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Phytochemistry in the Current Scenario

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Abstract:

Phytochemistry is the study of phytochemicals, which are chemicals derived from plants. Phytochemists strive to describe the structures of the large number of secondary metabolites found in plants, the functions of these compounds in human and plant biology, and the biosynthesis of these compounds. Plants synthesize phytochemicals for many reasons, including to protect themselves against insect attacks and plant diseases. The compounds found in plants are of many kinds, but most can be grouped into four major biosynthetic classes: alkaloids, phenylpropanoids, polyketides, and terpenoids.

Phytochemistry can be considered a subfield of botany or chemistry. Activities can be led in botanical gardens or in the wild with the aid of ethnobotany. Phytochemical studies directed toward human (i.e. drug discovery) use may fall under the discipline of pharmacognosy, whereas phytochemical studies focused on the ecological functions and evolution of phytochemicals likely fall under the discipline of chemical ecology. Phytochemistry also has relevance to the field of plant physiology.

Keywords: phytochemistry, secondary metabolites, diseases, ethnobotany, pharmacognosy, plants, ecology.

Introduction

Techniques commonly used in the field of phytochemistry are extraction, isolation, and structural elucidation (MS, 1D and 2D NMR) of natural products, as well as various chromatography techniques (MPLC, HPLC, and LC-MS). Many plants produce chemical compounds for defence against herbivores. The major classes of pharmacologically active phytochemicals are described below, with examples of medicinal plants that contain them.[1] Human settlements are often surrounded by weeds containing phytochemicals, such as nettle, dandelion and chickweed.[2][3]Many phytochemicals, including curcumin, epigallocatechin gallate, genistein, and resveratrol are pan-assay interference compounds and are not useful in drug discovery.[4][5]. Alkaloids are bitter-tasting chemicals, widespread in nature, and often toxic. There are several classes with different modes of action as drugs, both recreational and pharmaceutical.[6][7]

Medicines of different classes include atropine, scopolamine, and hyoscyamine (all from nightshade), the traditional medicine berberine (from plants such as Berberis and Mahonia), caffeine (Coffea), cocaine (Coca), ephedrine (Ephedra), morphine (opium poppy), nicotine (tobacco), reserpine (Rauvolfia serpentina), quinidine and quinine (Cinchona), vincamine (Vinca minor), and vincristine (Catharanthus roseus). Glycosides Anthraquinone glycosides are found in senna, rhubarb, and Aloe. [8]

The cardiac glycosides are phytochemicals from plants including foxglove and lily of the valley. They include digoxin and digitoxin which act as diuretics. Polyphenols of several classes are widespread in plants, including anthocyanins, phytoestrogens, and tannins. Terpenes and terpenoids of many kinds are found in resinous plants such as the conifers. They are aromatic and serve to repel herbivores. Their scent makes them useful in essential oils, whether for perfumes such as rose and lavender, or for aromatherapy. Some have had medicinal uses: thymol is an antiseptic and was once used as a vermifuge (anti-worm medicine). Contrary to bacteria and fungi, most plant metabolic pathways are not grouped into biosynthetic gene clusters, but instead are scattered as individual genes. Some exceptions have been discovered: steroidal glycoalkaloids in Solanum, polyketides in Pooideae, benzoxazinoids in Zea mays, triterpenes in Avena sativa, Cucurbitaceae, Arabidopsis, and momilactone diterpenes in Oryza sativa.[9]

The phytochemical category includes compounds recognized as essential nutrients, which are naturally contained in plants and are required for normal physiological functions, so must be obtained from the diet in humans.[17][18]Some phytochemicals are known phytotoxins that are toxic to humans;[19][20] for example aristolochic acid is carcinogenic at low doses.[21] Some phytochemicals are antinutrients that interfere with the absorption of nutrients.[22] Others, such as some polyphenols and flavonoids, [10][11]may be pro-oxidants in high ingested amounts.[23]Non-digestible dietary fibers from plant foods, often considered as a phytochemical,[24] are now generally regarded as a nutrient group having approved health claims for reducing the risk of some types of cancer[25] and coronary heart disease.[26]Eating a diet high in fruits, vegetables, grains, legumes and plant-based beverages has long-term health benefits,[17] but there is no evidence that taking dietary supplements of non-nutrient phytochemicals extracted from plants similarly benefits health.[4] Phytochemical supplements are neither recommended by health authorities for improving health[5][27] nor approved by regulatory agencies for health claims on product labels.[28][29].

