Ecological Role of Alkaloids

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Shaily Goyal

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Abstract

Plant secondary metabolites are well recognized to provide protection against harmful organisms. Alkaloids are one of the most diverse groups of secondary metabolites. They are produced by a large variety of organisms, including bacteria, fungi, plants, and animals. Positive or negative effects of alkaloids can be seen among different herbivores and insects. Alkaloids being toxic in nature help the plants, herbivores, and insects to ward off their enemies or competitors and facilitate their own survival in the ecosystem. Some herbivores and insects sequester them to defend against their own enemy illustrating the flow of alkaloids through different trophic levels. Among plants, alkaloids work as allelopathic compounds, and this property makes some of the plants a potential natural weedicide. This chapter highlights the ecological roles of alkaloids and their possible role in chemical management of pests.

S. Goyal
Laboratory of Bio-Molecular Technology, Department of Botany, M. L. Sukhadia University, Udaipur, India
e-mail: goyalshaily@gmail.com

K.G. Ramawat, J.M. Mérillon (eds.), *Natural Products*,
DOI 10.1007/978-3-642-22144-6_98,

Keywords
Alkaloids • allelopathy • endophytes • pyrrolizidine alkaloids • quinolizidine alkaloids

Abbreviations

BIA	Benzylisoquinoline alkaloids
MLA	Methyllycaconitine
PA	Pyrrolizidine alkaloids
QA	Quinolizidine alkaloids

1 Introduction

Plant secondary metabolites are structurally highly diverse chemical compounds. They exert various biological effects even at very low concentration and, hence, play an important role in ecological communications. Unlike in the twentieth century, ecologists now are well aware of the impact secondary metabolites (SM) can have through their interaction with the biotic and abiotic environment in which they exist [1]. SM provides protection against harmful organisms like herbivores, insects, and microbes and helps the plant to tolerate stress and to survive in the ecosystem [2, 3]. Such roles of SM are important as the plants have to compete with their competitor plants for light, water, and nutrients. In nature, SM play different ecological functions, e.g., they serve as signal compounds to attract pollinating or seed dispersing insects and animals and can mediate the interactions between symbiotic bacteria and their plant hosts (e.g., rhizobia) [4]. They can also perform some physiological functions such as nitrogen storage, nitrogen transport, and UV protection. As secondary metabolites have group-specific distribution in the plant kingdom, these physiological functions are not common to all but are unique and additional to certain compounds.

Plants are attacked by herbivores and pathogens. They deter both by direct and indirect defenses. These organisms often share the same individual plant, mainly when feeding insects are vectors or their feeding wounds allow establishment of pathogens. Thus, there are many opportunities for direct interactions to affect the fitness and ecology of plants [5, 6]. Plants themselves are not simply passive hosts. They participate truly in these three-way interactions. As part of direct defenses morphological structures or SM are used to inhibit attack by insects and pathogens [7]. With indirect defenses, against herbivores, damaged plants emit volatile compounds that attract the enemies of their enemies [8].

Variations in plant nutrients and herbivore-deterrent plant secondary metabolites (PSMs) across a landscape create a chemically complex environment that may influence the distribution and abundance of animal species [9]. The defensive and nutritional chemistry of not majority, but many plant populations are highly variable [10]. Spatial hotspots of highly palatable or highly unpalatable plants are ecologically important, because the probability of a plant being eaten depends not only on its own characteristics but also on the environment in which it occurs [11]. Plants experience associational defense or associational resistance from unpalatable neighboring plants when herbivores make foraging decisions at the scale of a patch of plants, or by association with palatable neighbors if they act as attractant-decoys when herbivores forage at an individual-plant scale. Some plants can experience associational susceptibility if the association is disadvantageous [12] whether such associational effects occur, and whether spatial patches of trees of similar palatability are of any significance to foraging herbivores thus depends upon the scale of the herbivore's foraging movements [13].

In comparison with flavonoids, the distribution of alkaloids is more restricted, with only 20–30 % of plants (mostly angiosperms) producing this major class of metabolite. A subdivision of the alkaloids with respect to their biosynthetic origin from a particular amino acid precursor (usually phenylalanine/tyrosine, tryptophan, ornithine, lysine, histidine, or anthranilic acid) further restricts the distribution of each subclass. More information about alkaloids types and distribution is available in other chapters of the book. Most alkaloids are physiologically active compounds having a variety of toxic effects on animals and allelopathic effects on plants. Alkaloids with allelopathic properties include aconitine, berberine, caffeine, cinchonine, colchicine, cytisine, ergometrine, gramine, harmaline, hyoscyamine, lobeline, lupanine, narcotine, nicotine, papaverine, quinidine, quinine, salsoline, sanguinarine, sparteine, strychnine, theophylline, and yohimbine [14, 15]. These compounds are originated from aerial parts of plants and released into the environment through foliar leaching by rain, residue decomposition, and debris incorporation. However, some alkaloids of plant origin are produced by roots and are released directly into the soil and have marked effects on positive and negative interactions between plants and soil-borne organisms [16].

2 Ecological Role of Alkaloids on Plants

The absence of secondary metabolites generally does not immediately kill plants but can have profound effects on a species' ecology and evolution. It is often found that particular secondary metabolites are restricted to individual species or narrow sets of species within a phylogenetic group, providing the potential for biochemically mediated behavior almost as diverse as the plant kingdom. Alkaloids strengthen the competitiveness of invasive plant species by inhibiting the growth of neighboring plants (this phenomenon is known as allelopathy). Most of the structural types of alkaloids can exhibit allelopathic effect. Allelopathy in crop plants can help in warding off weeds. In plants, allelopathy is often related to harmful effects on germination and seedling growth [17]. Some authors suggest that allelopathic effects can also contribute to promote shifts in density, dominance, and spatial patterns of plant populations [18, 19]. Thus, allelopathic plants may have a differential role in species coexistence and in forest succession [20, 21].

