Allelochemics: Chemical Interactions between Species

Chemical agents are of major significance in the adaptation of species and organization of communities.

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It is not simply true that nature is red in tooth and claw. Not only are cooperation and differentiation toward the reduction of competition important in the function of natural communities, the means of antagonism between animals are far more varied than carnage. Many interactions of attack, defense, and behavioral response involve not physical force but chemical agents. The study of these interactions, and of the arrays of chemicals on which they are based, is the subject of the new and rapidly expanding field of chemical ecology (*1*). Chemicals that serve as messages between members of a species are termed pheromones (*2*). We review here a class of interactions termed allelochemic (*3, 4*), involving chemicals by which organisms of one species affect the growth, health, behavior, or population biology of organisms of another species (excluding substances used only as foods by the second species).

Allelopathy in Higher Plants

Such effects appear, for example, in the suppression of the growth or occurrence of some higher plants by chemicals released from another higher plant —the phenomenon of allelopathy (*3–11*).

Allelopathic effects in shrub communities have been studied by C. H. Muller and others in the hills near Santa Barbara, California. In one shrub type, the hard chaparral, rainwash carries a variety of more or less toxic substances, many of them phenolic compounds, to the soil where they inhibit the germination and growth of herb seeds present in the soil. The effectiveness of the inhibition can be seen after a fire, for destruction by fire of those parts of the shrubs above ground releases the herb seeds from inhibition. Annual herbs bloom in profusion for a few years after fires until regrowth of the shrubs subjects the herbs to new inhibition (*12*). The other major shrub community of the area, the soft chaparral, invades grasslands; on some soils in dry periods the invading shrub patches are surrounded by belts of bare soil 1 to 2 meters wide and devoid of herbs and wider belts in which growth of the grassland plants is reduced. The search for a cause of the bare belts led to a study of the volatile terpenes (camphor, cineole, and so forth) that are released from the leaves into the air and which give the community its characteristic fragrance (*5, 13*). The terpenes are adsorbed from the air onto soil particles, and on certain clay soils the terpenes accumulate in the soil during the dry season to amounts effective in inhibiting germination and growth of herb seedlings (*14*).

Walnut trees (*Juglans* spp.) produce allelopathic effects through a chemical agent, juglone, washed from leaf surfaces to the soil (*15*). Allelopathic effects have also been observed for other trees (*16–19*), shrubs (*20, 21*), and herbs (*22, 23*), including cereal crops and weeds (*6, 10, 24, 25*). Some of these effects are produced by substances released from the living plant by rainwash or root exudation (*26*); others result from decomposition of litter and dead remains of roots (*6, 27*). Some effects are indirect, such as those observed in successions on abandoned farm fields in Oklahoma. Phenolic acids released by the grass *Aristida oligantha* (and other old-field species) inhibit the nitrogen-fixing bacteria and blue-green algae of the soil. Low concentrations of available nitrogen in the soil, to which the *Aristida* itself is tolerant, slow the invasion and replacement of this grass community by other species (*22*).

These and other observations suggest a number of general points on allelopathic phenomena (*3, 5*):

1) *Variety of routes of release.* Allelopathic materials are variously released by rainwash or by fog drip (*17*) from leaf surfaces and glands, by volatilization from leaves, by excretion or exudation from roots, and by decay of above-ground or below-ground plant parts, or both. The poison will out: accumulations of potentially toxic materials in plants will find their way into the soil sooner or later, by one route or another.

2) *Widespread occurrence.* Allelopathetic effects have been reported for agricultural and wild species of most varied growth forms and kinds of communities from rain-forest trees (*18*) to desert shrubs (*21*). It is reasonable to judge that allelopathic effects are common and that the observed cases stand out from a background of more widespread, less conspicuous effects on plant growth and populations (*3*).

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3) *Significance in plant communities* (*3, 5*). Allelopathy may consequently be of widespread significance in plant communities. In plant succession a dominant species may, by allelopathic suppression, speed its invasion of a preceding community and delay its replacement by other species. In both successional and climax communities strongly dominated by a single species, chemical effects of that species on the soil may limit the number of other species able to occur with it. In communities in which a number of canopy species are mixed together, these may form a mosaic of differing chemical effects on the soil which may contribute (along with microrelief, light differences, and so forth) to the patterning and species diversity of the undergrowth.

4) *Autotoxicity*. Allelopathic self-inhibition has been reported for a number of successional species (*23*) and agricultural plants (*7, 24*), for *Eucalyptus* (*19*), and for one climax rain-forest tree (*18*). Self-toxicity is an evolutionary paradox. One supposes that some selective advantage from production of toxic compounds outweighs the disadvantage of self-inhibition. Self-toxicity may be no serious disadvantage for successional species, since these are vagabond populations that dominate a community for only a short period in a given place.

5) *Chemical character of allelopathic substances*. The known agents of allelopathy belong to a few major groups of compounds among the secondary plant substances; these include phenolic acids, flavonoids, and other aromatic compounds, terpenoid substances, steroids, alkaloids, and organic cyanides.

6) *Treatment in the plant*. In general, allelopathic compounds (and other secondary substances) occur in plants in ways that protect the plant against their effects (*3, 5*). Many of these compounds occur as glycosides; the substance, which may be toxic, is combined with a sugar and thereby rendered innocuous within the plant. Innocuous or not, the glycosides are commonly in solution in vacuoles of cells, and therefore further separated from protoplasmic function. Other secondary substances occur as polymers (tannins, lignins, resins, and rubbers) or as crystals (calcium oxalate raphides). Many of the substances are deposited outside living cells in the dead heartwood, in dead cells or spaces between cells, in ducts, or in the glandular hairs found on the surfaces of many plants. Some substances are, finally, discharged from the plant by leaching from the leaf surface, exudation from the roots, or volatilization. The secondary substances are thus treated like toxic wastes to be inactivated in or excreted from the plant, or both. The search for an evolutionary interpretation of plants' copious production of substances against which they must protect themselves may well lead to study of the interactions of higher plants with other organisms.

Land Plants and Their Enemies

The curious naturalist may wonder why, in the face of depredations by countless animal consumers, green plants are dominant over much of the earth's land surface. One answer is that herbivores are not limited by their food supply, but rather by other factors (such as predation and disease) that prevent their populations from increasing until their food supply is consumed (*28*). We prefer a second answer, suggested as early as 1888 by Stahl (*29*), which holds that not all that is green is palatable to animals. The evolution of thorns and spines by so many plant species attests to the strength of selection exerted by herbivores. Though the majority of plants, apparently as successful as thistles and roses, lack defensive thorns, it is increasingly clear that they do not lack defense.

The storybook picture of a cow contentedly chewing a buttercup is misleading. Buttercups (*Ranunculus* spp.) are strongly distasteful to grazing animals and are rejected until other forage is gone. Several species are known to release protoanemonin, an irritant which can lead to fatal convulsions in livestock (*30*). Cattle on western ranges frequently fall victim to larkspurs (*Delphinium* spp.) containing neurotoxic alkaloids such as delphinine (*31*). Nicotine and other alkaloids cause paralysis of aphids on tobacco plants (*32*). Steroid cardiac glycosides lead to convulsive heart attacks in vertebrates eating foxglove (*Digitalis purpurea*) or certain other plants, and a single leaf of oleander (*Nerium oleander*) is potentially lethal to man (*30, 33*).

The action of toxic plant substances is sometimes less direct. Tannins bind proteins into indigestible complexes which contribute to the growth-inhibitory properties of mature oak leaves for vertebrates (*34*) and moth larvae (*35*). Tannins also inhibit fungal growth and virus transmission (*36*), thus providing many plants with a broad-spectrum defense against both animal and microbial enemies (*37*).

Normal growth and development of insects depends on the precisely timed waxing and waning of amounts of molting and juvenile hormones (*38*). Several plant species, mostly gymnosperms, are now known to contain substantial amounts not only of the molting hormones, α- and β-ecdysone, but also of analogs of even greater activity (*39*). If a certain critical dose of these phytoecdysones is exceeded, insect metamorphosis is fatally accelerated (*38*); larvae of the *Cecropia* moth, for example, are doomed by ingestion of food containing only 1 part of ponasterone-A per billion (*40*). Juvenile hormone activity also is present in some plants. The "paper factor" (juvabione), present in the pages of *Science* and other products of American paper pulp, was finally isolated from the balsam fir *Abies balsamea* (*41*). Applied to bugs of the family Pyrrhocoridae, this substance arrests development at an immature stage and prevents the formation of a normal adult (*38, 42*). The insect hormones and analogs occurring in plants are now believed to represent a fiendishly subtle mechanism of defense (*38*).