While health authorities encourage consumers to eat diets rich in fruit, vegetables, whole grains, legumes, and nuts to improve and maintain health,[17] evidence that such effects result from specific, non-nutrient phytochemicals is limited or absent.[4] For example, systematic reviews and/or meta-analyses indicate weak or no evidence for phytochemicals from plant food consumption having an effect on breast, lung, or bladder cancers.[30][31] Further, in the United States, regulations exist to limit the language on product labels for how plant food consumption may affect cancers, excluding mention of any phytochemical except for those with established health benefits against cancer, such as dietary fiber, vitamin A, and vitamin C.[32]Phytochemicals, such as polyphenols, have been specifically discouraged from food labeling in Europe and the United States because there is no evidence for a cause-and-effect relationship between dietary polyphenols and inhibition or prevention of any disease.[28][33]Among carotenoids such as the tomato phytochemical, lycopene, the US Food and Drug Administration found insufficient evidence for its effects on any of several cancer types, resulting in limited language for how products containing lycopene can be described on labels.[34]

Plants synthesize a variety of phytochemicals, but most are derivatives: [12][13]

- Alkaloids are a class of chemical compounds containing a nitrogen ring. Alkaloids are produced by a large variety of organisms, including bacteria, fungi, plants, and animals, and are part of the group of natural products (also called secondary metabolites). Many alkaloids can be purified from crude extracts by acid-base extraction. Many alkaloids are toxic to other organisms.
- Polyphenols (a.k.a. phenolics) are compounds that contain phenol rings. The anthocyanins that give grapes their purple color, the isoflavones, the phytoestrogens from soy and the tannins that give tea its astringency are phenolics.
- Glycosides are molecules in which a sugar is bound to a non-carbohydrate moiety, usually a small organic molecule. Glycosides play numerous important roles in living organisms. Many plants store chemicals in the form of inactive glycosides. These can be activated by enzyme hydrolysis, which causes the sugar part to be broken off, making the chemical available for use.
- Terpenes are a large and diverse class of organic compounds, produced by a variety of plants, particularly conifers, which are often strong smelling and thus may have a protective function. They are the major components of resins, and of turpentine produced from resins. When terpenes are modified chemically, such as by oxidation or rearrangement of the carbon skeleton, the resulting compounds are generally referred to as terpenoids. Terpenes and terpenoids are the primary constituents of the essential oils of many types of plants and flowers. Essential oils are used widely as natural flavor additives for food, as fragrances in perfumery, and in traditional and alternative medicines such as aromatherapy. Synthetic variations and derivatives of natural terpenes and terpenoids also greatly expand the variety of aromas used in perfumery and flavors used in food additives. The fragrance of rose and lavender is due to monoterpenes. The carotenoids produce shades of red, yellow and orange in pumpkin, maize, and tomatoes.[14][15][16]

Discussion

The chemical ecology of plant-insect interaction is a significant subfield of chemical ecology.[2][4][5] In particular, plants and insects are often involved in a chemical evolutionary arms race. As plants develop chemical defenses to herbivory, insects which feed on them evolve immunity to these poisons, and in some cases, repurpose these poisons for their own chemical defense against predators. For example, caterpillars of the monarch butterfly sequester cardenolide toxins from their milkweed host-plants and are able to use them as an anti-predator defense. Whereas most insects are killed by cardenolides, which are potent inhibitors of the Na+/K+-ATPase, monarchs have evolved resistance to the toxin over their long evolutionary history with milkweeds. Other examples of sequestration include the tobacco hornworm Manduca sexta, which use nicotine sequestered from tobacco plants in predator defense;[4] and the bella moth, which secretes a quinone-containing froth to deter predators obtained from feeding on Crotalaria plants as a caterpillar.[17][18]

Chemical ecologists also study chemical interactions involved in indirect defenses of plants, such as the attraction of predators and parasitoids through herbivore-induced volatile organic compounds (VOCs). Plant interactions with microorganisms are also mediated by chemistry. Both constitutive and induced secondary metabolites are involved in plant defense against pathogens and chemical signals are also important in the establishment and maintenance of resource mutualisms. For example, both rhizobia and mycorrhizae depend on chemical signals, such as strigolactones and flavanoids exuded from plant roots, in order to find a suitable host.