Soil is arguably the most complex and difficult system to choose for the study of ecological functions of secondary metabolites. However, soil is also the ecosystem in which chemical interactions play the most substantial role, and from where major insights into the role of leaching alkaloids on neighboring plants can be revealed. There are many examples which show the effect of alkaloids on other plants. Some of the earlier studies showed numerous examples of allelopathic effect of Solanaceae family members, e.g., the germination of *Medicago sativa* L. (lucerne) was inhibited by *Solanum tuberosum* extract; the germination of *Triticum aestivum* L. (wheat) was inhibited by seeds of *Solanum melongena* L. (eggplant) and *Nicotiana tabacum*, while a mixture of 200 g of dried plant material from *Lycopersicon esculentum* in 100 mL of water inhibited the germination of *T. aestivum* by 42 %, and significantly reduced radicle and coleoptile growth. Studies on *Solanum rostratum* Dun. showed that fresh, alkaloid containing extract of *S. rostratum* had inhibitory action against symbiotic nitrogen-fixing bacteria (*Rhizobium* species), with a slightly less marked inhibition of the free-living nitrogen-fixing bacterium *Azotobacter*. The inhibition of symbiotic nitrogen-fixing bacteria by this weed could aid in its competition with plants relying on nodulation for their nitrogen supply [22, 23].

Alleopathic studies by Hussain and coworkers [24] showed that *Datura innoxia* significantly inhibited germination and growth of test species by root exudates, aqueous extracts from various aboveground parts, and substances volatilizing from the shoots. Gressel and Holm [25] found that aqueous extracts of ground seeds of *Datura stramonium* (thornapple) inhibited the germination of many crop species. It is generally believed that alkaloids of *Datura* often leach from seeds into the surrounding soil and make the surrounding environment toxic to some plants and may be favorable to others due to decreased competition. *D. stramonium* inhibits germination and root growth of *Helianthus annuus*; the strength of its effects depends on the amount of alkaloid adsorbing clay in the soil [26]. As compared to leached alkaloids, the inhibitory effect can be absent for the endogenously produced alkaloids, as was reported for quinolizidine alkaloids in lupins [27] and colchicines in *Colchicum autumnale*. However, in case of alkaloid sensitive plants, both high and low concentration of alkaloid in soil is harmful. At lower concentration they inhibit or stimulate the growth of radicles and hypocotyls and at higher concentration marked reduction in the germination of seeds can be seen. The presence of *Datura* near wild cucurbits and other members of the complex of starchy seeds used by prehistoric occupants of the Eastern Woodlands [5] suggest that not all crop plants would be deleteriously affected by its proximity. By poisoning weeds in agricultural fields, *D. stramonium* instead might have had a positive effect on the growth of certain crop plants that can tolerate leached alkaloids. Depending on the susceptibility of various cultigens in the Eastern Woodlands to alkaloid poisoning and its deleterious effects on harmful invaders, prehistoric Americans may have left *Datura* as a useful weed.

Another plant with great allelopathic effect is the Barley. It is integrated with other crops to inhibit weed growth which is mediated by alkaloids released from barley plant components and/or exuded from living roots. High allelopathic effectiveness of barley has resulted in its wide adoption as a cover crop in sustainable agricultural systems for weed management. The allelopathic effectiveness varies among the barley cultivars, hence, selection programs might improve the allelopathic potential of new cultivars used for weed management [28]. In barley, alkaloids gramine (*N*,*N*-Dimethyl-3-aminomethylindole) and hordenine (*N*,*N*-dimethyl-4-hydroxyphenylethylamine) confer heritable self-defense capabilities against other plants [29]. In a study, effects of gramine and hordenine on white mustard were studied. The release of alkaloids by barley was quantified by HPLC. The alkaloids had a negative effect on white mustard which included reduction of radicle length and apparent reduction in health and vigor of radicle tips. The evidence of the morphological and primary effects of barley allelochemicals at the levels released by living plants indicates that the biologically active secondary metabolites of barley may lead to a significant role in self-defense by the crop [30]. In an experiment by Ovesi and coworkers [31] 17 Iranian barley cultivars of different developmental stages were undertaken to determine their allelopathic potential, and it was observed that barley leachates and residues decreased emergence and Germination Rate Index (GRI) of wild mustard (*Sinapis arvensis*) as the test plant. Although there were some fluctuations in the GRI value with time, the germination inhibitory effect has decreased as new, higher-yielding cultivars have been released. Taking into account of various laboratory studies on alkaloids, they have proved to play an important role in influencing neighboring plants. But in some cases there are discrepancies between the field and laboratory experiments. For example, in a study, the germination of *Ocimum* (a tropical herb), *Spermacoce* and *Catharanthus* (two tropical, alkaloid-producing plants), and *Cinchona* itself was strongly inhibited by the quinoline alkaloids of *Cinchona*, when applied at concentrations higher than about 0.3 mM. Although the roots of the plants contain high concentrations of these alkaloids (ca. 10 mM), only very low concentrations were found (ca. 0.02 mM) in the soil. Further, upon germination of seeds sown close by the plants, no toxic effects were observed. So, although several studies have reported inhibition of seed germination by *Cinchona* alkaloids under laboratory conditions, such results indicate that this property does not play a role under natural circumstances at realistic concentrations [32].

