract, careful examination of such data emphasizes, the need to clarify the influence of processing on the benefits of garlic. On the other hand, an array of garlic preparations is available on the market. This review clarifies the effects of garlic supplements and the chemical and biological differences among commercial preparations.	88	Journal articles, books	The health benefits of garlic and current confusion, the complex chemistry of garlic, garlic supplements and intake of garlic, commercial garlic precuts and its four categories: dehydrated garlic powder, garlic oil, garlic oil macerate and aged garlic extract (AGE), bioavailability of garlic compounds and safety and quality control of garlic preparations are critically reviewed in this paper.
31	Nutritive value and technology of spices: Current status and future perspectives	Subbulakshmi, G, Naik, M..	2002	J Food Sci Tech Mys	India is reputed for the production of 63 types of most important spices. Almost, all spices are grown in this country because of the varied climate-tropical, sub-tropical and temperate. Each of the states and union territories grows one or more spices in abundance. There are as many as 26 types of Indian spices that find a ready overseas market. Nutritive value and technology of those spices, their current status and future perspectives are reviewed in this paper	150	Journal articles, books	India is the world's largest exporter of spices and also emerged as a major supplier of spice products. Therefore, this review analyses: India, the spice bowl, export of spices and spice products form India, nutritive value of spices, antimicrobial properties of spices and spice products, role of spices in health and disease, processing of spices, pre-treatments, spice oils and oleoresins, shelf life of spices, microbiological safety of spices, quality control of spices and future perspectives in nutritive value and technology of spices.

Table 4. Chronologically summary of previous literature reviews on botanicals: General aspects or fundamentals and experimental models. Cont...

Attribute	Title	Author(s)	Year of publication	Publish in	Focus and objectives	Number of publications	Type of publications	Methodology
32	Reviews of articles on medicinal herbs	Sarris, J., Flaherty, J.	2002	Aust J Med Herbalism	Eight articles in recent issues of phytotherapy are summarized as follows: anti-inflammatory activities of isolated flavonoids, cellular immune suppression by <i>Tylophora indica</i> , cyclooxygenase inhibition with anthocyanins from cherries and berries, synergy and other interactions in Phytomedicines, the hypotensive and bradycardic action of <i>Mentha x villosa</i> essential oil, study of parsley seed laxative effects, <i>Valeriana edulis</i> and <i>V. officinalis</i> contrasted for efficacy in treating insomnia and hypericin in combination with photodynamic therapy used in the treatment of fibrosarcoma.	8	Journal articles, books	These abstracts are brief summaries of articles which have appeared in recent issues of phytotherapy journals, most of which are held in the NHAA library and can be obtained through the Medplant Update service in Australia.
33	Onions: A global benefit to health	Griffiths, G., Trueman, L., Crowther, T., Thomas, B., Smith, B.	2002	Phytother Res	Onion (<i>Allium cepa</i> L.) is botanically included in the Liliaceae and species are found across a wide range of latitudes and altitudes in Europe, Asia, N. America and Africa. Genetic diversity and geographic distribution, horticultural production, marketing and consumption trends are analyzed in the introduction of this review. However, its major emphasis is onion in the context of a range of health benefits in terms of: chemical composition and the key health compounds and its therapeutic and medicinal value. This review establishes a vision of onion in the perspective of human health.	121	Journal articles, books	This paper critically reviewed the agronomy of the onion crop, the biochemistry of the health compounds and reporting on recent clinical data obtained using extracts from this species. Where appropriate the authors compare the data with that obtained from garlic (<i>Allium sativum</i> L.) for which more information is widely available around the world.
34	Biological activities of lavender essential oil	Cavanagh, H.M.A., Wilkinson, J.N.	2002	Phytother Res	In this paper, the authors reviewed current research investigating the biological activities of lavender oil and highlight areas that require further investigation. Details about the current state of knowledge of the effect of lavender oils on psychological and physiological parameters and its use as an antimicrobial agent are addressed. These issues are discussed before they have a true picture of the biological activities of lavender essential oil.	67	Journal articles, books	A commercial value of lavender was recently confirmed when it was named 'Herb of the Year 1999' by the Herb Growing and Marketing Network in the United States of America. In this paper, lavender are critically analyzed in terms of: chemical composition of its EO, neurological effects, effects on the other body systems, lavender as an antimicrobial agent, its pecticidal activities and its dermatological uses.
35	Pharmacokinetics and bioavailability of herbal medicinal products	Bhattaram, V.A., Graefe, U., Kohlert, C., Veit, M., Derendorf, H.	2002	Phytomedicine	Pharmacokinetic and bioavailability studies that have been conducted for some of the most important or widely used phytopharmaceuticals are critically evaluated. Furthermore, various drug interactions are discussed which show that caution should be exercised when combining phytopharmaceuticals with chemically derived active pharmaceutical ingredients.	?	Journal articles, books	This review summarized the data available on bioavailability and pharmacokinetics of some commonly used Herbal Medicinal Products (HMPs) through the following issues: methodology of analysis; clinical studies, non-clinical studies and drug interactions of <i>Ginkgo biloba</i> , <i>St. John's wort</i> , horse chestnut, willow bark, milk thistle, quercetin and EO of peppermint oil, eucalyptus oil, pine oil and thyme oil.

Table 4. Chronologically summary of previous literature reviews on botanicals: General aspects or fundamentals and experimental models. Cont...