Hypericin is a crimson-colored dianthrone derivative secreted from glands on plants of the genus *Hypericum*. Hypericin is responsible for intense photosensitivity and skin irritation, leading sometimes to fatal blindness and starvation, when these plants are eaten by animals (*30*). Although plants containing hypericin are avoided by almost all herbivores, several beetles of the genus *Chrysolina* have evidently evolved a mechanism for detoxifying hypericin and thus have a food supply almost untouched by other herbivores. At least one species, *C. brunsvicensis*, has further turned the evolutionary scales on the plants by using the repellent as a cue to locate its food. The beetles explore leaf surfaces with their tarsal chemoreceptors until hypericin, present on the leaf surface, triggers feeding (*43*).

Similar coadaptation is now known or presumed to have developed between a wide variety of insects and their food plants (*29, 44, 45*). A significant portion of the entire insect and microbial community associated with the plant family Cruciferae owes its organization to a single set of chemicals, the mustard oils and their glycosides (*46*). Herbivores responding to these compounds include the cabbage white butterflies *Pieris rapae* and *P. brassicae* (*47, 48*); the diamondback moth, *Plutella maculipennis* (*48, 49*); the vegetable weevil *Listroderes costirostris* (*50*); the mustard beetle, *Phaedon cochleariae* (*51*); the flea beetles *Phyllotreta cruciferae* and *P. striolata* (*52*); and the cabbage aphid, *Brevicoryne brassicae* (*53*). The mustard oil allyl isothiocyanate acts also as an attractant for *Diaeretiella rapae* (Braconidae), a primary parasite of crucifer-feeding aphids (*54*), and as a germination stimulant for spores of the parasitic fungus *Plasmodiophora brassicae* (*55*). Mustard oils are irritants, capable of causing serious injury to animal tissue (*30*) and are also among the most potent antibiotics known from higher plants (*56*). Like hypericin, they are a chemical defense that has been exploited as a behavioral cue by some of the plants' enemies.

Most herbivore species attack few species of food plants from among the many available. Yet almost all plants are attacked by some species. Herbivores have evidently evolved the means of detoxifying most of the toxic materials in plants, but not all of them are detoxified by any one species. A specialist insect presumably gains an advantage by restricting its detoxification energies to one or a few potentially harmful substrates, whereas a polyphagous species must spend more of its energy and nutrients maintaining mechanisms of detoxification for a wide range of chemically defended plants (that is, it carries a higher "metabolic load"). The activity of a mixed-function oxidase system in the gut of moth and butterfly larvae is considerably higher in polyphagous species than in species restricted to one family of food plants. Pyrethrins are among the many insecticides metabolized by these enzymes. In *Chrysanthemum cinerariaefolium* flowers the occurrence alongside pyrethrins of the lignan sesamin, an inhibitor of mixed-function oxidases, suggests a further turn to the evolutionary arms race between plants and insects (*57*). Vertebrate herbivores may be less specialized than insects because of the lower cost of a general detoxifying ability relative to their total energy and nutrient budget and because they may rely more on phenotypic learning ability than on genetically programmed responses to specific chemical cues.

The roles of secondary substances in the adaptive linkages of plants and animals are thus variously ambivalent. Some chemicals are repellents or toxins, and others such as flower scents and fruit flavors are attractants for the advantage of the plants; of the repellents some have subsequently come to attract enemies of the plant. For the animals some substances are poisons or tolerated toxins and some (that may be among these toxins) are essential behavioral cues.

Defense and Attack in Animals

Most plant chemical defenses are passive: parts of the plant must be eaten before a repellent effect is felt. Animals, by contrast, cannot afford to allow parts of their bodies to be ingested before a predator realizes its mistake, and their chemical defenses are frequently forced to immediate attention through sprays, bites, or stings. North Americans are all too familiar with the odor of butyl mercaptan, the defense spray of the skunk that effects a posthumous revenge on passing motorists. Like many animals whose defense is directed primarily against predators with ability to learn (especially vertebrates), the skunk is aposematically colored to help the predator avoid future mistakes (*58*).

It is among the invertebrates, and especially the arthropods, that chemical defense seems to have reached its peak of diversification (*59, 60*). Bombardier beetles (*Brachinus* spp.) spray intruding predators with a secretion containing quinones. The moment the beetles are struck by a predator the hot secretion is discharged with an audible detonation, and the beetles are instantly rejected (*60*). In this genus of beetles, the quinones are formed by a reaction between the phenolic precursors and hydrogen peroxide, occurring in a special two-chambered gland. When the contents of the two chambers are mixed, catalase promotes the liberation of oxygen from the hydrogen peroxide and the phenols are oxidized to quinones in an exothermic reaction. The pressure of the liberated oxygen provides the explosive propellent for the spray (*60, 61*). Most insect defenses are less elaborate than the bombardier's spray. Compounds used include lower aliphatic acids, aldehydes, ketones, esters, lactones, hydrogen cyanide, phenols, and quinones. The defensive secretions of some pentatomid bugs comprise as many as 18 components (*62*).

Some species of milkweed (Asclepiadaceae), such as *Asclepias curassavica*, contain cardiac glycosides that have a digitalis-like action on the vertebrate heart. Monarch caterpillars reared on *A. curassavica* develop into adults which are strongly distasteful to birds (*63*). The monarch, the grasshopper *Poekilocercus bufonius*, and several other insect species associated with milkweeds evidently retain the toxic compounds from their food and use them for their own defense (*63*).

Many animals use venoms to capture and kill their prey. The active components of snake venoms are mixtures of proteins or peptides of two general categories, toxins and hydrolytic enzymes (*64*). The neurotoxins and cardiotoxins, possessed by only some species, act directly on the vertebrate nervous system to produce paralysis and respiratory failure. As little as 0.12 microgram of neurotoxin from cobra venom will kill a mouse (*65*). The venoms of some parasitic wasps and solitary bees are used regularly for the paralysis of their victims and, when necessary, for defense. These venoms rival in potency some bacterial toxins; one part of *Bracon hebetor* venom in 200 million parts of host blood causes permanent paralysis in late instar larvae of *Galleria mellonella* (*66*). The reduviid *Platymeris rhadamanthus* of East Africa and other predatory bugs inject insect prey with toxic salivary secretions which, like snake venoms, consist of mixtures of tissue-destroying enzymes (*67*). In *Platymeris*, the secretion doubles as a defensive spray against vertebrate predators (*67*).

Many mammals hunt with the aid of a keen sense of smell and probably respond to a combination of many components characterizing the scent of their prey. Sometimes, however, specific chemicals emanating from animals are used as sensory cues by other species. When feeding on ponderosa pine, male *Ips confusus* bark beetles release in their frass three terpene alcohols which are aggregating pheromones; they bring about mass infestations of a tree by the beetles. Two of the compounds serve also to attract both sexes of the beetle *Enoclerus lecontei*, a predator of *Ips confusus*. Evidently the predators use the bark beetle pheromones as a cue to find high densities of their prey (*68*).

Interspecific use of intraspecific pher-

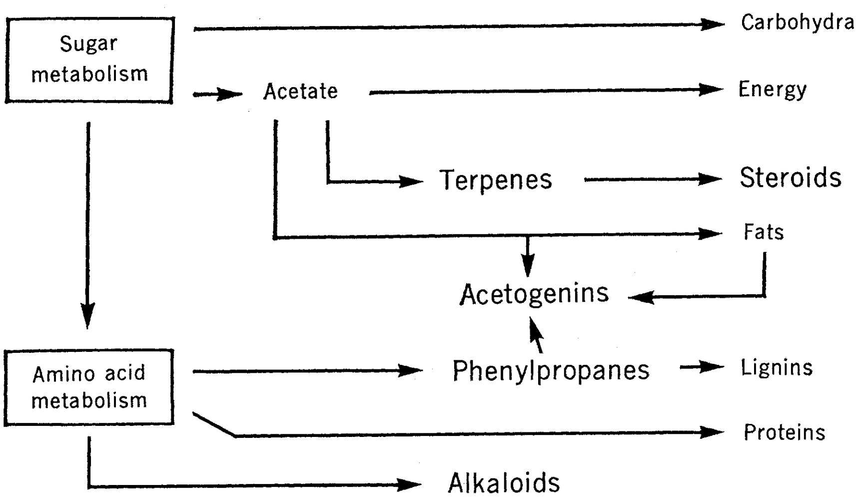

Fig. 1. Metabolic relationships of the major groups of secondary compounds (shown in large type) to primary metabolism.

omones may be widespread. *Camponotus beebei* ants are able to exploit the system of odor trails of *Azteca chartifex* ants, although the *Azteca* ants are unable to follow the trails of *Camponotus* (*69*). Nymphs and females of the roach *Attaphila fungicola* inhabit fungus gardens of the ant *Atta texana* and are attracted to the ant's odor-trail pheromones (*70*). The female polyphemus moth, *Antheraea polyphemus*, will only release a sex pheromone when she has first responded to an odor (*trans*-2-hexenal) from red-oak leaves, which are suitable food for her larvae (*71*). The sex pheromone of the moth *Bryotopha similis* (Gelechiidae) is *cis*-9-tetradecenyl acetate; that of a closely related sibling species (previously not recognized as a separate species) is the geometrical *trans* isomer of the same compound. The pheromone of either species actually repels males of the other species, thus reinforcing reproductive isolation between the two species (*72*). Trail odors are left in areas searched for hosts by parasitic wasps of the genera *Pleolophus, Endasys*, and *Mastrus*, and these odors serve as cues for avoidance of duplicated effort in searching both by the species that has left them and by other wasp species parasitic on the same host (*73*).