Similarily, *Lupinus albus* L. was mentioned to have allelopathic effects, limiting the growth of *Spergula arvensis* L., *Rumex obtusifolius* L., and *Chenopodium album* L. Such effect was attributed to the presence of quinolizidine alkaloids in *L. albus*. Some crops such as barley (*Hordeum vulgare* L.) [33] and pearl millet (*Pennisetum glaucum* (L.) R.Br.) [34] were reported to have self-toxicity effects and that type of effect was expected in *Lupinus* species because alkaloids are present in all plant components. However, in a work by Nava and coworkers [35] the occurrence of plants of *L. campestris* in the experimental areas before seed sowing did not affect seed germination. This result suggested that *L. campestris* does not present self-toxicity despite having alkaloids. There are many experiments which showed allelopathic effect of different plants, e.g., alkaloid content of mesquite (*Prosopis juliflora*) leaves showed allelopathic activity against root growth of lettuce (*Lactuca sativa*) and barnyard grass (*Echinochloa crus-galli*) [36]. Caffeine (1,3,7-trimethylxanthine), a purine alkaloid found naturally in over 100 plant species showed to possess phytotoxicity against plant species. A study proved the effect of caffeine on the rooting of hypocotyl cuttings of mung bean (*Phaseolus aureus*) and the associated biochemical changes. At 1,000 μM caffeine concentration, there was a 68 % decrease in the number of roots/primordia per cutting and 80 % decrease in root length. However, no root formation occurred at 2,000 μM caffeine [37]. Research on wheat allelopathy has progressed rapidly from the initial evaluation of allelopathic potential to the identification of allelochemicals and genetic markers associated with wheat allelopathy. Benzoxazinones, a novel class of alkaloids, along with other allelochemicals were identified as biologically active agents conferring weed suppression. Recent advances in metabolomics, transcriptomics, and proteomics will greatly assist in the identification of novel allelopathy genes. Ultimately, the allelopathy genes could be manipulated to regulate the biosynthesis of allelochemicals, thereby resulting in better weed suppression via elevated levels of allelopathic potential in commercial wheat cultivars [38].

3 Ecological Role of Alkaloids on Herbivores and Insects

Plant allelochemicals are nonnutritional compounds, synthesized by a plant species that are able to affect growth, health, and behavior or population biology of another species either as a stimulator or an inhibitor [39]. Most progress in the past decade in understanding how secondary metabolites influence herbivores has come from systems where the plant chemistry is well characterized through partnerships between chemists and ecologists [40, 41]. Up to 90 % of the energy flow through feeding in terrestrial ecosystems occurs at the interface between plant primary producers and animal primary consumers, thus this sector of the system includes many alkaloids produced by plants to repel, reduce, regulate, or redirect the pressure put on them by herbivores (consumers). Most known alkaloids in almost all classes were first isolated from edible parts of photosynthetic plants and have notable effects on the physiology and behavior of animals that normally or potentially feed on these plant parts (leaves, stems, sap, bark, roots, flowers, shoots, fruits, seeds). Among plant secondary metabolites, pyrrolizidine alkaloids (PAs), mainly those with a 1,2-double bond in the necine base moiety (1,2-dehydropyrrolizidines), are one of the best-studied examples of the flux of chemical compounds through trophic levels (In ecology, the trophic level is the position that an organism occupies in a food chain). In natural contexts, PAs are important elements of ecosystem and plant–animal relationships [42]. PAs flow through different trophic levels, suffering metabolic modifications and mediating many ecological interactions. Herbivorous species that are associated with PA-plants may have developed different ways to deal with these potentially toxic compounds. Some species like *Tyria jacobaeae, Zonocerus variegatus, Oreina* leaf beetles, *Mitopus morio*, and many more became PA-specialists and overcame this chemical barrier by detoxifying and incorporating PAs in their tissues [43]. Moreover, they use these toxic compounds for their own benefit as odor signal in intraspecific communication, and as a taste signal in interspecific interactions [44]. The reason behind the tolerance to toxic PAs by the organisms can be that the PAs are almost always stored as their *N*-oxides and not as a free base. Because PA *N*-oxides cannot diffuse freely across biomembranes, they can be easily stored and retained in specific organs or tissues, in general the integuments (as seen in different species of arctiid moths: *Spilosoma lubricipeda, Arctia caja, Phragmatobia fuliginosa, Callimorpha dominula, Diacrisia sannio*, and *T. jacobaeae, Creatonotos transiens*) [45]. In plants, PAs and other toxins occur in low concentrations (usually less than 1 % of the dry weight), so they are assumed to be a cheap defense. Digestibility reducers (e.g., trypsin protease inhibitor) occur in higher concentrations and are more expensive for the plant to produce [46] as the costs of secondary metabolites increase with their concentration [47]. Besides being beneficial traits, defense products can also lead to so-called ecological costs, such as increased susceptibility to other types of herbivores and pathogens, and deleterious effects on pollinators and herbivore predators and parasitoids [48].

The ragwort species, common or Tansy ragwort (*Jacobaea vulgaris*, formerly *Senecio jacobaea*), Marsh ragwort (*S. aquaticus*), Oxford ragwort (*S. squalidus*), and Hoary ragwort (*S. erucifolius*), members of Asteraceae family, are native to Europe, but invaded North America, Australia, and New Zealand as weeds. The abundance of ragwort species is increasing in west-and central Europe. Ragwort species contain different groups of secondary plant compounds defending them against generalist herbivores, contributing to their success as weeds [49]. They are mainly known for containing pyrrolizidine alkaloids, which are toxic to grazing cattle and other livestock causing considerable losses to agricultural revenue. Consequently, control of ragwort is obligatory by law in the United Kingdom, Ireland, and Australia. Cattle confront alkaloid poisoning primarily through the consumption of hay poisoned with *Senecio* material. The livers of mammals can be severely damaged by toxic pyrrols, the breakdown products of PAs, which are formed in the gut. Ragwort is one of the most frequent causes of plant poisoning of livestock. It is responsible for over 90 % of the complaints on injurious weeds in the United Kingdom [50, 51]. PAs also occur in other families, e.g., Boraginaceae and Leguminosae. Besides herbivores and insects, microorganisms are also affected by PAs [52].