Attribute	Title	Author(s)	Year of publication	Publish in	Focus and objectives	Number of publications	Type of publications	Methodology
36	Development of a Chinese herbal medicine toxicology database	Bensoussan, A, Myers, S.P., Drew, A.K., Whyte, I.M., Dawson, A.H.	2002	Clin Toxicol	The purpose of this review was to develop methods to retrieve and evaluate available scientific evidence on the toxicity of Chinese Herbal Medicine (CHM) from various sources, to assess the quality of this evidence, to grade the toxicity of individual Chinese herbs and finally, to make relevant data on each herb available via a searchable electronic database. This database should help promote safer practice of CHM in the West by making data available to guide selection and use, and minimize the risk of adverse reactions. This article outlines the methodologies used in developing the database and presents initial findings.	28	Journal articles, books	English and Chinese primary studies were systematically retrieved via journal abstracting databases and key toxicity texts. Partial translation of published research was achieved via an audited process utilizing data extraction forms. Methods for grading herb toxicity (in therapeutic use or overdose) were developed based on a combination of the quality of reports, severity of adverse reaction, supporting animal studies, extrapolation from pharmacology and empirical evidence.
37	Guidance for the safety assessment of botanicals and botanical preparations for use in food and food supplements	Schilter, B., Andersson, C., Anton, R., Constable, A., Kleiner, J., O'Brien, J., Renwick, A.G., Korver, O., Smit, F., Walker, R.	2003	Food Chem Toxicol	The present guidance focuses both on botanical preparations as ingredients and on the actual food application. The safety of botanicals bred with the assistance of genetic engineering technology, or which would be classed as Novel Foods are addressed by existing guidelines. However, aspects of the present document would be relevant when assessing the safety of such products with physiological (or functional) health benefits. The aim is to provide a general framework in which to establish the safety of functional botanical products for human consumption. It is not intended to address claim substantiation or regulatory issues. The present guidance focuses both on botanical preparations as ingredients and on the actual food applications.	75	Journal articles, books	The guidance paper was developed by an expert group of the Natural Toxin Task Force of the European Branch of the International Life Sciences Institute—ILSI Europe and discussed with a wider audience at a workshop held on 13–15 May 2002 in Marseille, France. This paper critically reviewed the following areas: product specification/characterization (i.e. recommendations); history of use (i.e. recommendations); product comparison (i.e. recommendations); intended use, dietary exposure, dietary consequences; hazard identification and characterization (i.e. test material, use of toxicity data on unrefined extracts, use of toxicity data on purified ingredients, human data, experimental studies, recommendations, epidemiological data, animal data, matrix effects, modes or mechanisms of toxicity), risk characterization, post launch monitoring and subsequent investigations and the decision tree approach.
38	Antibacterial and Antifungal Properties of EO	Kalemba, D., Kunicka, A.	2003	Curr Med Chem	This paper gives an overview on the activity of EO derived from various plants as well as their constituents against a wide variety of bacteria and fungi. Two main aspects are in the scope of interest of the authors: a wide variety of methods used and antimicrobial activity in relation to the possible application of EO in medicine and food, cosmetic and pharmaceutical industries.	273	Journal articles, books	This paper reviews the classical methods commonly used for the evaluation of EO antibacterial and antifungal activities. The agar diffusion method and the dilution method as well as turbidimetric and impedimetric monitoring of microorganism growth in the presence of tested EO are described. Also the review gives an overview on the factors influencing the estimation of EO antimicrobial activity, the susceptibility of microorganisms to EO, synergistic effects of EO their components and other agents and activity of EO towards microorganism.
39	Quality, efficacy and safety of complementary medicines: fashions, facts and the future. Part I. Regulation and quality	Barnes, J.	2003	Brit J Clin Pharmacol	This paper reviews the extent of use of complementary medicines, and issues related to the regulation and pharmaceutical quality of these products.	69	Journal articles, books	This review discusses, mainly from a UK perspective, various types of complementary medicines, particularly trends in their use, regulation, and issues surrounding quality. It has a particular focus on European herbal medicines as these are among the most widely used 'complementary medicines' in the UK and, from a biomedical perspective, herbal medicines (rather than, for example, homeopathic remedies) are likely to have the greatest potential in terms of both risks and benefits.