We have discussed only a small fraction of the known cases of allelochemic interactions among the higher plants and animals. Yet they illustrate both the remarkable variety of secondary chemicals and the vital role of such chemicals in many kinds of interspecific interactions, including predation, parasitism, selection of habitat and food, competition, dispersal, defense, and organization of communities. The natural environment is a maze of chemical stimuli, unappreciated by man but of vital importance for the survival of many plant and animal species. The role of form and color in adaptation has long been known, but more recent research with current chemical techniques has been necessary to elucidate some of the wealth of chemical adaptations that are of at least equal significance in the interrelations of species in natural communities.

Chemistry of Secondary Substances

Most allelochemic interactions involve the diverse secondary substances (*3, 29*), which do not occur in all living matter but appear sporadically throughout the living world. They are contrasted with the primary substances, such as various proteins, carbohydrates, nucleic acids, and fats, which are of general occurrence and metabolic importance (*74*). With few exceptions, secondary chemicals can be classified on biosynthetic grounds into five major groups: phenylpropanes, acetogenins, terpenoids, steroids, and alkaloids. Generally speaking, these compounds are offshoots from metabolic pathways with important functions in primary metabolism (Fig. 1). The great diversity of natural products arises from surprisingly few starting materials, chief of which are acetic acid and a few common amino acids. The following outline omits the details of biosynthesis and of stereochemistry so that the overall pattern of metabolic origins will be more apparent. No attempt is made to distinguish the groups of organisms in which particular pathways have been established. The overall assumption is that secondary compounds have broadly similar origins in all living matter.

Phenylpropanes arise from phenylalanine and its congeners, themselves derived from simple carbohydrates via the shikimic acid (No. **1**) pathway (*75*). Deamination of phenylalanine and tyrosine (No. **2**), for example, leads to the simple phenylpropanes cinnamic and *p*-coumaric (No. **3**) acids, respectively (*76*). The benzene ring may retain the 3,4,5-substitution pattern of shikimic acid, or this may be reduced as in ferulic (No. **4**), *p*-coumaric (No. **3**), and cinnamic acids. The more volatile phenylpropanes contribute characteristic odors and flavors to many herbs and spices, such as cinnamon (cinnamaldehyde) and cloves (eugenol, No. **5**) (*77*).

The shikimic acid pathway also gives rise to a wide variety of simple phenols such as protocatechuic and gallic (No.

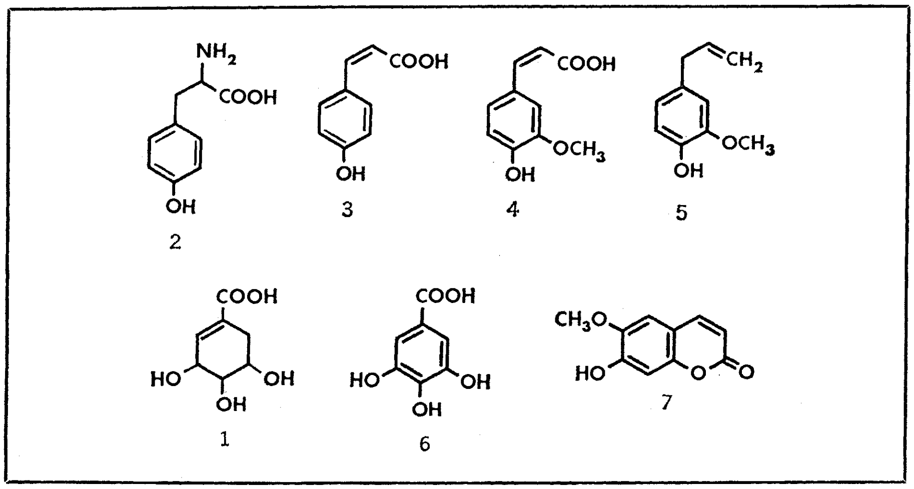

Fig. 2. Some representative phenylpropanes.

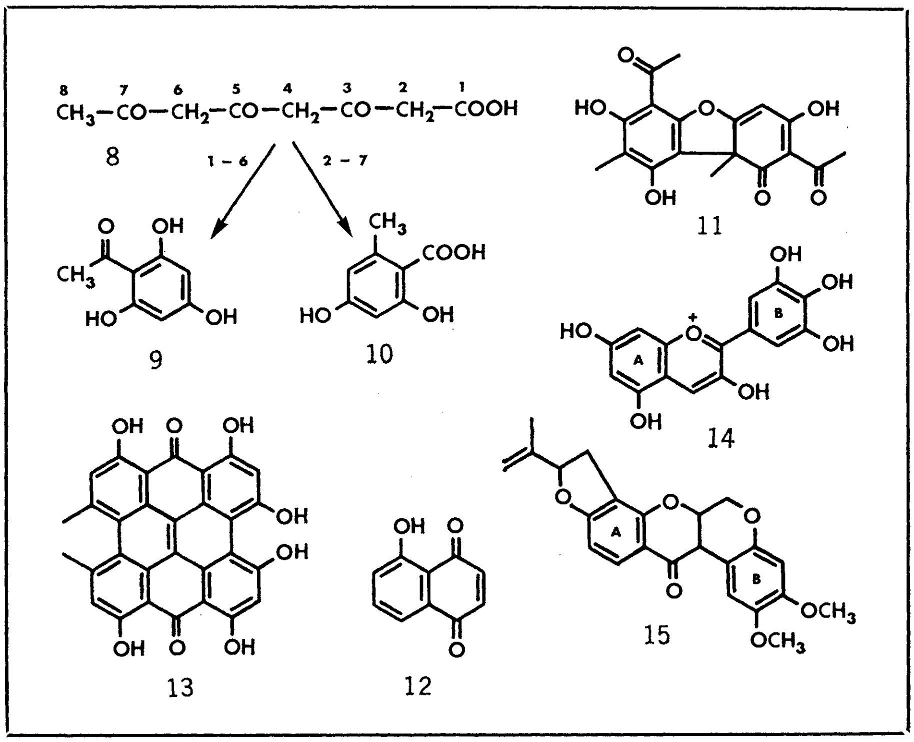

Fig. 3. Some representative acetogenins.

6) acids (*78*). The widely occurring hydrolyzable tannins (contrasted from condensed tannins by their susceptibility to hydrolysis by dilute acids) are esters of phenolic acids (often gallic acid) and sugars (*79*). The phenylpropane skeleton is probably the basis of scopoletin (No. **7**), umbelliferone, and other natural coumarins. These lactones (internal esters) of *o*-hydroxycinnamic acids occur widely in grasses, orchids, citrus fruits, and legumes (*77*).

Acetogenins comprise more than 1000 compounds, initially formed by head-to-tail condensation of malonyl units to an acetyl starter group, forming linear polyketide chains of alternating ketone (carbonyl) and methylene (CH_2) groups (No. **8**). Biosynthesis of fats is similar, but the carbonyl groups are reduced to methylene groups as the chain lengthens (*74, 80*). The chief source of diversity arises from internal cyclization of the polyketide chain, usually leading to the formation of a benzene ring. This mechanism and the shikimic acid pathway are apparently the only pathways to aromatic compounds in nature (*80*). Further diversity arises from the ability of the polyketide chain to cyclize in two different ways. The simple eight-carbon chain (No. **8**), for example, gives rise either to phloracetophenone (No. **9**) or to orsellinic acid (No. **10**). Nuclei originating from such cyclizations can be detected in a wide range of derivatives, such as usnic acid (No. **11**), a widespread antibiotic of lichens (*74, 80*).