For controlling *Senecio* different factors affecting its growth were explored. A study showed that nutrients level in soil can determine the outcome of competition between plants. For example, *Chenopodium album* competes most successfully with the *S. vulgaris* when potassium levels are high [53]. In agriculture, one might want to reduce weed pressure of *Senecio* species by adapting nutrient supply. Nutrients affect both the variety and the levels of PAs in the plant. Nutrient-poor pastures were found to be much more invaded by the weeds *S. jacobaea* and *S. aquaticus* than nutrient-rich pastures [54]. Apparently, the low amount of nutrients caused gaps in the vegetation which enabled propagules to invade the pastures. The effect of nutrients on competitiveness of *Senecio* even depends on its species, e.g., *S. madagascariensis* actually has increased competitive advantage over oats with increasing nitrogen and phosphorus levels [55]. Moreover, improved nutrient status in the field lowers the PA concentration in the *Senecio* plants and thereby pathogen did respond positively to the plants, and such plants are more susceptible to pathogens, though it remains to be seen whether this can improve biocontrol of *Senecio* weeds [52].

The most prominent insect for control of common ragwort is the cinnabar moth (*Tyria jacobaeae*, Arctiidae). The larva of cinnabar moth is specialized on feeding on common ragwort. It uses the PAs contained for host detection, sequestering, and detoxifying them through N-oxidation [43]. The cinnabar moth can have a major impact on the population dynamics of *S. jacobaea*. The caterpillars periodically completely defoliate their host plant and in certain years cause extinction of *S. jacobaea* on a local scale [56]. If the cinnabar moth has been a selective force in the evolution of different PAs of its host plant *S. jacobaea*, we expect that structurally related PAs differ in their effects on the moth. Other insects capable of deterring PA effect are Ragwort stem and crown boring moth (*Cochylis atricapitana*) and Ragwort plume moth (*Platyptilia isodactyla*) [51]. Toxins are rare within natural communities, but they exert profound effects on species interactions at multiple trophic levels and thus could function in keystone roles [57].

In a study, induced direct defenses in wild populations of the alpine plant *Adenostyles alliariae*, a species that possesses constitutive chemical defense (pyrrolizidine alkaloids mainly seneciphylline and senecionine) and specialist natural enemies (two species of leaf beetle, *Oreina elongata* and *Oreina cacaliae*, and the phytopathogenic rust *Uromyces cacaliae*), were tested. The host plant suffers a high proportion of leaves consumed by leaf beetles, and infection by the phytopathogenic rust. *O. cacaliae* spends the entire reproductive season on *A. alliariae*, whereas *O. elongata* also feeds on *Cirsium spinosissimum*. It was observed that the beetles were not deterred by the PAs in their host, and in fact sequestered them for their own defense. Such plants possesses inducible resistance involving the jasmonic acid and salicylic acid pathways that is capable of reducing the rate of beetle and rust attack that were undeterred by the pyrrolizidine alkaloids produced by the plant [11].

During the study on other specialist organisms, Van Dam and coworkers [58] observed adults of the monophagous weevil, *Mogulones cruciger* (Curculionidae) feeding preferentially on young leaves of *Cynoglossum officinale* (Boraginaceae) with a high PA (heliosupine, echinatine, and 30-acetylechinatine) content. Concerning the adult stage, PAs were demonstrated to be an oviposition stimulant to females of *T. jacobaeae* and the danaine butterfly, *Idea leuconoe*. In 1982, Eisner demonstrated for the first time that PAs were involved in the chemical defense of warning colored insects. He showed that the orb-weaver spiders *Nephila clavipes* (Nephilidae) and the domesticated scrub jays *Aphelocoma coerulescens* (Corvidae) rejected adults of the arctiid moth *Utetheisa ornatrix* as a food source, which contain PAs sequestered from their larval host plants, *Crotalaria* spp. When the larvae of *U. ornatrix* fed on artificial diet without PAs, the adults were predated by the orb-weaving spiders [59]. Cardoso [60] showed that mealworms treated with monocrotaline were tasted and afterward visually rejected by the pileated finch, *Coryphospingus pileatus* (Emberizidae). Thus, the unpalatability was learned, since in subsequent trials the birds started to reject visually palatable prey with the same coloration as the unpalatable ones. The insectivorous bat *Eptesicus fuscus* (Vespertilionidae) is also deterred by PAs present in arctiids. This bat species learned to associate the sounds emitted by PA-containing moths with unpalatability, thus using auditory cues signaling aposematism [61]. The protection conferred by these alkaloids is not totally effective. Tanager birds (*Pipraeidea melanota*, Thraupidae) have been found preying heavily on distasteful species of ithomiine butterflies, by discarding the cuticle and ingesting the abdominal contents, which is suggested to have a low PA content. In the overwintering sites of the danaine butterfly, *Danaus plexippus* in Mexico, these butterflies were preyed upon by the mouse *Peromyscus melanotis* (Cricetidae) that presented the same predatory behavior as the tanager birds [62]. The PA-derivatives, dihydropyrrolizines and b- and c-lactones have a sexual function as pheromones in males of ithomiines, danaines and arctiids. In these butterflies, females choose mate depending upon the amount of PAs on their bodies. This is ecologically significant, since males transfer PAs to females during mating. In turn females transfer PAs to the eggs, conferring protection for both [63]. These examples depict the flow of PAs through different trophic levels. Further example of tritrophic interaction can be seen in Ladybirds (*Coccinella*). These insects sequestered PA from *Aphis jacobaeae* feeding on PA rich *S. jacobaea*. It is likely that in ladybirds, besides the endogenously produced coccinellines the PA also serve as chemical protectants.

Some plants contain a diverse array of alkaloids that deter vertebrate herbivores. However, mammalian folivores have evolved a complex of physiological and behavioral strategies to counter these compounds, leading to the development of an “evolutionary arms race.” Many alkaloids exhibit a bitter or pungent taste for vertebrates and a bitter or pungent diet is normally instinctively avoided [64]. Unlike most mammals, insect herbivores are more selective feeders. The majority of insects are specialized feeders of some sort, specializing on particular plant species, genera, or families or on particular plant organs [65]. As for example, lupins occur in two varieties, one which is alkaloid free (sweet lupins) and the other which is alkaloid rich (bitter lupins). They produce quinolizidine alkaloids (QA) in leaf chloroplasts and export them via the phloem all over the plant where they accumulate in epidermal tissues and especially in reproductive organs. Aphids passively feed on sap of phloem vessels in plants. Aphid like, *Myzus persicae* only suck sap from phloem of “sweet” lupins but not from alkaloid-rich varieties with high alkaloid contents in the phloem. Also many other animals, from leaf miner flies (Agromyzidae) to rabbits (*Oryctolagus cuniculus*) showed a similar discrimination. Sweet lupins were always highly susceptible and selected as favorable food [64]. The defense potential of bitter lupin is due to quinolizidine alkaloids which interfere with the nervous system of animals, affecting mainly nicotinic and muscarinic acetylcholine receptors and inhibiting Na^+ and K^+ channels.