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Attribute	Title	Author(s)	Year of publication	Publish in	Focus and objectives	Number of publications	Type of publications	Methodology
40	Quality, efficacy and safety of complementary medicines: fashions, facts and the future. Part II. Efficacy and safety	Barnes, J.	2003	Brit J Clin Pharmacol	This review is the second of two papers which review issues concerning complementary medicines. This one considers evidence for the efficacy of several well-known complementary medicines, and discusses complementary-medicines pharmacovigilance.	72	Journal articles, books	There is a view that the criteria for efficacy and safety of complementary medicines should be the same as those for conventional drugs. In this sense, this paper analyses the efficacy of herbal medicinal products, their safety and the future of complementary medicines.
41	Garlic as an antioxidant: the good, the bad and the ugly	Banerjee, S. K., Mukherjee, P. K., Maulik, S. K.	2003	Phytother Res	A literature search on garlic and its antioxidant potential churned up a surprisingly large amount of data, some of it good, some bad and some of it definitely ugly. Various preparations of garlic, mainly aged garlic extract, have been shown to have promising antioxidant potential. However, the presence of more than one compounds in garlic, with apparently opposite biological effects, has added to the complexity of the subject. Raw garlic homogenate has been reported to exert antioxidant potential but higher doses have been shown to be toxic to the heart, liver and kidney. So where do we stand today on this issue of garlic? Is garlic always good for health? How safe is it? Is it necessary to isolate the antioxidant compounds for its medicinal use in a more effective way?	99	Journal articles, books	This paper critically reviews garlic in the context of its potential antioxidant compounds (i.e. raw garlic homogenate, allicin, heat treated garlic, garlic powder aged garlic extract, S-allyl cysteine, garlic oil, garlic protein), the other side of the coin and future directions of research with garlic.
42	Efficacy, chemistry and pharmacology of Chinese herbal medicine for allergic rhinitis	Xue, C.C.L., Hugell, H.M., Li, C.G., Story, D.F.	2004	Curr Med Chem	The review consists of three parts: a critical appraisal of clinical studies on the efficacy of Chinese herbal medicines in allergic rhinitis; a review of the key chemical compounds present in the individual herbs used; and consideration of the known biological effects of the herbs, and, where possible, the pharmacology of their constituents	57	Journal articles, books	Some questions are solved through the review: How does Chinese Medicine understand allergic rhinitis?, Is Chinese herbal Medicine effective for allergic rhinitis?, How Does Western Medicine understand allergic rhinitis?, Is Chinese herbal medicine effective for seasonal allergic rhinitis? And Chinese herbal medicine effective for perennial allergic rhinitis?. Conclusions drawn from 6 clinical studies are shown. EO, lignans, flavonoids and saponins are chemical classes that are frequently represented in individual herbs of the 6 Chinese herbal formulae used in trials. The chemical structures characterizing these classes of compound and the pharmacological actions of these and other constituents of the herbs, relevant to allergic rhinitis, have been reviewed.
43	Digestive stimulant action of spices : A myth or reality?	Platel, K., Srinivasan, K.	2004	Indian J Med Res	This review highlights the available information on the influence of spices on the digestive secretions and enzymes.	48	Journal articles, books	The authors briefly describe the effect of spices on the digestive system, such as: Influence on salivary and gastric secretions, stimulation of bile secretion, stimulation of pancreatic enzymes, influence on digestive enzymes of small intestinal mucosa, effect on transit time and the stimulant action of spice mixes.
44	A review of common herbs and potential interactions	Magee, K., Loiacono, C.	2004	Int J Dent Hygiene	Complementary and alternative medicine (CAM) encompasses a diverse group of medical treatment such as acupuncture, aromatherapy, massage therapy, meditation, hydrotherapy and herbal therapy. In this paper, authors have chosen to focus on herbal therapy, also known as phytotherapy or phytomedicine	26	Journal articles, books	This paper offers a review of herbal therapy, possible oral and systemic health complications and potential biomedical medication interactions.

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Attribute	Title	Author(s)	Year of publication	Publish in	Focus and objectives	Number of publications	Type of publications	Methodology
45	Antimicrobial and chemopreventive properties of herbs and spices	Lai, P.K., Roy, J.	2004	Curr Med Chem	This review discusses recent data on the antimicrobial and chemopreventive activities of some herbs and spices and their ingredients.	128	Journal articles, books	The authors present a review on the antimicrobial and chemopreventive properties of herbs and spices with specific references to mostly those of used in Asia in terms of: antimicrobial agents, structural aspects of antimicrobial phytochemicals, cancer chemopreventive, structural aspects of chemopreventive phytochemicals, information on extract's concentration and synergism and traditional herbal remedies and drug development.
46	EO: their antibacterial properties and potential applications in foods: A review	Burt, S.	2004	Int J Food Microbiol	The purpose of this paper is to provide an overview of the published data on the antibacterial activity of EO (EO) and their components that could be considered suitable for application in or on foods, and to describe their possible modes of action. The current knowledge on potential antagonists and synergists is presented; legal and safety aspects are discussed and areas for future research are proposed. Although some data are presented on spoilage flora, this paper will focus chiefly on the antibacterial effect of EO on food borne pathogens and, in particular, those for which food animals are the major reservoir.	195	Journal articles, books	This paper reviews the studies that have related to composition of EOs, in vitro test of antibacterial activity, test of antibacterial activity of EO in food systems, mode of antibacterial action, susceptibility of gram-negative and gram-positive organisms, synergism and antagonism between components of EO, synergism and antagonism between EO components and food preservatives or preservation methods, legal aspects of the use of EO and their components in foods, safety data, organoleptic aspects, future perspectives and areas for future research.
47	Commonly used herbal medicines in the United States: A review	Bent, S., Ko, R.	2004	Am J Med	This paper reviews the herbal medicines that are widely used in the United States. Herbs are considered to be dietary supplements in the United States and therefore are subjected to a very limited form of regulation and oversight. Although herbs are often believed to be "natural" and therefore safe, many dangerous and lethal side effects have recently been reported, including direct toxic effects, allergic reactions, effects from contaminants, and interactions with drugs and other herbs. Of the ten most commonly used herbs in the United States, systematic reviews have concluded that only four are likely to be effective, and there is very limited evidence to evaluate the efficacy of the approximately 20,000 other available herbal products.	78	Journal articles, books	The purpose of this paper is to provide an overview of the published data on prevalence/epidemiology for using commonly herbal medicines in the United States, the complexity of herbal products (regulations, efficacy, safety, research) and future directions.
48	Oregano: Properties, composition and biological activity	Arcila-Lozano, C.C., Loarca-Pina, G., Lecona-Urbe, S., Gonzalez-Mejia, E.	2004	Arch Latinoam Nutr	The oregano spice includes various plant species. The most common are the genus <i>Origanum</i> , native of Europe, and the <i>Lippia</i> , native of Mexico. Among the species of <i>Origanum</i> , their most important components are the limonene, beta-cariofilene, rho-cymenene, canfor, linalol, alpha-pinene, carvacrol and thymol. In the genus <i>Lippia</i> , the same compounds can be found. The oregano composition depends on the specie, climate, altitude, time of recollection and the stage of growth. Some of the properties of this plant's extracts are being currently studied due to the growing interest for substituting synthetic additives commonly found in foods. All of those aspects are aimed in this review written in Spanish language.	103	Journal articles, books	This review covers in Spanish language the following aspects of oregano: chemical composition, methods of extraction and analyses of EO, biological activities of oregano compounds and uses and industrial applications of oregano as plant or through its compounds.