Chain initiation by a fatty acid, instead of acetic acid, leads to the poison-ivy toxins such as urushiol (*74*). Chain initiation by cinnamic acid (phenylpropane in origin) leads to the stilbenes, which occur in conifers and are toxic to fungi, fish, insects, and small mammals (*77, 80*). The polyacetate route is probably the origin of most quinones (*81*), and more complex cyclizations lead to a variety of polycyclic aromatics, including naphthoquinones, such as juglone (No. **12**) from walnut, and anthraquinones, which occur widely as plant and fungal pigments. Still more complex are the dimeric quinones like hypericin (No. **13**) and the tetracycline antibiotics such as aureomycin (*74, 80, 82*).

The flavonoids have a basic C_6-C_3-C_6 skeleton, in which one benzene ring (A) is of polyketide origin and the other (B) ring of shikimic (phenylpropane) origin (No. **14**) (*83*). In most flavonoids, the central C_3 chain is linked to the A ring in the form of a central pyran ring, different oxidation states of which characterize the catechins, leucoanthocyanidins, flavanones, flavanonols, flavones, anthocyanidins (for example, delphinidin, No. **14**), and flavonols. The chalcones and dihydrochalcones lack the oxygen bridge of the pyran ring (*77*). The isoflavonoids, including rotenone (No. **15**), arise initially from the flavonoids by migration of the B ring to the next position on the pyran ring (*76*). Condensed tannins are polymers of catechin and other flavonoid units (*79*).

A variety of simple aliphatic paraffins (alkanes), olefins (alkenes), acetylenes (alkynes), alcohols, ketones, and esters occur naturally, for example, in insect defensive secretions (*60*) and along with terpenoids as components of the flavors and odors of fruits and flowers (*84*). Most are probably acetogenins, either formed directly from acetyl chains or via fatty acids (*77*). The roots of several umbelliferous plants owe their great toxicity to long-chain acetylenic alcohols (*77*), which may arise from long-chain fatty acids (*74, 85*).

Terpenoids arise from a linear chain of isoprene units, themselves derived from the branched condensation of three acetic acid molecules to form mevalonic acid (No. **16**). Decarboxylation and dehydration of mevalonic acid leads to the true 5-carbon isoprene unit (Nos. **17** and **17a**), in the form of isopentenyl pyrophosphate (*80*). Head-to-tail union of from two to eight isoprene units yields the skeletons of the monoterpenoids (C_{10}), sesquiterpenoids (C_{15}), diterpenoids (C_{20}), triterpenoids (C_{30}), and tetraterpenoids (C_{40}). Rubber consists of much longer linear chains of isoprene units. The linear terpene chains may cyclize, giving rise to the wide variety of cyclic terpenoids (*77*).

Typical linear monoterpenoids are nerol (No. **18**), found in cyclamen oil, and its geometrical isomer geraniol, which is a constituent of rose oil. Citral, a major component of lemon grass oil, is a mixture of the corresponding aldehydes, neral and geranial. Monocyclic and bicyclic monoterpenoids include menthol (No. **19**) and menthone, both found in peppermint oils, 1:8-cineole, nepetalactone from catnip, camphor (No. **20**), and α-pinene (*86*). Although the monoterpenoids are characteristically found in the essential oils of plants, animal sources include the defensive secretions of insects and the scent glands of alligators (*60, 87, 88*). Diterpenoids, based on the skeleton of geranylgeraniol (No. **21**), include many cyclic compounds, such as manoöl and gibberellic acid (*74*). Dimerization of (sesquiterpene) farnesol units yields squalene (No. **22**), the fundamental triterpenoid and source of all other triterpenoids and steroids. Dimerization of C_{20} units leads to the carotenoids and other tetraterpenoid compounds (*89*). Many secondary compounds are partly

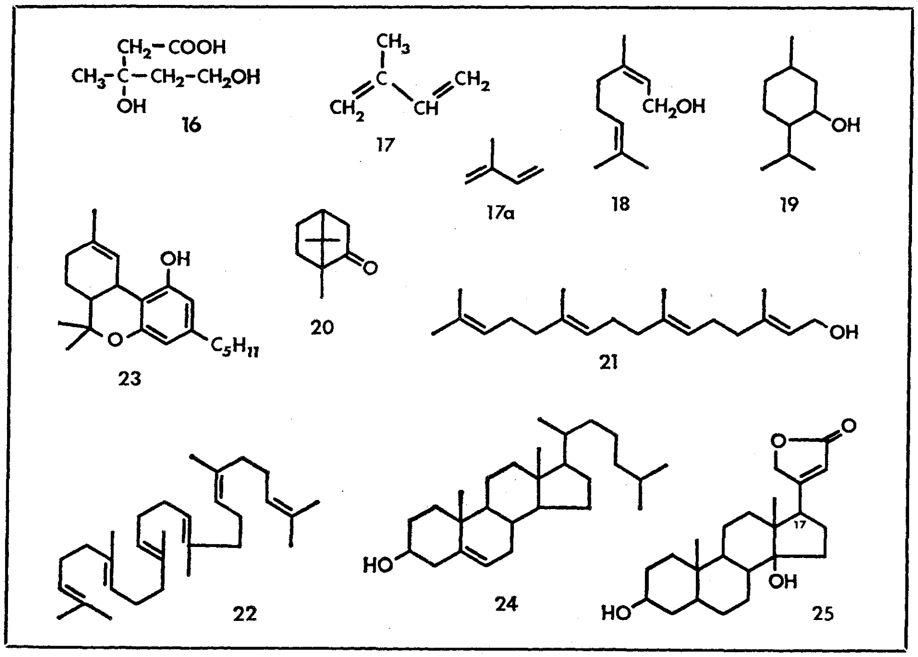

Fig. 4. Some representative terpenoids and steroids.

terpenoid in origin. The physiological action of marihuana, for example, is largely due to Δ^1-tetrahydrocannabinol (No. **23**), a substituted cyclic monoterpenoid (*90*).

The widespread importance of terpenoids as agents of chemical communication both between and within species probably results from their volatility combined with the extraordinary structural diversity (and therefore specificity) attainable through a very small number of enzymatic steps (*87*).

Steroids originate from lanosterol, itself formed by cyclization of squalene (No. **22**). The biosynthesis of steroids includes removal of three methyl groups from lanosterol, leading to cholesterol (No. **24**), various changes in oxidation state at sites on the tetracyclic nucleus, and breakdown of the side-chain from C_8 to C_5 (bile acids), C_4 (some cardiac glycosides), C_2 (cortical hormones), or none (sex hormones) (*80*). Many terpenoid and steroid alcohols (sterols) occur naturally as glycosides. The saponins, for example, are named because of their soaplike properties; they are powerful surface-active agents, foaming when shaken with water and able to cause hemolysis of red blood cells. Plants containing them have been used for centuries as fish poisons (*77*). The cardiac glycoside heart poisons are characterized by an unsaturated lactone ring, attached to the steroid nucleus at carbon No. 17. In the aglycone of cardenolides, such as digitoxigenin (No. **25**), the ring is five-membered; in the bufanolides, such as scillarenin, the ring is six-membered. Cardenolides occur in several plant families, notably the Asclepiadaceae (milkweeds), Apocynaceae, and Scrophulariaceae (genus *Digitalis*); bufanolides have a more restricted distribution in plants (Liliaceae, genus *Scilla*; Ranunculaceae, genus *Helleborus*) but occur also as toad poisons (*91*).

Alkaloids, found primarily in the higher plants, are grouped together largely because they contain basic nitrogen (frequently in a heterocyclic ring), not because of shared metabolic origin. Nevertheless, the origin of alkaloids from relatively few amino acids permits their classification into three large groups (*80*). The simplest are those derived from the aliphatic amino acids, ornithine (No. **26**) and lysine (No. **27**), and include simple pyrrolidine and piperidine alkaloids, such as hygrine (No. **28**) and *N*-methylisopelletierine (No. **29**), respectively, as well as tropane alkaloids such as tropine (No. **30**) and cocaine (*74, 80*). The aliphatic rings of nicotine (No. **31**) and anabasine arise from ornithine and lysine, respectively; the aromatic ring in both cases is derived from nicotinic acid (*74*). Combination of two ornithine or two lysine units leads, respectively, to pyrrolizidine alkaloids and lupin alkaloids (for example, lupinine, No. **32**) (*80, 92*).