Bitter lupins are not used as a diet because of their toxicity. However, they may have alternative uses as potential sources of natural insecticides. In a study, quinolizidine alkaloids of three Mexican *Lupinus* species: *L. montanus* (HBK), *L. stipulatus* (Agardh), and *L. aschenbornii* (Schauer), were analyzed by capillary

Gas chromatography-mass spectrometry. Sparteine was found in high amounts in both *L. montanus* and *L. aschenbornii* while aphylline and an epiaphylline-like compound in *L. stipulatus*. When extracts of these plants were tested for their insecticidal activity using larvae of the Fall Armyworm, *Spodoptera frugiperda* (Smith); (Lepidoptera, Noctuidae) as a model pest; it was found that extract of *L. stipulatus* was most toxic against the larvae of *S. frugiperda* in comparison to two others. This suggests that the various QA act differently on caterpillars, and could be used to control *Spodoptera* populations [66].

Besides being toxic, alkaloids of lupins are helpful to some plants and animals in direct or indirect ways. For example, specialized aphid, *Macrosiphum albifrons*, which lives on lupins and sequesters the dietary alkaloids and uses them for defense against predators [67]. Another beneficial effect of bitter lupin in maintaining the ecology of an area can be anticipated by studies on *Castilleja indivisa*, a hemiparasitic annual plant. Herbivory can result in decreased pollination by reducing resources available for floral displays, or by damaging attractive tissues. Preference of pollinators for less damaged plants has been found in systems with floral herbivory and with leaf herbivory [68]. Decreased pollination indirectly results in low seed set and disturb the normal seed number and thereby ecology of the particular area. In a study by Adler [69] alkaloids were manipulated experimentally in the *Castilleja indivisa* by growing these parasites with bitter or sweet alkaloid isogenic lines of the host *Lupinus albus* in the field. Over the flowering season, pollinators visited a greater percentage of *C. indivisa* with bitter (high-alkaloid) hosts than sweet (low alkaloid) hosts, and also visited more *C. indivisa* that had been sprayed with insecticide compared to natural herbivory controls, regardless of alkaloid content. Analysis indicated that the benefit of alkaloids was due to their effect on herbivory. Herbivory and pollination had both direct and indirect effects on lifetime seed set of a parasitic plant, *Castilleja indivisa*. Similar host plant effects on herbivores of a hemiparasite were seen in generalist herbivore cabbage looper (*Trichoplusia ni*) and the specialist Nymphalidae butterfly (*Euphydryas anicia)*. Both type of herbivores showed decreased performance on *Castilleja sulphurea* containing alkaloids from the host *Delphinium occidentale* compared to *Castilleja* parasitizing hosts without alkaloids [68].

Besides avoiding, some insects can tolerate the defense chemistry of their host. The potato beetle (*Leptinotarsa decemlineata*) lives on *Solanum* species containing steroidal alkaloids, which are tolerated but not stored by this species. The bruchid beetle, *Bruchidius villosus*, predates seeds of QA rich plants, such as *Laburnum anagyroides*. This beetle eliminates most of the dietary cystisine with the faces. Certain aphids can store the dietary alkaloids, for example, QA in *Aphis cytisorum*, *A. genistae*, and *Macrosiphum albifrons* and PA in *Aphis jacobaeae* and *A. cacaliaster* [70].

There are many examples which show that besides pyrrolizidine and quinolizidine alkaloids other classes of alkaloids are also quite toxic to herbivores and insects. In North America, reed canarygrass (*Phalaris arundinacea*) is important livestock forage on wet and poorly drained soils. It is often unpalatable and supports lower animal performance than would be predicted from its nutrient content. It contains at least eight different alkaloids, including five indole alkaloids and three *p*-carbolines. These alkaloids all contain an indole nucleus. Reed canarygrass also contains hordenine. Marten and coworkers [71] concluded that the threshold level for total indole alkaloid concentration in reed canarygrass at or above which diarrhea and reduced growth rate occurs is about 0.2 % of the dry weight. The low palatability of reed canarygrass is associated with the hordenine content. *Phalaris* spp. has caused animal mortalities in various parts of the world by affecting the animals in different ways. Low larkspurs (*Delphinium nuttallianum* Pritz., *Delphinium andersonii* Gray) and plains larkspur (*Delphinium geyeri* Greene) often poison cattle grazing on western North American rangelands. The dominant toxic alkaloid in larkspur is methyllycaconitine (MLA); other very toxic alkaloids in low and plains larkspurs are nudicauline and geyerline. Concentrations of toxic alkaloids in *D. nuttallianum*, *D. andersonii*, and *D. geyeri* often did not significantly decline during the growing season as typically found in tall larkspurs. Thus, risk to grazing cattle may remain high until these plants are dormant [72].