Table 5. Chronologically summary of previous literature reviews on botanicals: Innovation, extension and new approaches.

Attribute	Title	Author(s)	Year of publication	Publish in	Focus and objectives	Number of publications	Type of publications	Methodology
1	Molecular biology for the improvement of medicinal and aromatic plants	Lewinsohn, E.	1996	Acta Hort. (ISHS)	In this paper, the emerging opportunities for the incorporation of genetic engineering into existing breeding programs for the full exploitation of the biosynthetic potential of aromatic and medicinal plants, is reviewed.	85	Journal articles, books, Encyclopedia	The author describes how Molecular Biology offers promising tools for the creation of novel crop varieties with improved nutritional value, resistance to herbicides, pests, diseases, pollutants and adverse climatic conditions taking into account the following thematic areas: physiological roles of natural products in the plants that produce them; techniques used to obtain genetically engineered crops; examples of introduction of useful agronomic traits to crops by genetic resistance to insect pests, fungal and viral diseases, "resistance of herbicides and pollutants", metabolic engineering to improve product preservation and characteristics, products of industrial materials and pharmaceuticals, and manipulation of biosynthetic pathways in medicinal and aromatic plants.
2	Industry perspectives on the use of natural antimicrobials and inhibitors for food applications	Gould, G. W.	1996	J Food Protect	The roles of natural antimicrobials are analyzed in the context of their potential for preserving foods. Natural antimicrobial systems are covered including animals, plants and microorganisms; as well as new physical procedures such as high hydrostatic pressure and manothermosonication.	54	Journal articles, books	The author reviews the current preservation technologies and natural antimicrobial systems (animal-derived antimicrobials, plant-derived antimicrobials, microorganism-derived antimicrobials, and new physical procedures), and the wide range of extremely effective naturally occurring antimicrobial systems include those derived from animals (e.g., enzymes such as lysozyme and lactoperoxidase; other proteins such as lactoferrin, lactoferricin, ovotransferrin, and serum transferrins; small peptides such as histatins and magainins; and the immune system), those derived from plants (e.g., phytoalexins, low-molecular-weight components of herbs and spices; phenolics such as oleuropein; and EO) and those derived from microorganisms (e.g., bacteriocins such as nisin and pediocin).
3	Analysis of active ingredients in medicinal herbs with high-performance liquid chromatography and related technologies: A review	Tsai, T. H., Hong, C. Y., Chen, C. F.	1997	J Food Drug Anal	This review discusses the liquid chromatographic systems, and capillary electrophoresis as well as related technologies that have been applied in various medicinal herb analysis, particularly on the herbal drugs used in traditional Chinese medicine,	70	Journal articles, books	This review is written in Chinese language and comprises a summary of HPLC techniques, and their application to various herbal medicines from the traditional Chinese medicine. Chromatograms are shown in relation to analytical methods. Chemical structure of the main components of medicinal herbs from China are also shown.
4	EO and 'aromatherapy': their modern role in healing	Lis-Balchin, M.	1997	J R Soc Health	The author describes why aromatherapy is one of the most actively growing forms of alternative medicine combining massage together with counseling and a nice odor. The actual mode of action of EO in vivo is still far from known, although there is strong in vitro evidence that EO can act as an antimicrobial or antioxidant agent or have a pharmacological effect on various tissues including an effect on brain waves and behavior.	33	Journal articles, books	The author describes five clinical studies on aromatherapy and point out 6 scientific evidences of EO efficacy in terms of aromatherapy, and their further analyze for future clinical application of aromatherapy.

Table 5. Chronologically summary of previous literature reviews on botanicals: Innovation, extension and new approaches. Cont...