The second major group of alkaloids is derived from phenylalanine and tyrosine (No. **2**). Condensation of an amine and an aldehyde molecule derived from these amino acids leads to benzylisoquinoline alkaloids such as laudanosine (No. **33**), papaverine, berberine, morphine, and tubocurarine, a major component of South American curare poison (*80*). Several much simpler alkaloids, such as ephedrine and mescaline (No. **34**), also arise from phenylalanine and tyrosine (*74*).

Alkaloids of the last major group are derived from tryptophan, the indole nucleus of which can be detected in such representatives as psilocybin, reserpine, yohimbine, strychnine, and bufotenine

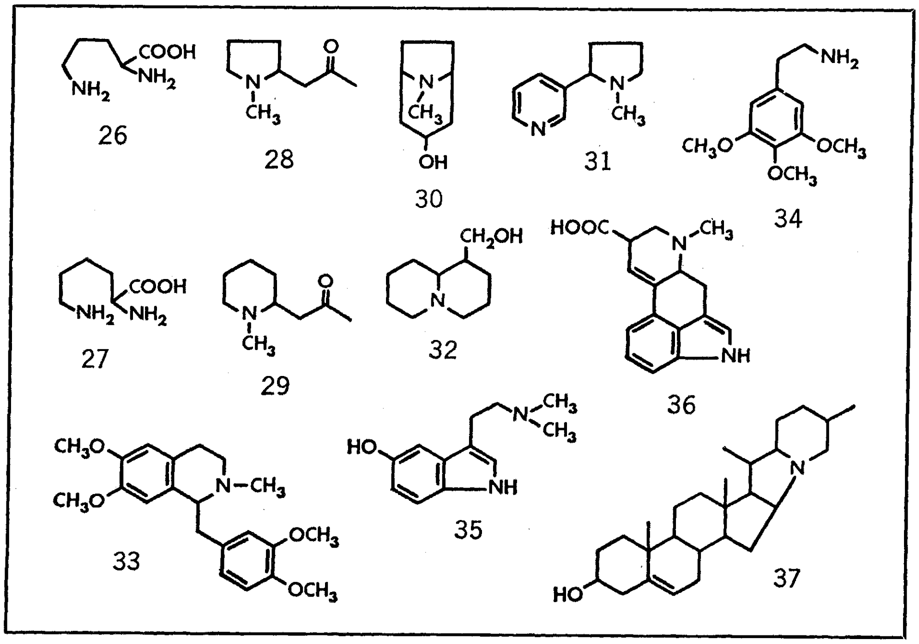

Fig. 5. Some representative alkaloids.

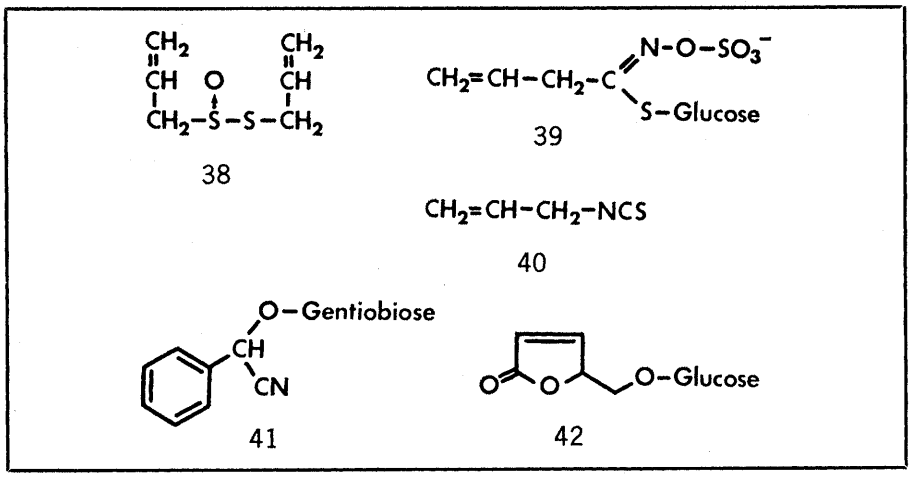

Fig. 6. Examples from some smaller groups of secondary compounds.

(No. **35**), the last occurring in plants (*Piptadenia peregrina*), fungi (*Amanita mappa*), and toads (*Bufo vulgaris*) (*93*). Alkaloids from the ergot fungus are amides of lysergic acid (No. **36**), formed from tryptamine and mevalonic acid (*80, 93*).

Apart from these three major groups of alkaloids, there is a small group of acetogenin alkaloids and a larger group of terpenoid and steroid alkaloids, such as delphinine from larkspur, and solanidine (No. **37**), which occurs as the glycoside, solanine, in potato and other *Solanum* species (*30*).

There are groups of compounds which do not readily fit any of the five main categories of secondary substances so far discussed. Thiols, for example, include *n*-propyl mercaptan from onion (*Allium cepa*) and butyl mercaptan from the skunk. Allicin (No. **38**), formed enzymically when garlic plants are crushed, is one of several sulfoxides known to be bactericidal (*94*). Other naturally occurring sulfur compounds include the sulfides (thioethers), polysulfides, and methylsulfonium compounds. The mustard oil glycosides (glucosinolates) occur only in plants of the Cruciferae and a few other families. When cellular damage occurs, the glycosides are hydrolyzed by the enzyme myrosinase to release the mustard oils. The glycoside sinigrin (No. **39**), for example, yields the mustard oil allyl isothiocyanate (No. **40**) (*46*).

Cyanogenic glycosides are common in the Rosaceae; on hydrolysis many do not yield the aglycone as such, but after a secondary reaction release hydrogen cyanide. Amygdalin (No. **41**), for example, from peach and related plants yields benzaldehyde and hydrogen cyanide (*30*).

Many simple organic acids probably arise from acetate, by way of the acids that make up the citric acid cycle (*95*). They include formic, acetic, butyric, oxalic, and malonic acids, occurring free or as esters or salts. Some hydroxy acids occur only as their lactones, often in the form of glycosides (*77*). The innocuous glycoside ranunculin (No. **42**), found in buttercups, is such a lactone and breaks down to release the aglycone protoanemonin, a strongly irritant oil accounting for up to 2.5 percent of the dry weight of some buttercup species (*30, 96*).

Despite the diversity of the metabolic repertory, there are striking convergences of chemical defenses in different phyla (*60*). The cardiac glycosides in plants are similar to those in toads; 2-hexenal is found in insect defensive secretions and also in plants. Cyclopentanoid monoterpenes similar to nepetalactone from catnip are synthesized by several insects (*60, 97*). Related cyanogenic compounds occur in plants and in arthropods. Quinazolinone alkaloids, similar to those occurring in certain plants, are synthesized by a millipede *Glomeris marginata* (*98*).

The evolution of allelochemic agents must depend on a balance between metabolic cost and natural selection. Metabolic costs would depend, for example, on the distance of the chemical from some metabolic pathway already in use, on the new enzyme systems required, and on associated morphological changes as well as on the food energy that is incorporated in the compound or expended in its biosynthesis. Expense may be reduced by the use of a waste or by-product for which a pathway already exists, by combination of two or more roles for the same chemical, by retention of a suitable chemical from the food, or by mimicry that takes advantage of another species' expenditure on chemical defense. If the balance between metabolic cost and selection is as sensitive as we believe, one would expect to find variations in quality and quantity of allelochemics over the range of some species, in response to changes in the environment. The cline in venom composition of the toad *Bufo regularis* from East Africa to South Africa (*99*), the occurrence of the cardiac aglycone sarverogenin in seeds of Nigerian *Strophanthus sarmentosus* plants growing in forest environments but not in seeds of the same species in savanna habitats (*100*), and the difference in composition of the defensive secretion of American and Australian populations of the pentatomid bug *Nezara viridula* (*62*) may be such expressions of the fine tuning of the chemistry of defense to shifting selective pressures.

Antibiotics and the Soil System

Many secondary substances are concentrated into the roots of plants; the pungent oils of the onion and horseradish are familiar cases. There is evidence for the protective function of some of these substances in roots (*101, 102*). Exudation and decay of dead roots release these substances and foods into the soil (*8, 9, 103–106*). Foods and secondary substances also reach the soil by decay of litter and by rainwash from plant surfaces above ground (*10, 107*). The secondary substances too are subject to microbial degradation in the soil, but most soils contain significant amounts of potentially toxic materials from higher plants, notably phenolic acids (*108*). Inhibition of nitrogen-fixing bacteria by old-field grasses (*22*) and of mycorrhizal fungi (and thereby of the trees dependent on them) by substances from the heath *Calluna vulgaris* (*104, 109*) are striking cases of effects of secondary substances on the microbial community of the soil.