For microbes to gain access to the plant, they must be able to penetrate the layer of wax that forms a hydrophobic barrier on the plant's surface. Many plant-pathogenic microbes secrete enzymes that break down these cuticular waxes. Mutualistic microbes on the other hand may be granted access. For example, rhizobia secrete Nod factors that trigger the formation of an infection thread in receptive plants. The rhizobial symbionts can then travel through this infection thread to gain entrance to root cells.[19][20]

Mycorrhizae and other fungal endophytes may also benefit their host plants by producing antibiotics or other secondary metabolites that ward off harmful fungi, bacteria and herbivores in the soil. Some entomopathogenic fungi can also form endophytic relationships with plants and may even transfer nitrogen directly to plants from insects they consume in the surrounding soil.

Chemical ecology has been utilized in the development of sustainable pest control strategies. Semiochemicals (especially insect sex pheromones) are widely used in integrated pest management for surveillance, trapping and mating disruption of pest insects. Unlike conventional insecticides, pheromone-based methods of pest control are generally species-specific, non-toxic and extremely potent. In forestry, mass trapping has been used successfully to reduce tree mortality from bark beetle infestations in spruce and pine forests and from palm weevils in palm plantations. In an aquatic system, a sex pheromone from the invasive sea lamprey has been registered by the United States Environmental Protection Agency for deployment in traps. A strategy has been developed in Kenya to protect cattle from trypanosomiasis spread by Tsetse fly by applying a mixture of repellent odors derived from a non-host animal, the waterbuck.

The successful push-pull agricultural pest management system makes use of chemical cues from intercropped plants to sustainably increase agricultural yields. The efficacy of push-pull agriculture relies on multiple forms of chemical communication. Though the push-pull technique was invented as a strategy to control stem-boring moths, such as *Chilo partellus*, through the manipulation of volatile host-finding cues, it was later discovered that allelopathic substances exuded by the roots of *Desmodium spp.* also contribute to the suppression of the damaging parasitic weed, *Striga*. [21][22]

A large proportion of commercial drugs (e.g. aspirin, ivermectin, cyclosporin, taxol) are derived from natural products that evolved due to their involvement in ecological interactions. While it has been proposed that the study of natural history could contribute to the discovery of new drug leads, most drugs derived from natural products were not discovered due to prior knowledge of their ecological functions. However, many fundamental biological discoveries have been facilitated by the study of plant toxins. For example, the characterization of the nicotinic acetylcholine receptor, the first neurotransmitter receptor to be identified, ensued from investigations into the mechanisms of action of curare and nicotine. Similarly, the muscarinic acetylcholine receptor takes its name from the fungal toxin muscarine.

Ethnopharmacology is a related field which studies ethnic groups and their use of plant compounds. It is linked to pharmacognosy, phytotherapy (study of medicinal plants) use and ethnobotany, as this is a source of lead compounds for drug discovery. Emphasis has long been on traditional medicines, although the approach also has proven useful to the study of modern pharmaceuticals. [23][24][25]

It involves studies of the:

1. identification and ethnotaxonomy (cognitive categorisation) of the (eventual) natural material, from which the candidate compound will be produced
2. traditional preparation of the pharmaceutical forms

3. bio-evaluation of the possible pharmacological action of such preparations (ethnopharmacology)
4. their potential for clinical effectiveness
5. socio-medical aspects implied in the uses of these compounds (medical anthropology).[26]