Attribute	Title	Author(s)	Year of publication	Publish in	Focus and objectives	Number of publications	Type of publications	Methodology
5	An overview of supercritical fluid extraction in Chinese herbal medicine: From preparation to analysis	Chen, Y. T., Ling, YC	2000	J Food Drug Anal	Current state of supercritical fluid extraction (SFE) in the preparation and analysis of Chinese herbal medicine (CHM) and similar matrices considering applications in preparations and analyses are reviewed; as well as the possible solutions to the draw backs and foreseeable trends. Successful applications of SFE require the proper use on many experimental parameters. These parameters are organized in this review to facilitate the development of SFE based process and method in future works.	75	Journal articles, books	This paper carried out a literature review by searching the science citation index from the Institute for Scientific Information. SFE of useful ingredients from herbs and plants were presented as well as SFE from residual pesticides from herbs and plants.
6	Gas chromatographic technologies for the analysis of EO	Marriott, P.J., Shellie, R., Cornwell, C	2001	J Chromatogr A	There are two primary considerations when the authors discussed the analytical separation of EO. Firstly, they recognize that among chromatographic methods, primarily gas chromatography will be the most appropriate analytical instrumental approach, thus one must decide whether the performance of the separation will be adequate for the problem. Secondly, once the method has been chosen, the techniques used for characterization of the separated components needs to be considered. This will largely be the realm of mass spectrometry. Discussion of precursor biological compounds and biosynthetic pathways leading to EO generation is out to scope of this review.	132	Journal articles, books	This review is devoted to Gas Chromatographic technologies then it analyses de following aspects: gas chromatography techniques-a review, phases, aspects of sample handling for extraction and introduction of samples, hyphenated and multidimensional analysis of EO and comprehensive two-dimensional gas chromatography.
7	Supercritical fluid extraction in herbal and natural product studies: A practical review	Lang, Q.Y., Wai, C.M.	2001	Talanta	Supercritical Fluids Extraction (SFE) has become an acceptable extraction technique used in many areas. SFE of active natural products from herbal, or more generally, from plant materials has also become one of the most important application areas. In addition, with the increasing public interest in herbal medicines and natural products, numerous SFE-related research papers in herbal or natural product studies have been published in recent years. In this context, a practical review of the recent development in this area is presented by the authors and some of the interesting research results published within the last decade were addressed	82	Journal articles, books	This review presents the major advantages of SFE, fluid materials and modifiers, sample preparation, extraction conditions, collection methods, clean-up of pesticides from herbal plants and other samples, on-line fractionation an coupling with chromatographic methods and SFE modeling.
8	Microbial contamination of medicinal plants: A review	Kneifel, W.Czech, E., Kopp, B	2002	Planta Med	The intention behind this review paper is to discuss the following items: 1. To give an extensive survey of published data regarding the microbial load associated with herbal medicinal drug. 2. To elucidate some microbial criteria and methodological aspects which may useful to be further integrated in modern quality assurance of medicinal plants. 3. To consider the different modes of manipulation, which are usually applied for preparing medicinal drugs such as treatment with boiling water, cold water extraction and ethanol extraction, which usually affect the microbiological nature of the products thereby obtained. 4. To use this surveys a basis for proposing tailor-made quality standards for herbal medicinal plants.	42	Journal articles, books	This study intends to contribute to this knowledge by giving survey of published data regarding the microbial contamination of herbal plants in terms of: microbial contaminants associated with medicinal plants, microbial quality standards, class plans and sampling guidelines, methodological aspects, and influences of different preparation techniques on the microbiological quality.

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Attribute	Title	Author(s)	Year of publication	Publish in	Focus and objectives	Number of publications	Type of publications	Methodology
9	A review of modern sample-preparation techniques for the extraction and analysis of medicinal plants	Huie, C.W.	2002	Anal Bioanal Chem	In this article recent developments and applications of modern sample-preparation techniques for the extraction, clean-up, and concentration of analytes from medicinal plants or herbal materials are reviewed. These modern techniques include solid-phase microextraction, supercritical- fluid extraction, pressurized-liquid extraction, microwave- assisted extraction, solid-phase extraction, and surfactant-mediated extraction. Emphasis is placed on brief description of the unique capabilities and advantages and disadvantages of each modern sample-preparation techniques and of how these techniques were exploited to improve the extraction and analysis of a variety of medicinal plants.	81	Journal articles, books	In this review, recent developments and applications of modern sample-preparation techniques for the extraction, clean-up, and concentration of analytes from medicinal plants or herbal materials are reviewed. These modern techniques include solid phase, microextraction, supercritical-fluid extraction (SFE), pressurized-liquid extraction, microwave-assisted extraction, solid-phase extraction, and surfactant-mediated extraction.
10	Herbal bioactivation: the good, the bad and the ugly	Zhou, S., Koh, H. L., Gao, Y., Gong, Z. Y., Lee, E. J.	2004	Life Sci	This review highlights the role of formation of reactive intermediates via bioactivation in herbal toxicity using aristolochic acids, pulegone and germander as examples. In addition, mechanism- based inhibition of cytochrome P450 (CYPs) by many herbal constituents and the clinical and toxicological relevance are discussed.	286	Journal articles, books	This paper critically highlights herbal bioactivation in terms of formation of toxic metabolites, mechanism- based herbal inhibitors of cytochrome P450s, mechanism-based inhibition of CYPs and herb-drug interactions, and mechanism-based inhibition of CYPs and herbal chemoprevention.
11	Role of proline-linked pentose phosphate pathway in biosynthesis of plant phenolics for functional food and environmental applications: a review	Shetty, K.	2004	Process Biochemistry	Plants are excellent sources of phenolic phytochemicals, especially as antioxidants. These phenolic phytochemicals can be targeted for designing functional foods and in order to design consistent food-grade phytochemical profiles for safety and clinical relevancy, novel tissue culture and bioprocessing technologies have been developed. These are based on the model that phenolic metabolites in plants are efficiently produced through an alternative mode of metabolism linking proline synthesis with the pentose phosphate pathway. Using this system, techniques have been developed to isolate high phenolic clonal lines of food-grade plants from single heterozygous seeds. Applying the same model, elicitation concepts and techniques have been used to over-produce phenolic metabolites in seeds and sprouts. In both clonal and seed sprout systems, exogenous treatment of phenolic phytochemicals from a non-target species elicited endogenous stimulation of phenolic synthesis and potentially an antioxidant response. All of these aspects related with the proposed model are addressed in this review.	128	Journal articles, books	A strategy has been reviewed by the author in order to generate consistent phenolic antioxidants from food-grade plants for design of functional foods to provide better ways to potentially manage (through prevention) oxidation-linked and infectious diseases. This strategy to generate consistent phenolic antioxidants has also provided plant systems models, where synthesis of ATP, RE, NADPH ₂ and sugar phosphates for cellular metabolism is probably regulated through an alternative proline-linked pentose phosphate pathway.