The bacteria and fungi are engaged in their own biochemical combats. Their secondary substances are the antibiotics and other toxins, chemicals produced by bacteria and fungi that are inhibitory to other organisms. Antibiotics are produced by a variety of soil fungi, actinomycetes, and other bacteria (*110–112*) and lichens (*113*). Complex networks of antibiotic antagonisms and tolerances appear under experimental conditions among groups of soil actinomycetes and blue-green algae (*114*). Antibiotics are in some experiments inhibitory to the organism producing them (*115*). Some fungi produce staling substances that, by inhibiting growth of hyphae toward one another, may produce a more even spacing of hyphae through a food source (*116*). Many soils contain substances, presumably accumulated antibiotics, which exert a moderate, general, background inhibition of bacteria and fungi (*117*). The phenomenon is suggestive of the apparent antibiotic quality of seawater (*118*). Some antibiotics have inhibiting effects on higher plants (*119*).

The metabolic and evolutionary significance of the antibiotics has been subject to question paralleling that regarding the secondary plant substances (*120*). Although it is easy to show the effectiveness of antibiotics as chemical antagonists in vitro and in human disease, it is not easy to establish these effects in the complex ecosystem of the soil at concentrations that occur in the soil. The most plausible selective justification of antibiotics is as agents of competition among soil organisms. An actinomycete or fungus established in a decaying root fragment in the soil can, by antibiotic production, delay invasion of its food supply by other species. The effect would be local, relative, and normally obscure among the complexity of interactions in the soil (*110, 121, 122*). Analogy with the secondary substances suggests another question as yet unstudied: whether antibiotics may offer some fungal species relative protection against nematodes and small arthropods (springtails, certain mites, and so forth) that consume soil and litter fungi. One may also ask whether the devilish poison systems of *Amanita* mushrooms (*123*) are evolutionary accidents, whether they give selective advantage by discouraging vertebrate consumption, or whether they are concentrations into the reproductive organs of chemicals evolved for defense of the underground mycelia.

It is probable that antibiotic production is more characteristic of free-living soil fungi and less in evidence among root-parasitic fungi (*111, 124*). The contrast of free-living and root-parasitic fungi is too simple, however, for the soil fungi form a spectrum from free-living forms metabolizing organic compounds in the soil, through facultative parasites that may inhabit both living and dead roots and soil, and the mycorrhizal fungi of root surfaces with varying kinds of symbiotic relationships to the host plant, to the obligate root parasites (*121, 125*). Although the spectrum is one of increasing dependence of fungi on organic compounds obtained from living roots, some fungi in the middle of the spectrum contribute to the plant nutrients and organic materials taken up through mycorrhizal surfaces (*103, 104, 126, 127*).

The layer of organisms and chemical interchanges near the root surface is termed the rhizosphere, and the bacteria and fungi of the soil are strongly concentrated toward the surfaces of roots (*103, 111, 128*). What is involved, however, is a biochemical and ecological gradient from the root surface, through the layer more densely occupied by mycorrhizal filaments and bacteria responding to substances from the root, to the intervening soil space. Different species of soil organisms—animals and protists as well as bacteria and fungi—occupy different positions, in different biochemical adaptations to the plant root and other food sources and to one another, along this gradient. Such gradients are a major feature of the internal patterning of the soil ecosystem. Additional complexity of patterning is imposed on the soil system by differences in secondary chemistry of the roots, leaf litter, and decaying wood of different plant species, and by a time-gradient: during the progress of wood decay different microbial species occupy the dead wood, differently utilizing its chemical components in different competitive relations to other microbial species.

Occupation by species of different spatial, biochemical, and other functional positions in this patterning represents niche differentiation in the soil community. Other aspects of biochemical relations of bacteria and fungi to other organisms should be mentioned. Allelopathic and antibiotic substances in the soil that are repellent to some species may be used as food, or as chemical signals for the location of food, by other species. Nematodes and fungal zoospores are attracted to the root by exudates as chemical cues; resting spores and sclerotia of many soil fungi germinate only under the stimulation of root exudates (*55, 106, 129*) or substances from other bacteria and fungi (*130*). Seeds of some plant parasites will germinate only under the influence of secondary chemicals released into the soil by the host species (*9, 126*). Some species of nematode-trapping fungi (Moniliales) develop hyphal loops as snares only when stimulated by a chemical released by the nematodes and signaling to the fungus their presence in its environment (*131*). Effects in the opposite direction include the auxins synthesized and released by rhizosphere fungi and bacteria; these auxins tend to reduce root growth and may contribute to mycorrhiza formation (*9, 132*).

These comments may illustrate the diversity and significance of chemical interactions in the soil community. In the darkness of the soil, colors and differences in structure among organisms are much less prominent than they are above ground. The space to which soil organisms relate is defined largely by chemical gradients and it is clearly necessary to approach through biochemical adaptation both the niche differentiation of soil organisms and their integration into the soil community as a functional system.

Hosts and Parasites

The influences of bacteria and fungi on plant roots are part of the broader phenomenon of chemical interplay of parasite and host. Evolutionary trends of parasitism include: (i) close chemical fit of parasite to host, including metabolic adaptation to the host as food source, tolerance of host defensive chemicals, and use of host chemistry for cues governing life-cycle and behavior; (ii) evolution by hosts of chemical defenses giving relative protection against parasites; and (iii) evolution of a host and parasite pair toward tolerance of one another's chemical characteristics, hence toward an avirulent and relatively stable relationship.

The chemistry of parasite and host has been most studied in the interactions of man and his microbial invaders (*133*). Defenses of the human body against invasion begin with the skin and its fatty acids. Lysozyme, an enzyme that by digesting the cell wall lyses some bacteria, occurs in the skin, mucus membranes, and fluids (tears, saliva, nasal secretions). It is familiar that the blood functions as a chemical moat capable of drowning bacteria in its chemical defenses. The blood antibodies are proteins that are formed as counteractants to foreign proteins (and some polysaccharides) as antigens; the antibodies serve in several defensive roles. Blood complement is a complex of proteins destroying bacterial cells by lysis, an internal venom. Certain of the leucocytes or white blood cells move upon bacteria in response to chemicals released by them, and then attack the bacterial prey by ingestion and with the protein phagocytin and the digestive enzymes. Bacteria in contact with individual cells of tissues encounter the further chemical defenses of these, which include basic polypeptides and polyamines and a recently identified ketoaldehyde (*134*).

This impressive defensive system exists for protection against invaders whose only weapons are chemical. External enzymes of the bacteria—hyaluronidases and collagenases—permit penetration and spread through tissues; these and other chemical agents facilitating invasion and spread of the pathogen are aggressins. Leucocidins, bacterial repellents that kill leucocytes, are produced by virulent staphylococci and streptococci. Many bacteria produce capsules or sheaths of polysaccharides and other substances that provide relative protection against ingestion by leucocytes (*135*). To the capsule polymers, as bacterial defenses-for-attack, are opposed the host's antibodies as agents of attack-for-defense. By combining with these polymers the antibodies coat the bacterial cell (opsonization) and facilitate ingestion by leucocytes.

A few other observations on parasites may be in order. The yellow fever mosquito, *Aedes aegypti*, is drawn to feed on human beings by chemical cues (*136*). Lactic acid is most important among the organic acids of the skin to which the mosquitoes respond; carbon dioxide is a supporting substance which is not an attractant by itself, but the presence of which makes the attraction by lactic acid effective. For cellulose-digesting flagellates of termites and wood roaches the molting hormone (ecdysone) of their hosts is a behavioral inductant, to which they respond by encystment and development of sexual stages (*137, 138*). In the rabbit flea *Spilopsyllus cuniculi* maturation of the eggs is dependent on ingestion of blood with sufficient amounts of corticosteroid hormones from the pregnant host (*139*). Behavioral inductants are released also by parasites. Infective stages of the fish tapeworm *Ligula intestinalis* cause its intermediate host, the rudd, to leave its school and swim in the surface water, an easy prey for fish-eating birds and mammals in which the tapeworm's cycle may be completed (*138*).