Despite such toxic effects, alkaloids are sequestered by herbivores and insects for their own benefit which in a way is important in maintaining the ecosystem of the habitat. Pitohuis, a passerine bird, is thought to sequester the alkaloid, homobatrachotoxin, from beetles in their diet into the feathers and skin. The utilized batrachotoxin helps the bird in deterring its predators and avoidance of this bird as food by natives of New Guinea. It is predicted by a group of workers that the rarity of examples of secondary metabolites sequestration in birds and mammals demonstrates that other predator-avoidance strategies such as cryptic behavior and physical “fight or flight” mechanisms are less costly than ingesting and sequestering these toxic compounds in these mobile animals [73]. Another example of alkaloid driven benefit was seen in wild tobacco. As assumed short visitation (time period of visits) times by legitimate pollinators due to increased level of alkaloid and phenols, do not necessarily represent a fitness disadvantage for plants. For example, nicotine in floral nectar of wild tobacco was found to decrease consumption rates by certain pollinators but consequently increased the number of individual visits and, thus, the number of successful pollen transfers. Likewise, nectar odors play a role in the attraction of mutualists to both floral nectar and extrafloral nectar, but repellent functions have to protect nectar from unintended consumption. Nectar chemistry serves both, the attraction of nectar visitors that exert a positive effect on plant fitness and the repellence or putative intoxification of exploiting organisms [74].

Numerous plant alkaloids with antiherbivore properties are classified according to their mode of action (e.g., toxins, antifeedants, antidigestive proteins, etc.) and have been used in agriculture to control insect pests. The pyridine alkaloid nicotine is one of the best-studied putative plant resistance traits. Because it can interact with the acetylcholine receptors in the nervous systems of animals, nicotine is extremely toxic to most herbivores and, consequently, was one of the first insecticides used to control pests in agriculture. Evidence for the resistance value of nicotine arises from the agricultural practice of using nicotine sprays and genotypes of cultivated tobacco differing in nicotine levels [75]. Similarly, experiments indicate a statistically significant dose dependent decrease in the survival rate and an increase in the percentage mortality of ants and aphids in the presence of *Datura alba*. This property of *Datura* suggests that alkaloid-rich extract of *Datura alba* at suitable concentration could potentially be useful to local farmers [76]. Another alkaloid, caffeine has recently been viewed as a safe chemical for management of pests including molluscs, slugs, snails, bacteria, and as a bird deterrent.

Work by Chaniago and coworkers [77] showed that barley has the potential for self-defense against broiler chickens and other species through its biologically active secondary metabolites, gramine and hordenine. Similar type of defense was also seen against aphid *Rhopalosiphum padi* (L.). The population growth rate of *R. padi* was negatively correlated with gramine content in leaves of barley seedlings. In wheat indole alkaloids and phenolics are important in the resistance to insects. The indole alkaloid (i.e., gramine) can be toxic to *Schizaphis graminum*, *R. padi*, and *Sitobion avenae*. Compared to total phenolics, the indole alkaloid content is highly correlated with the number of *S. avenae* infesting wheat ears [78]. Cotton bollworm is one of the most important pest insects in many countries of world and is responsible for destroying a lot of crop plants. In an experiment, when secondary compound gramine was incorporated into artificial diets of cotton bollworm (*Helicoverpa armigera*) larvae. The results showed that it decreased the mean larval and pupal weights of cotton bollworm [79]. Such types of studies make the background to attempt to breed crop varieties with increased level of allelochemicals that would be resistant to pests.

4 Ecological Role of Alkaloids on Microorganisms

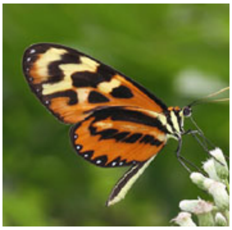
The existing evidence on the role of alkaloids against microorganisms is scarce especially in comparison to ecological studies on insects. However, there are many classes of alkaloids known to show antimicrobial activities, one of such classes is benzylisoquinoline alkaloids (BIAs). It is a large and diverse alkaloid group with more than 2,500 defined structures. The BIAs berberine, sanguinarine, and palmatine were specifically shown to confer protection against herbivores and inhibit the multiplication of bacteria, fungi, and viruses [80]. Other class with potential antibacterial activity is quinolizidine alkaloids. Recently, Erdemoglu and coworkers [81] reported that quinolizidine alkaloid extracts from the aerial parts of *Lupinus angustifolius* and *Genista vuralii* showed significant activity against several different bacterial species and moderate activity against the fungi; *Candida albicans* and *C. krusei*. In a work, alkaloid extracts of aerial parts and seeds of *Sophora alopecuroides* showed promising antimicrobial activities against different bacteria tested [82]. Tyski and coworkers [83] tested lupin alkaloids against a number of Gram-positive and Gram-negative bacteria, including one strain of *Bacillus thuringiensis* isolated from soil and concluded that the alkaloids present in lupins may have an allelopathic function against bacteria. Sepulveds and

Table 6.1 Selected examples of alkaloid containing plants and animals and their role in ecology

Alkaloid	Plants/animals	Ecological roles
Gramine, Hordenine	 *Hordeum vulgare* L. (Barley)	Allelopathic potential; Weed management
Quinolizidine alkaloids	 *Lupinus* sp. (Bitter lupins)	Allelopathic potential, natural insecticides
3-oxo-juliprosine, secojuliprosopinal, etc.	 *Prosopis juliflora*	Allelopathic potential
Benzoxazinones	 *Triticum* sp.	Allelopathic potential
Pyrrolizidine alkaloids	 *Jacobea vulgaris*	Toxic to cattles and other livestock

(*continued*)

Table 6.1 (continued)

Alkaloid	Plants/animals	Ecological roles
Indole alkaloids	 *Phalaris arundinacea* (Reed canarygrass)	Animal mortalities
Methyllycaconitine, nudicauline, geyerline	 *Delphinium* sp. (Low Larkspurs)	Cattle poisoning
PA-derivatives (dihydropyrrolizines, b- and c-lactones)	 Ithomiines, danaines, arctiids males	Phermones
Pyrrolizidine alkaloids	 *Coccinella* (ladybirds)	Sequester PA
Homobatrachotoxin	 Pitohuis (a passerine bird)	Sequester from beetles and deter its predators

Corcuera [84] identified gramine as being inhibitory to the growth of the bacterium *Pseudomonas syringae*, and Krischik and group [85] found nicotine to be toxic to five species of *Pseudomonas*: *P. syringae*, *P. syringae* pv. *angulata*, *P. syringae* pv. tabaci, *P. fluorescens*, and *P. solanacearum*, all plant pathogens. Wink [86] listed 183 alkaloids with antibacterial properties but indicated that many of these may have been investigated for possible pharmaceutical use rather than to elucidate their ecological roles.