Table 6. Chronologically summary of previous literature reviews on botanicals: Specific application and case studies.

Attribute	Title	Author(s)	Year of publication	Publish in	Focus and objectives	Number of publications	Type of publications	Methodology
1	Improving foods with herbs and spices extracts	Todd, Paul H.	1996	Acta Hort. (ISHS)	This paper reviews the preparation of botanical material for extraction, extraction and refinement of the material, pharmacologically active constituents which may improve the nutritional quality of foods, the application of extracts in the preparation of foods, and the role which horticulturalists are playing in improving food quality.	29	Journal articles, books	The author analyzes the following aspects: preparation of the extract, preparation of extracts and refining of EO and how extracts employs various aspects of fairly conventional technology; the nutritional value of certain herb and spice extracts as subject of much discussion in the literature and in symposia; how the potential effect of these condimental extracts when used in food varies with the botanical source, and the use of extracts in foods, and the role of horticulturalists.
2	Phytochemistry and bioactive properties of plant volatile oils: antibacterial, antifungal and antioxidant activities	Dorman, H.J.D.	1999	University of Strathclyde, Ph.D. dissertation	The aims of this thesis were to investigate the antibacterial, antifungal and antioxidant activities of the plant volatile oils and their components, where possible, from members of the Labiatae, Misticaceae, Myrtaceae, Piperaceae and Umbelliferae families. In addition the possible effects upon lipid composition in a pregnant rat model and their neonates.		Journal articles, books	This is a PhD thesis comprises the following articles: plant volatile oil composition analysis using gas chromatography and mass spectroscopy, antibacterial effects of selected plant volatile oils and their phytoconstituents upon a range of bacterial organism, antimycotic effects of selected plant volatile oils upon three fungal organisms, antioxidant properties of plant volatile oils: an in vitro assessment and effect of dietary supplementation of plant volatile oils upon tissue fatty acid composition in a pregnant rat model.
3	Dietary strategies to counteract the effects of mycotoxins: a review	Galvano, F., Piva, A., Ritiene, A., Galvano, G.	2001	J Food Protect	A wide range of chemical, physical and biological approaches has been experienced in the attempt to reduce the toxicity of mycotoxins. Nutritional approaches, such as supplementation of nutrients, food components or additives with protective properties against mycotoxin toxicity and addition of nonnutritive sorbents or bacteria, yeast and modified yeast cells capable of reducing the bioavailability of mycotoxins are reviewed. In particular, some studies highlighted the capability of several extracts from medicinal herbs and plants to counteract the aflatoxin B1 toxicity.	113	Journal articles, books	Antioxidant substances (selenium, vitamins), food components and additives (piperine, coumarins, chlorophyll and its derivatives, aspartame cyproheptadine, and allyl sulfides), mycotoxin-binding agents (Hydrate sodium calcium aluminosilicate (HSCAS), zeolites, bentonites, clays, activated carbons cholestyramine, polyvinylpyrrolone, bovine serum albumin and microbiological binding agents) are critically reviewed in this paper.
4	Plants and plant extracts for improving animal productivity	Greathead, H	2003	Proc Nutr Soc	The present review considers the background to the recent surge of interest in the use of plants and their extract as alternative performance enhancers, as well as the non-nutrient bioactive compounds of plants, the secondary metabolites. Possible ways of manipulating rumen and peripheral metabolites are discussed in relation to what is currently known about the bioactive roles of these compounds.	80	Journal articles, books	Background to the current interest in the use of plants and their extracts as alternative performance enhancers, plant secondary metabolites, manipulation of rumen metabolism and delivery of bioactive plants and their extract to animals are addressed in this review.

References reviews by category

General aspects or fundamentals and experimental models - Review (48)