Some interactions of bacteria and fungi with higher plants involve aggressins, toxic compounds which kill the tissue to be invaded and decomposed. Some toxins of pathogenic fungi are, like many antibiotics, peptides (*140*). A terpenoid aldehyde has been identified as a toxin of the fungus *Colchiolobus sativus*, the pathogen of root rot of cereal crops (*140, 141*). The pathogenic bacterium *Pseudomonas tabaci* of the wildfire disease of tobacco produces halos of dead and dying tissue surrounding loci of infection on leaves. The toxin producing the halos, a modified dipeptide lactone, may act primarily by inhibition of the enzyme glutamine synthetase (*141, 142*). Such toxins intergrade with inductants that are released by the bacterium or fungus and produce a modification of living tissues of the host advantageous to the bacterium or fungus.

Plants are capable of producing in some of their tissues increased quantities of defensive substances in response to invasion. Orchid tubers under attack by fungi produce orchinol (*143*); potatoes produce chlorogenic and caffeic acids (*144*). These and other defensive responses of plants (*102, 145*) involve phenolic compounds that are present in the skin of the protected organ as a first defense, and are produced in quantity in the deeper tissues surrounding a fungal penetration through the skin, as a second defense. Such substances have been termed "phytoalexins" (*102*). Comparison of phytoalexins with antibodies may emphasize the functional parallels involving widely different chemical mechanisms among allelochemic phenomena. The fact that orchids both accept penetration of roots by fungi forming mycorrhizae, and reject (with orchinol) penetration of the tuber by these same fungal species, reflects the balance of defense and tolerance in chemical accommodation, the chemical coupling of symbionts to one another.

Ectocrines in Aquatic Communities

A given volume of water from a lake or the sea generally contains far more organic matter in solution than in plankton organisms in the water. Some of this dissolved organic matter is released by bacterial decomposition of dead organisms or particles, and some of it is excreted from animals. A large share of it, however, is released into the water through the membranes of phytoplankton cells. Lucas (*146, 147*) has discussed the importance of organic compounds as bases of competition, succession, community integration, and symbiosis in the plankton. He suggested the term ectocrine (*146*) for these external metabolites, broadening the concept beyond that of allelochemic to include also foods, pheromones, and respiratory gases.

Phytoplankton cells are leaky living systems, which release substantial fractions of their metabolites—sugars, amino acids, fatty acids, and vitamins—into the water. The leakage is a small fraction (less than 1 to 5 percent) for some species in rapid growth, a large fraction (25 to 40 percent and sometimes more) for other species and less favorable growth conditions (*148*). The leakage is not a net loss to the plankton community, for many of these same phytoplankton (along with colorless plankton organisms) are actively taking up organic matter from the water. Nutrition of photosynthetic plankton organisms is in various ways auxotrophic. Some take up and utilize when available, and some require, certain vitamins from the water; others depend on supplementing their nutrition with other food compounds (*149*). The phytoplankton species differently combine photosynthetic production of some with absorptive uptake of other organic compounds. The phytoplankton is a community whose members support themselves in part by taking in one anothers' leachates. The phytoplankton species are consequently (along with animals, bacteria, and fungi of the plankton) interrelated by a network of chemical exchanges. Different positions in this biochemical network represent different functional positions in the community, or niches (*150, 151*).

Foods, and other chemical agents or allelochemics, are not sharply separated among the ectocrines; for substances that are toxic to one species are food for another (*152*). Release of toxins that are the planktonic parallels of allelopathic and antibiotic compounds is widespread among phytoplankton (*153*). The substances released by *Chlorella* and other algae slow the filtering rate of *Daphnia* (*154*). The inhibition is not effective in younger and less dense cultures of the algae, but becomes effective in dense, senescent, nondividing cultures. It may thus be possible for a rapidly growing algal population to escape control by microcrustacean grazing and reach a density that inhibits the microcrustacea from consuming it. Such effects may account for the low densities of zooplankton that often occur with high densities of phytoplankton in lakes and the sea (*146, 154, 155*).

Some other effects of ectocrines should be mentioned. Davenport (*156, 157*) has shown by experiment the responses of commensal annelid worms to chemical cues from their hosts. Certain water mites that live on the gills of freshwater clams reverse their response to light under chemical influence. They move toward the light in the absence of, but away from the light (and hence downward toward the host) in the presence of, chemical cues from the clams (*157, 158*). A predatory rotifer (*Asplanchna*) releases into the water a substance that causes uncleaved eggs of another rotifer (*Brachionus calyciflorus*) to develop into individuals with a pair of long, movable spines that are otherwise absent. In contact with a predatory *Asplanchna* the spines can be extended to make ingestion of the *Brachionus* more difficult; they give *Brachionus* partial protection against predation (*159*). Distinctive escape substances appear in the inks released by squid, and in surface-tension swimming. The beetle *Stenus* and the bug *Velia*, while supported on the surface film of freshwater, release substances that reduce the surface tension behind them so that they are drawn by the tension away from a potential predator (*60, 160*). We predict that research into the relations of multicellular marine algae and their consumers will reveal chemical defenses and responses paralleling those of higher plants and animals on land.

From the wealth of life in the sea a single group, the coelenterates, may be chosen to illustrate chemical relations. For jellyfish and sea anemones the toxins of their stinging cells are both venoms against prey and repellents against predators. Certain nudibranchs that feed on coelenterates concentrate the undischarged stinging cells in their tissues, thus appropriating as a repellent the chemical weapon system of another species (*161*). The means of disarming and rearming the stinging cells are unknown, but presumably chemical. Certain fish are able, once the individual has accommodated itself to an anemone, to live as commensals of anemones, swimming among the tentacles protected from discharge of the stinging cells, which is lethal to unprotected fish, by an unknown, heat-labile chemical (*156, 157, 162*). The sea anemone *Calliactis parasitica* is commensal with a hermit crab (*Eupagurus bernhardus*) and lives attached to the snail shell which the crab occupies. *Calliactis* attaches itself to the snail shell in response to the chemistry of its periostracum or coating; the anemone will attach to pieces of shell apart from hermit crabs, but not to shells boiled in alkali, or stripped of the periostracum, or coated with plastic (*156, 163*). The sea anemone *Stomphia coccinea* is preyed upon by starfish and responds to chemical cues from them. Upon the approach of a starfish (or stimulation by starfish mucus in the seawater) the anemone detaches itself and moves through the water with a random threshing that might, with respect to the limitations of an anemone's capacities, be called swimming (*156, 164*).

Autotoxicity and Civilization

The secondary substances include a vast array of molecules of special designs that man may exploit to his own purposes. The scents of flowers are appropriated for their attraction to man. Compounds presumably evolved as repellents are used as flavors of foods and drinks or as scents of incense. Caffeine and nicotine, both alkaloids, are appreciated as mild stimulants. Man's ability to tolerate many secondary substances in food, and even to welcome some of them in moderation, does not discount the protective values of secondary substances to the plant. From plants' secondary substances come a miscellany of other useful substances—rubber, turpentine, resins and waxes, tannins, pesticides, and so on. The antibiotics have been of incalculable value in medical practice, and from the higher plants have come many valuable medicines and drugs. Implications of the increasing abuse of some of these substances, as consequences of and contributions to psychological erosion among members of a wealthy and complex civilization, cannot yet be judged. Among the alkaloids are also such effective poisons as strychnine. Some secondary substances have since prehistoric times been appropriated by man for use as venoms on poison-tipped arrows.

Man is engaged also in a great enterprise in antibiosis—the release of poisons and inhibitors against the insects that compete with him for use of crop plants as foods, and against other unwanted species populations. Some of the most effective pesticides are secondary substances appropriated by man (*165*). The synthesis of many other pesticide compounds has been an achievement in the shorter-term benefit of chemistry to agriculture but also (given the necessities of agriculture for overpopulation) in longer-term detriment to the human environment. The restriction of use of DDT in the Western nations will be an accomplishment in the control of environmental abuse by rationality, but an incomplete solution to the worldwide increase in use of an increasing variety of chlorinated hydrocarbons. Along with the broadcasting into the environment of intentional poisons, civilized man is releasing into the environment rapidly increasing quantities of industrial wastes and combustion products, and many of these substances are both toxic and now worldwide contaminants. The needs of civilization for power imply accelerating release of combustion pollutants for the foreseeable future (*166*) and of radioisotopes from increasing numbers of nuclear power plants as well.