Alkaloids also exhibit antifungal effects. There are many bioassay experiments which proved their efficacy. Ma and coworkers [87] showed that the isoquinoline alkaloids, corynoline and acetylcorynoline, inhibited the fungal growth of *Cladosporium herbarum*. Zhou and group [88] reported that steroidal alkaloids from the rhizomes and roots of *Veratrum taliense* inhibited the growth of the phytopathogenic fungi, *Phytophthora capisis* and *Rhizoctonia cerealis*. The alkaloid extract of the seeds of the plant *Sophora alopecuroides* showed significant activity against *Candida krusei* (MIC = 62.5 μg/mL) [89]. PAs produced by *Heliotropium subulatum* showed to be active against *Aspergillus fumigatus, Aspergillus niger, Rhizoctonia phaseoli*, and *Penicillium chrysogenum* [90].

Alkaloidal plant extracts from *J. vulgaris*, when tested never stopped fungal growth totally. After initial growth-delay the fungi were able to adapt and grow normally within 30 days. Hol and van Veen [91] hypothesized that this temporary growth-delay may have serious ecological significances. This delay may impact the competition between microorganisms in the rhizosphere and will give plant roots extra time to raise its defenses or escape. Experimental studies have proved that high-PA-containing plants (1.13–3.92 mg/g dw) with jacobine as the major root PA suppressed the development of some microorganisms in the rhizosphere and thereby play a role in the selection processes. This selection might favor those microorganisms that are tolerant or resistant to these defense compounds or in some cases even can degrade or utilize them. Such selections shape the soil-borne microbial community present in the rhizosphere. Despite all such findings the exact role that alkaloids play in plant protection against root-infecting bacteria and fungi is still not fully understood. Measuring low levels of chemical compounds that occur in the rhizosphere of the plant is still a challenge study area because of inadequate methods for analysis. Some examples of alkaloid containing plants and animals have been shown in (Table 6.1).

5 Ecological Role of Endophytic Alkaloids

Symbiotic interactions of green plants with bacteria and fungi are widespread. Enhanced nutrient uptake, greater stress tolerance, and protection from pests are among many benefits obtained by infected hosts. Most endophytes (organism that lives inside of a plant) produce one or more alkaloid classes that likely play some role in defending the host plant against pests. The bioprotective alkaloids in grass/endophyte symbiota are generally grouped as pyrrolizidines, ergot alkaloids, indole diterpenes, and pyrrolopyrazines. Such a production of alkaloid toxins by endophytes provides a clear mechanism for altered host physiology and ecology. Controlled and natural experiments suggest that endophyte symbiosis can have large effects on plant communities and their associated consumers [92]. An interesting example can be seen in ergot alkaloids. These alkaloids are mainly produced by saprophytic fungi: *Claviceps purpurea* and related species (Clavicipitaceae) which are symbionts on grasses. Rye is especially affected among cereals. *Claviceps* is a symbiotic organism that takes nutrients from its host but provides chemical defense against herbivores as compensation. Field experiments have shown that such a fungal infection is an ecological advantage for grasses in the wild.

The endophyte that has sparked the greatest research interest is *Neotyphodium coenophialum* (formerly *Acremonium coenophialum*), which is a ubiquitous symbiont of tall fescue (*Festuca arundinacea* = *Lolium arundinaceum*; a long-lived perennial bunchgrass species). It provides a wide range of host benefits and produces three of the four known classes of endophyte associated alkaloids which provide them protection against various pathogens. For example, infected tall fescue is more resistant to seedling blight caused by *Rhizoctonia* and crown rust caused by *Puccinia coronata* relative to uninfected plants [93]. The widespread occurrence of all four alkaloid classes among asexual endophyte species, and the hybrid origins of many such endophytes, it is reasonable to speculate that hybridization may have led to the proliferation of alkaloid-production genes among asexual endophytes, favoring hybrids. The ergot alkaloids ergovaline, lolitrems, and lolines are produced by only a single sexual species, *Epichloe festucae*, but they are common in seed-transmitted endophytes, suggesting that *E. festucae* contributed genes for their synthesis [94]. Alternatively, asexual hybrids may also be favored by the counteracting of the accumulation of deleterious mutations.

Other symbiotic fungi such as *Balansia* and *Myriogenspora* (Clavicipitaceae) also infect grasses and produce alkaloids. Ergot alkaloids (such as agroclavine, chanoclavine, ergine, ergosine, and ergometrine) are also common in some genera of the Convolvulaceae (including *Argyreia*, *Ipomoea*, *Turbina corymbosa*, *Stictocardia tiliafolia*). This is due to the ergot alkaloid formation by endophytic clavicipitaceous fungus, which is in symbiotic relationship with certain species in this plant family [95]. Loline, another alkaloid found in a grass *Lolium pratense*, e.g., *Festuca pratensis*, which has symbiotic relation with endophytic fungus *Neotyphodium uncinatum*. A study proved that endophyte infection increased persistency and competitive ability of *F. pratensis* [96] thus; help the grass and its hemiparasite to ward off herbivores. Besides endophyte/grass symbiota, loline alkaloids have also been identified in some other plant species; namely, *Adenocarpus* species (Fabaceae) and *Argyreia mollis* (Convolvulaceae). Loline alkaloids are less widely distributed among endophyte-infected grasses than ergot alkaloids but are generally found in higher concentrations than other alkaloids (exceeding 1 % of plant dry weight biomass. Further, Peramine, the only pyrrolopyrazine alkaloid found in endophyte-infected grasses, is more widely distributed in *Epichloe* and *Neotyphodium* host grasses than other alkaloids. Peramine has a relatively even distribution in the plant and over the growing season, and there is evidence of host genotype control of peramine concentrations [97]. Recently, a fungal endophyte, *Embellisia* spp., was isolated from locoweeds (*Astragalus* and *Oxytropis* spp.) and shown to produce toxic alkaloid swainsonine [98].