Results

Archaeological evidence indicates that the use of medicinal plants dates back to the Paleolithic age, approximately 60,000 years ago. Written evidence of herbal remedies dates back over 5,000 years to the Sumerians, who compiled lists of plants. Some ancient cultures wrote about plants and their medical uses in books called *herbals*. In ancient Egypt, herbs are mentioned in Egyptian medical papyri, depicted in tomb illustrations, or on rare occasions found in medical jars containing trace amounts of herbs. In ancient Egypt, the Ebers papyrus dates from about 1550 BC, and covers more than 700 compounds, mainly of plant origin. The earliest known Greek herbals came from Theophrastus of Eresos who, in the 4th century BC, wrote in Greek *Historia Plantarum*, from Diocles of Carystus who wrote during the 3rd century BC, and from Krateuas who wrote in the 1st century BC. Only a few fragments of these works have survived intact, but from what remains, scholars noted overlap with the Egyptian herbals. Seeds likely used for herbalism were found in archaeological sites of Bronze Age China dating from the Shang dynasty[11] (c. 1600–1046 BC). Over a hundred of the 224 compounds mentioned in the *Huangdi Neijing*, an early Chinese medical text, are herbs. Herbs were also commonly used in the traditional medicine of ancient India, where the principal treatment for diseases was diet. *De Materia Medica*, originally written in Greek by Pedanius Dioscorides (c. 40–90 AD) of Anazarbus, Cilicia, a physician and botanist, is one example of herbal writing used over centuries until the 1600s.

There are many forms in which herbs can be administered, the most common of which is a liquid consumed as a herbal tea or a (possibly diluted) plant extract. [27][28]

Herbal teas, or tisanes, are the resultant liquid of extracting herbs into water, though they are made in a few different ways. Infusions are hot water extracts of herbs, such as chamomile or mint, through steeping. Decoctions are the long-term boiled extracts, usually of harder substances like roots or bark. Maceration is the cold infusion of plants with high mucilage-content, such as sage or thyme. To make macerates, plants are chopped and added to cold water. They are then left to stand for 7 to 12 hours (depending on herb used). For most macerates, 10 hours is used.

Tinctures are alcoholic extracts of herbs, which are generally stronger than herbal teas.[27] Tinctures are usually obtained by combining pure ethanol (or a mixture of pure ethanol with water) with the herb. A completed tincture has an ethanol percentage of at least 25% (sometimes up to 90%).[26] Non-alcoholic tinctures can be made with glycerin but it is believed to be less absorbed by the body than alcohol based tinctures and has a shorter shelf life. Herbal wine and elixirs are alcoholic extract of herbs, usually with an ethanol percentage of 12–38%. Extracts include liquid extracts, dry extracts, and nebulisates. Liquid extracts are liquids with a lower ethanol percentage than tinctures. They are usually made by vacuum distilling tinctures. Dry extracts are extracts of plant material that are evaporated into a dry mass. They can then be further refined to a capsule or tablet. [29][30]

The exact composition of an herbal product is influenced by the method of extraction. A tea will be rich in polar components because water is a polar solvent. Oil on the other hand is a non-polar solvent and it will absorb non-polar compounds. Alcohol lies somewhere in between.

Many herbs are applied topically to the skin in a variety of forms. Essential oil extracts can be applied to the skin, usually diluted in a carrier oil. Many essential oils can burn the skin or are simply too high dose used straight; diluting them in olive oil or another food grade oil such as almond oil can allow these to be used safely as a topical. Salves, oils, balms, creams, and lotions are other forms of topical delivery mechanisms. Most topical applications are oil extractions of herbs. Taking a food grade oil and soaking herbs in it for anywhere from weeks to months allows certain phytochemicals to be extracted into the oil. This oil can then be made into salves, creams, lotions, or simply used as an oil for topical application. Many massage oils, antibacterial salves, and wound healing compounds are made this way. Inhalation, as in aromatherapy, can be used as a treatment.

Examples of herbal treatments with likely cause-effect relationships with adverse events include aconite (which is often a legally restricted herb), Ayurvedic remedies, broom, chaparral, Chinese herb mixtures, comfrey, herbs containing certain flavonoids, germander, guar gum, liquorice root, and pennyroyal. Examples of herbs that may have long-term adverse effects include ginseng, the endangered herb goldenseal, milk thistle, senna (against which herbalists generally advise and rarely use), aloe vera juice, buckthorn bark and berry, cascara sagrada bark, saw palmetto, valerian, kava (which is banned in the European Union), St. John's wort, khat, betel nut, the restricted herb ephedra, and guarana. [31][32]

There is also concern with respect to the numerous well-established interactions of herbs and drugs. In consultation with a physician, usage of herbal remedies should be clarified, as some herbal remedies have the potential to cause adverse drug interactions when used in combination with various prescription and over-the-counter pharmaceuticals, just as a customer should inform a herbalist of their consumption of actual prescription and other medication.