Civilized man is consequently faced with a phenomenon new in history—progressive toxication of the biosphere. We are cast, like some pathogens and successional species, in the role of an unstable dominant population that can effect its own demise by autotoxicity and degradation of the environment. The city of the world proposed by Doxiadis (*167*) cannot come about. The signals, environmental and cultural, of approaching limits on the growth of technological civilization are many, and the intensities of these signals are now sharply increasing. The present combination of large and increasing populations with expanding technologies represents an unstable and ultimately self-destructive course. The limitations on this course are no longer distant, and the problems produced are no longer soluble with piecemeal tactical remedies (*151, 168*). A strategy for survival is needed (*169*) to replace man's present role as an unrestricted superdominant of the biosphere, for this role is a strategy for self-defeat.

Conclusion: Chemical Evolution

Table 1 offers a classification of chemical agents by function and adaptive relationship. The table classifies functions, not chemicals. The term pheromone (*2*) is well established for chemical messages between individuals of a species; these and other intraspecific effects are separated from allelochemics (*3, 4*) which affect individuals or populations of a different species than their source. Among allelochemics a principal division is made between allomones (chemical agents of adaptive value to the organism producing them) and kairomones (chemical agents of adaptive advantage to the receiving organism) (*170*).

A great many chemical agents can be assigned two or three roles in the outline (*170*). It is because chemical agents combine roles indicated in almost all conceivable directions that classification of the agents by their roles, as distinguished from classification of the roles, becomes almost impossible. Function as both allomone and kairomone is common among secondary plant substances that have a repellent function but which also are used as signals by animals adapted to consumption of the plants; and some of these substances may also have allelopathic or autotoxic effects (or both). Cases have been mentioned in which hormones, pheromones, or food compounds released by one species are also kairomones for a second species. The versatility with which evolution has produced many chemical agents for particular functions is reemphasized by the versatility with which these functions are combined (*170*).

This versatility is of great meaning for the diversity of life. Our discussions of different ecosystems have shown how chemical interactions may be essential aspects of niche differentiation. The manner of evolution of chemical interrelations between terrestrial plants and animals has been discussed by Ehrlich and Raven (*44, 151*). The metabolism of a plant species produces wastes and some chemical accidents, substances that may result from mutation and are not part of normal metabolism, but are not so deleterious that the genes determining them are promptly selected out of the gene pool. Some of these wastes and accidents are unpalatable to the animals consuming the plants. Selection by reduced consumption of more effectively protected individuals of the plant species increases the concentration of these substances in the tissues of descendent individuals.

When a plant species has "discovered" one or more protective agents, and selection has increased the concentration of these (and related compounds arising from later mutations), the plant is protected by a distinctive set of chemicals—secondary substances. From the plant species are evolved in time a group of other species with similar protective systems. As the defensive chemistry of the plants evolves, intensifies, and differentiates through time, the chemical adaptations of existing consumers of the plants must evolve, if these consumers are not to become extinct. An additional animal species will at times discover a plant species of the group as an alternative food to which it is reasonably preadapted; with further chemical accommodation this species may become adapted to consumption of that plant species. An animal species newly adapted to one of a group of chemically similar plants may find itself relatively free from competition with similar consumers. Its descendents can diversify as consumers of the plants.

From these processes the following result: (i) the irregular occurrence of plant secondary substances that we observe, as these are products of past genetic occurrences and metabolic differences intensified by selection; (ii) the high concentrations in plant tissues of toxic materials that must be treated as wastes, and that may become autotoxic; (iii) the occurrence of groups of related animal species feeding on groups of re-

Table 1. Classes of interorganismic chemical effects. Adaptive advantage is indicated by +, detriment by −, and adaptive indifference by 0, for the releasing organism first and the receiving organism second. The virgule (/) indicates that adaptive advantage or detriment is not specified for one side of the relationship.

I. Allelochemic effects
  A. Allomones (+ /), which give adaptive advantage to the producing organism
    1. Repellents (+ /), which provide defense against attack or infection (many secondary plant substances, chemical defenses among animals, probably some toxins of other organisms)
    2. Escape substances (+ /) that are not repellents in the usual sense (inks of cephalopods, tension-swimming substances)
    3. Suppressants (+ −), which inhibit competitors (antibiotics, possibly some allelopathics and plankton ectocrines)
    4. Venoms (+ −), which poison prey organisms (venoms of predatory animals and myxobacteria, aggressins of parasites and pathogens)
    5. Inductants (+ /), which modify growth of the second organism (gall, nodule, and mycorrhiza-producing agents)
    6. Counteractants (+ /), which neutralize as a defense the effect of a venom or other agent (antibodies, substances inactivating stinging cells, substances protecting parasites against digestive enzymes)
    7. Attractants (+ /)
      a. Chemical lures (+ −), which attract prey to a predator (attractants of carnivorous plants and fungi)
      b. Pollination attractants, which are without (+ 0) or with (+ +) advantage to the organism attracted (flower scents)

  B. Kairomones (/ +), which give adaptive advantage to the receiving organism
    1. Attractants as food location signals (/ +), which attract the organism to its food source, including (− +) those attracting to a food organism (use of secondary substances as signals by plant consumers, of prey scents by predators or chemical cues by parasites), (+ +) pollination attractants when the attracted organism obtains food, and (0 +) those attracting to nonliving food (response to scent by carrion feeder, chemotactic response by motile bacteria and by fungal hyphae)
    2. Inductants (/ +), which stimulate adaptive development in the receiving organism (hyphal loop factor in nematode-trapping fungi, spine-development factor in rotifers)
    3. Signals (/ +) that warn of danger or toxicity to receiver [repellent signals (A, 1) that have adaptive advantage to the receiver; scents and flavors that indicate unpalatability of nonliving food, predator scents]
    4. Stimulants (/ +), such as hormones, that benefit the second organism by inducing growth

  C. Depressants (0 −), wastes, and so forth, that inhibit or poison the receiver without adaptive advantage to releaser from this effect (some bacterial and parasite toxins, allelopathics that give no competitive advantage, some plankton ectocrines)

II. Intraspecific chemical effects
  A. Autotoxins (− /), repellents, wastes, and so forth, that are toxic or inhibitory to individuals of the releasing populations, with or without selective advantage from detriment to some other species (some bacterial toxins, antibiotics, ectocrines, and accumulated wastes of animals in dense culture)

  B. Adaptive autoinhibitors (+ /) that limit the population to numbers that do not destroy the host or produce excessive crowding (staling substance of fungi)

  C. Pheromones (+ /), chemical messages between members of a species, that are signals for:
    1. Reproductive behavior
    2. Social regulation and recognition
    3. Control of caste differentiation
    4. Alarm and defense
    5. Territory and trail marking
    6. Food location

lated plant species (for example, a butterfly genus on a plant family) (*44*) or on plants that are taxonomically distant but related in secondary substance chemistry; (iv) development of supplemental adaptation to the plant's chemistry by the animals as, for example, in the use of the plant's defensive allomones as kairomones of food location or mating behavior, and sometimes as defensive allomones for the animal; (v) development of relatively stable accommodations of plant and animal species (*171*) (the plant evolves toward balance of metabolic expenditure for secondary substances against loss to animal consumption; the animal evolves both toward chemical accommodation and a population level regulated in part by the plant's palatability, and individual and seasonal differences in palatability, and toward nondestructiveness to the plant population); (vi) accumulation through time of increasing numbers of insect species adapted to a plant species (that may be regarded as a chemically bounded island being invaded by insect species) (*172*); (vii) formation of chemical complexes of species, each comprising a plant species with its distinctive chemistry, the animal, fungus, and bacterial species accommodated to this chemistry, and additional species (predators, parasites, mimics) adapted to the species adapted to the plant; and (viii) contribution to high species diversity by these complexes. The community comprises a number of sets of heterotroph species in parallel niches—species similar in mode of feeding and temporal and spatial position in the community, but differing in chemical adaptation to plant food.

Though their evolutionary significance may differ from one major group of organisms to another, the devices of chemical interaction appear in all major groups. Means of chemical defense in particular have been mentioned for all five kingdoms (*173*) of organisms, and cases of chemical defense and response involving most combinations of two of these kingdoms can be found. In all communities chemical interrelations are important aspects of the adaptation of species to one another; in some communities chemical relations seem to be the principal basis of species niche differentiation and community organization. Ecologists consider that ecosystems are given functional unity by the transfer of energy, inorganic nutrients, and foods between environment and organisms. To these two classes of materials in community transfer, inorganic nutrients and foods, should be added the third, allelochemics. An intricate pattern of exchanges of materials of all three classes relates the organisms of a community to the environment and to one another. If the inorganic and organic nutrients provide the essential fabric of this pattern, the allelochemics provide much of the color and detail of its design.

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