Endophytic symbionts need to cope with the secondary metabolites of their host plant. Usually fungi inactivate the toxins of its host by the ability to utilize the compounds as substrate for energy and biomass production or storage for their own defense against attackers. Werner and group [99] showed that endophytic fungi were able to metabolize the polyamine alkaloid aphelandrine. Several fungi were capable to use part of the polyamine alkaloid as nitrogen source. Nearly all fast-growing endophytes of the family of Nectriaceae were able to degrade and to grow on this alkaloid while slow-growing endophytes could only partially degrade aphelandrine.

Endophyte infection affects the host plants and these changes may negatively affect co-occurring plant species and their consumers as seen in some greenhouse experiments. White clover (*Trifolium repens*) was competitively suppressed by perennial ryegrass in infected pastures but not in uninfected pastures, making endophyte-infected grass/clover mixtures difficult to sustain [100]. Grasses and grasslands are dominant features of our landscape and some endophyte symbioses potentially have large-scale consequences. Clay and Holah [101] showed how infected tall fescue in successional fields increased in dominance over a 4-year period, resulting in a decline in plant species richness compared to plots with uninfected tall fescue. Large tall fescue grasslands in the eastern United States present a good example of endophyte-induced dominance.

Much attention has been focused on endophyte alkaloids during the last 25 years as these alkaloids play direct or indirect role in changing the ecology of the environment in which it exists. Toxicity in cattle grazing tall fescue and of sheep grazing perennial rye grass by endophytic infection is quite common. Chinese grass *Achnatherum inebrians* (drunken horse grass), infected by a *Neotyphodium* endophyte, is rapidly increasing its geographic range and frequency of afflicted livestock. Indigenous livestock rarely eat the grass because they have learned to avoid it, but naive animals are frequent victims of intoxication or death. Endophyte-infected *Echinopogon* species native to Australia are reported to cause stock poisonings much like those seen with perennial ryegrass [102]. Besides them, wild herbivores such as voles and rabbits, and Canada geese are also negatively affected by endophyte-infected tall fescue. In an experimental study, sex ratio and the reproductive status of female prairie voles was significantly affected by endophyte infection in field plots of tall fescue [103]. Laboratory studies with several passerine birds found strong avoidance of endophyte-infected tall fescue seeds in choice tests, and reduced survival and weight gain in nonchoice tests [104].

Community-wide effects on endophytes may be extended beyond herbivores to their associated parasites and predators in other trophic levels. For example, *Neotyphodium* endophytes of *Lolium multiflorum*, lower plant quality, reduce the densities of aphid herbivores, and indirectly reduce the rate of parasitism on aphids by parasitoids [105]. The potential for alteration of the interactions of grasses with herbivores and their natural enemies will clearly depend on many factors, including the frequency of infected hosts within the community, the types and relative levels of bioprotective alkaloids, and the spatial distribution of grasses and herbivores.

However, little is currently known about the impact of endophytes on food web dynamics in any natural ecosystem. There is a potential for the grass/endophyte symbiosis to impact more than the associated animal and plant communities. The ecosystem level consequences of endophytes have begun to be considered by a few researchers [106]. These consequences include carbon flow into soil food webs, such as the endophyte effects on litter decomposition and soil microbial activity and changes in soil nutrients availability and secondary compounds that may feedback to the plant community. The two agronomic species *L. arundinaceum* and *L. perenne* investigated the most are not native to places where they have been studied (United States and New Zealand) [106]. Further studies in natural ecosystem remain to be done before realistic ecological impact of endophytes can be studied.

6 Conclusion

Although the biological activities of many alkaloids have not yet been studied and their ecological functions remain to be discovered or proven, alkaloids have proved to play an important role in the ecosystem. Recognizing the potential of alkaloids, studies on the ecological effects of alkaloids have received considerable attention over the last few decades. Some alkaloid-rich plants, such as *Senecio* spp., *Crotalaria* spp., *Lupinus* spp., wheat, and barley, have provided a concise background to understand how alkaloids mediate ecological interactions. Most of the structural types of alkaloids can exhibit allelopathic effects. Numerous examples of allelopathic effects can be seen in members of the Solanaceae plant family. In crop plants, allelopathy can help in warding off weeds. Allelochemicals in barley make it a potential candidate as a natural herbicide. Integrating barley cover cropping with other cultural practices can possibly improve the sustainable agricultural systems for weed management. Taking into account various laboratory studies on alkaloids, they have proved to play an important role in influencing neighboring plants. But in some cases there are discrepancies between the field and laboratory experiments, as in the case of *Cinchona* and *Lupinus campestris*. However, recent advances in metabolomics, transcriptomics, and proteomics will greatly assist in the identification of novel allelopathy genes. Ultimately, the allelopathy genes could be manipulated to regulate the biosynthesis of allelochemicals, thereby resulting in better weed suppression via elevated levels of allelopathic potential. Among plant–animal relationships, pyrrolizidine alkaloids and quinolizidine alkaloids are the most studied examples of the flux of chemical compounds through trophic levels. Herbivorous species that are associated with alkaloid-rich plants may have developed different ways to deal with these toxic compounds. Some species became alkaloid specialists and overcame this chemical barrier by detoxifying and incorporating these toxins in their tissues. Regardless of this, there are numerous plant alkaloids with antiherbivore, insecticidal, and antimicrobial properties and are classified according to their mode of action (e.g., toxins, antifeedants, antidigestive proteins, etc.) and have been used in agriculture as safe chemicals for management of pests including molluscs, slugs, snails, bacteria, and as a bird deterrent. Thus, the field of alkaloids in relation to ecology presents a great potential for research and development of environmental friendly weeds/herbivores/insects/microbes management practices, without disturbing the ecosystem.

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