For example, dangerously low blood pressure may result from the combination of an herbal remedy that lowers blood pressure together with prescription medicine that has the same effect. Some herbs may amplify the effects of anticoagulants. Certain herbs as well as common fruit interfere with cytochrome P450, an enzyme critical to much drug metabolism. [35]

In a 2018 study, FDA identified active pharmaceutical additives in over 700 of analyzed dietary supplements sold as "herbal", "natural" or "traditional". The undisclosed additives included "unapproved antidepressants and designer steroids", as well as prescription drugs, such as sildenafil or sibutramine. In some countries, formalized training and minimum education standards exist for herbalists, although these are not necessarily uniform within or between countries. In Australia, for example, the self-regulated status of the profession (as of 2009) resulted in variable standards of training, and numerous loosely formed associations setting different educational standards.One 2009 review concluded that regulation of herbalists in Australia was needed to reduce the risk of interaction of herbal medicines with prescription drugs, to implement clinical guidelines and prescription of herbal products, and to assure self-regulation for protection of public health and safety. In the United Kingdom, the training of herbalists is done by state-funded universities offering Bachelor of Science degrees in herbal medicine. In the United States, according to the American Herbalist Guild, "there is currently no licensing or certification for herbalists in any state that precludes the rights of anyone to use, dispense, or recommend herbs." However, there are U.S. federal restrictions for marketing herbs as cures for medical conditions, or essentially practicing as an unlicensed physician.[33][34]

Conclusions

Paraherbalism is the pseudoscientific use of extracts of plant or animal origin as supposed medicines or health-promoting agents. Phytotherapy differs from plant-derived medicines in

standard pharmacology because it does not isolate and standardize the compounds from a given plant believed to be biologically active. It relies on the false belief that preserving the complexity of substances from a given plant with less processing is safer and potentially more effective, for which there is no evidence either condition applies. [36]

Phytochemical researcher Varro Eugene Tyler described paraherbalism as "faulty or inferior herbalism based on pseudoscience", using scientific terminology but lacking scientific evidence for safety and efficacy. Tyler listed ten fallacies that distinguished herbalism from paraherbalism, including claims that there is a conspiracy to suppress safe and effective herbs, herbs can not cause harm, that whole herbs are more effective than molecules isolated from the plants, herbs are superior to drugs, the doctrine of signatures (the belief that the shape of the plant indicates its function) is valid, dilution of substances increases their potency (a doctrine of the pseudoscience of homeopathy), astrological alignments are significant, animal testing is not appropriate to indicate human effects, anecdotal evidence is an effective means of proving a substance works and herbs were created by God to cure disease. Tyler suggests that none of these beliefs have any basis in fact. [37][38]

In India, Ayurvedic medicine has quite complex formulas with 30 or more ingredients, including a sizable number of ingredients that have undergone "alchemical processing", chosen to balance dosha. In Ladakh, Lahul-Spiti, and Tibet, the Tibetan Medical System is prevalent, also called the "Amichi Medical System". Over 337 species of medicinal plants have been documented by C.P. Kala. Those are used by Amchis, the practitioners of this medical system. The Indian book, Vedas, mentions treatment of diseases with plants.

Herbalists tend to use extracts from parts of plants, such as the roots or leaves, believing that plants are subject to environmental pressures and therefore develop resistance to threats such as radiation, reactive oxygen species and microbial attack to survive, providing defensive phytochemicals of use in herbalism. Chinese patent medicine (中成药; 中成藥; *zhōngchéng yào*) is a kind of traditional Chinese medicine. They are standardized herbal formulas. From ancient times, pills were formed by combining several herbs and other ingredients, which were dried and ground into a powder. They were then mixed with a binder and formed into pills by hand. The binder was traditionally honey. Modern teapills, however, are extracted in stainless steel extractors to create either a water decoction or water-alcohol decoction, depending on the herbs used. They are extracted at a low temperature (below 100 degrees Celsius) to preserve essential ingredients. The extracted liquid is then further condensed, and some raw herb powder from one of the herbal ingredients is mixed in to form an herbal dough. This dough is then machine cut into tiny pieces, a small amount of excipients are added for a smooth and consistent exterior, and they are spun into pills.[39][40]

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