- Salzer, U. J. 1977. The analysis of EO and extracts (oleoresins) from seasonings--a critical review. *CRC Crit Rev Food Sci Nutr* 9: 345-373.
- Wagner, H., and A. Proksch. 1985. Immunostimulatory drugs of fungi and higher plants. In: H. Wagner, H. Hikino and N. R. Farnsworth (eds.) *Economic and medicinal plant research No. 1*. p 113-153. Academic Press Limited, London.
- Nikaido, H., and M. Vaara. 1985. Molecular basis of bacterial outer membrane permeability. *Microbiol Rev* 49: 1-32.
- Farnsworth, N. R., A. D. Kinghorn, D. D. Soejarto, and D. P. Waller. 1985. Siberian ginseng (*eleutherococcus senticosus*): Current status as an adaptogen. In: H. Wagner, H. Hikino and N. R. Farnsworth (eds.) *Economic and medicinal plant research No. 1*. Academic Press Limited, London.
- Janssen, A. M., J. J. Scheffer, and A. B. Svendsen. 1987a. Antimicrobial activity of EO: A 1976-1986 literature review: Aspects of test methods. *Planta Med* 53: 395-398.
- Janssen, M. A., J. J. C. Scheffer, and A. B. Svendsen. 1987b. Antimicrobial activities of EO: A 1976-86 literature review on possible applications. *Pharm Weekbl Sci* 9: 193-197.
- Rios, J. L., M. C. Recio, and A. Villar. 1988. Screening methods for natural products with antibacterial activity: A review of the literature. *J Ethnopharmacol* 23: 127-149.
- Namiki, M. 1990. Antioxidants/antimutagens in food. *Crit Rev Food Sci Nutr* 29: 273-300.
- Mowrey, D. B. 1990. Echinacea for the immune system. *Guaranteed potency herbs: Next generation herbal medicine*. p 45-62. Keats Publishing Inc, New Canaan, Connecticut.
- Stahl-Biskup, E. 1991. The chemical composition of thymus oils: A review of the literature 1960-1989. *J Essent Oil Res* 3: 61-82.
- Kabara, J. J. 1991. Phenols and chelators. In: N. J. a. G. Russell, G.W (ed.) *Food preservatives*. p 200-214. Blackie, London.
- Bauer, R., and H. Wagner. 1991. Echinacea species as potential immunostimulatory drugs. In: H. Wagner and N. R. Farnsworth (eds.) *Economic and medicinal plant research No. 5*. p 253-322. Academic Press Limited, London.
- Conner, D. E. 1993. Naturally occurring compounds. In: P. M. Davidson and A. L. Branen (eds.) *Antimicrobials in foods*. p 441-468. Marcel Dekker, Inc., New York.
- Nychas, G. J. E. 1995. Natural antimicrobials from plants. In: G. W. Gould (ed.) *New methods of food preservation*. p 58-89. Blackie Academic Professional, London.
- Murray, M. T. 1995. Garlic. In: M. T. Murray (ed.) *The healing power of herbs: The enlightened person's guide to the wonders of medicinal plants*. p 121-129. Prima Publishing, Rocklin, CA.
- Hobbs, C. 1995. Echinacea. Botanica Press.
- Russo, M., and G. C. Galletti. 1996. Medicinal properties and chemical composition of *vitex egnus-castus l.*: A review. *Acta Hort. (ISHS)* 426: 105-112.
- Shahidi, F. 1997. Natural antioxidants: An overview. In: F. Shahidi (ed.) *Natural antioxidants chemistry; health effects and applications*. p 1-24. AOCS Press, Champaign, IL.
- Offord, E. A., F. Guillot, R. Aeschbach, J. Loliger, and A. M. A. Pfeifer. 1997. Antioxidant and biological properties of rosemary components: Implications for food and health. In: F. Shahidi (ed.) *Natural antioxidants chemistry; health effects and applications*. p 88-96. AOCS Press, Champaign, IL.

- Nakatani, N. 1997. Antioxidants from spices and herbs. In: F. Shahidi (ed.) Natural antioxidants chemistry; health effects and applications. p 64-75. AOCS Press, Champaign, IL.
- Bergner, P. 1997. Echinacea. Prima Publishing.
- Svoboda, K., P, and J. B. Hampson. 1999. Bioactivity of EO of selected temperate aromatic plants: Antibacterial, antioxidant, antiinflammatory and other related pharmacological activities. In: Speciality Chemicals for the 21st Century. Intermediary products, cosmetics and perfumes, medicinal applications. p 1-17.
- Iwu, M. M., A. R. Duncan, and C. O. Okunji. 1999. New antimicrobials of plant origin. In: J. Janick (ed.) Perspectives on new crops and new uses. p 457-462. ASHS Press, Alexandria, VA.
- Balentine, D. A., M. C. Albano, and M. G. Nair. 1999. Role of medicinal plants, herbs, and spices in protecting human health. *Nutr Rev* 57: S41-45.
- Shahidi, F. 2000. Antioxidant factors in plant foods and selected oilseeds. *Biofactors* 13: 179-185.
- Nakatani, N. 2000. Phenolic anti-oxidants from herbs and spices. *Biofactors* 13: 141-146.
- Williamson, E. M. 2001. Synergy and other interactions in phytomedicines. *Phytomedicine* 8: 401-409.
- Sangwan, N. S., A. H. A. Farooqi, F. Shabih, and R. S. Sangwan. 2001. Regulation of EOproduction in plants. *Plant Growth Regul* 34: 3-21.
- Saller, R., F. Iten, and J. Reichling. 2001. Dyspepsia and phytotherapy - a review of traditional and modern herbal drugs. *Forsch Komp Klas Nat* 8: 263-273.
- Amagase, H., B. L. Petesch, H. Matsuura, S. Kasuga, and Y. Itakura. 2001. Intake of garlic and its bioactive components. *J Nutr* 131: 955S-962S.
- Subbulakshmi, G., and M. Naik. 2002. Nutritive value and technology of spices: Current status and future perspectives. *J Food Sci Tech Mys* 39: 319-344.
- Sarris, J., and J. Flaherty. 2002. Reviews of articles on medicinal herbs. *Aust J Med Herbalism* 14: 1-4.
- Griffiths, G., L. Trueman, T. Crowther, B. Thomas, and B. Smith. 2002. Onions: A global benefit to health. *Phytother Res* 16: 603-615.
- Cavanagh, H. M. A., and J. N. Wilkinson. 2002. Biological activities of lavender essential oil. *Phytother Res* 16: 301-308.
- Bhattaram, V. A., U. Graefe, C. Kohlert, M. Veit, and H. Derendorf. 2002. Pharmacokinetics and bioavailability of herbal medicinal products. *Phytomedicine* 9: 1-33.
- Bensoussan, A., S. P. Myers, A. K. Drew, I. M. Whyte, and A. H. Dawson. 2002. Development of a chinese herbal medicine toxicology database. *Clin Toxicol* 40: 159-167.
- Schilter, B. et al. 2003. Guidance for the safety assessment of botanicals and botanical preparations for use in food and food supplements. *Food Chem Toxicol* 41: 1625-1649.
- Kalembe, D., and A. Kunicka. 2003. Antibacterial and antifungal properties of EO. *Curr Med Chem* 10: 813-829.
- Banerjee, S. K., P. K. Mukherjee, and S. K. Maulik. 2003. Garlic as an antioxidant: The good, the bad and the ugly. *Phytother Res* 17: 97-106.
- Barnes, J. 2003a. Quality, efficacy and safety of complementary medicines: Fashions, facts and the future. Part i. Regulation and quality. *Brit J Clin Pharmacol* 55: 226-233.
- Barnes, J. 2003b. Quality, efficacy and safety of complementary medicines: Fashions, facts and the future. Part ii. Efficacy and safety. *Brit J Clin Pharmacol* 55: 331-340.

- Xue, C. C. L., H. M. Hugell, C. G. Li, and D. F. Story. 2004. Efficacy, chemistry and pharmacology of chinese herbal medicine for allergic rhinitis. *Curr Med Chem* 11: 1403-1421.
- Platel, K., and K. Srinivasan. 2004. Digestive stimulant action of spices: A myth or reality? *Indian J Med Res* 119: 167-179.
- Magee, K., and C. Loiacono. 2004. A review of common herbs and potential interactions. *Int J Dent Hygiene* 2: 111-121.
- Lai, P. K., and J. Roy. 2004. Antimicrobial and chemopreventive properties of herbs and spices. *Curr Med Chem* 11: 1451-1460.
- Burt, S. 2004. EO: Their antibacterial properties and potential applications in foods: A review. *Int J Food Microbiol* 94: 223-253.
- Bent, S., and R. Ko. 2004. Commonly used herbal medicines in the united states: A review. *Am J Med* 116: 478-485.
- Arcila-Lozano, C. C., G. Loarca-Pina, S. Lecona-Urbe, and E. Gonzalez de Mejia. 2004. Oregano: Properties, composition and biological activity. *Arch Latinoam Nutr* 54: 100-111.

Innovation, extension and new approaches - Review (11)

- Lewinsohn, E. 1996. Molecular biology for the improvement of medicinal and aromatic plants. *Acta Hort. (ISHS)* 426: 443-467.
- Gould, G. W. 1996. Industry perspectives on the use of natural antimicrobials and inhibitors for food applications. *J Food Protect suppl. S*: 82-86.
- Tsai, T. H., C. Y. Hong, and C. F. Chen. 1997. Analysis of active ingredients in medicinal herbs with high-performance liquid chromatography and related technologies: A review. *J Food Drug Anal* 5: 303-317.
- Lis-Balchin, M. 1997. EO and 'aromatherapy': Their modern role in healing. *J R Soc Health* 117: 324-329.
- Chen, Y. T., and Y. C. Ling. 2000. An overview of supercritical fluid extraction in chinese herbal medicine: From preparation to analysis. *J Food Drug Anal* 8: 235-247.
- Marriott, P. J., R. Shellie, and C. Cornwell. 2001. Gas chromatographic technologies for the analysis of EO. *J Chromatogr A* 936: 1-22.
- Lang, Q. Y., and C. M. Wai. 2001. Supercritical fluid extraction in herbal and natural product studies - a practical review. *Talanta* 53: 771-782.
- Kneifel, W., E. Czech, and B. Kopp. 2002. Microbial contamination of medicinal plants: A review. *Planta Med* 68: 5-15.
- Huie, C. W. 2002. A review of modern sample-preparation techniques for the extraction and analysis of medicinal plants. *Anal Bioanal Chem* 373: 23-30.
- Zhou, S., H. L. Koh, Y. Gao, Z. Y. Gong, and E. J. Lee. 2004. Herbal bioactivation: The good, the bad and the ugly. *Life Sci* 74: 935-968.
- Shetty, K. 2004. Role of proline-linked pentose phosphate pathway in biosynthesis of plant phenolics for functional food and environmental applications: A review. *Process Biochemistry* 39: 789-803.

Specific applications and case studies - Review (4)

Todd, P. H. 1996. Improving foods with herbs and spices extracts. *Acta Hort. (ISHS)* 426: 259-271.

Dorman, H. J. D. 1999. *Phytochemistry and bioactive properties of plant volatile oils: Antibacterial, antifungal and antioxidant activities*, University of Strathclyde, Glasgow.

Galvano, F., A. Piva, A. Ritieni, and G. Galvano. 2001. Dietary strategies to counteract the effects of mycotoxins: A review. *J Food Protect* 64: 120-131.

Greathead, H. 2003. Plants and plant extracts for improving animal productivity. *Proc Nutr Soc* 62: 279-