

Review

What Is New for the Mechanisms of Plant Resistance to Paraquat After Decades of Research?

Liyun Zhang ^{1,†}, Chang Xu ^{1,†}, Heping Han ², Shawn Askew ³, Erik Ervin ⁴, Qin Yu ² and Kehua Wang ^{1,2,*} 

¹ The College of Grassland Science and Technology, China Agricultural University, Beijing 100193, China; zly20010527@163.com (L.Z.); bs20223241086@cau.edu.cn (C.X.)

² Australian Herbicide Resistance Initiative, School of Agriculture and Environment, University of Western Australia, Perth, WA 6009, Australia; heping.han@uwa.edu.au (H.H.); qin.yu@uwa.edu.au (Q.Y.)

³ School of Plant and Environmental Sciences, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061, USA; saskew@vt.edu

⁴ Department of Plant and Soil Sciences, University of Delaware, Newark, DE 19716, USA; eervin@udel.edu

* Correspondence: kehwa@cau.edu.cn

† These authors contributed equally to this work.

Abstract: Paraquat is one of the most widely used nonselective herbicides globally. Although the emergence of weed resistance to paraquat has progressed relatively slowly since the first reported case in Japan in 1980, it has been steadily increasing. Resistance in weedy plants is predominantly associated with non-target-site resistance (NTSR), particularly via reduced uptake and translocation to target sites (i.e., chloroplasts) and/or enhanced sequestration; increased antioxidant capacity is also a common mechanism by which plants cope with various stresses, including reactive oxygen species (ROS). However, direct evidence for paraquat transport mediated by membrane transporters in weeds has not been established. Over the past decade, research, especially in model plants such as *Arabidopsis thaliana*, has advanced our understanding of the mechanisms underlying plant resistance to paraquat. This brief review summarized recent studies on paraquat resistance, with a particular focus on uptake, translocation, and sequestration mechanisms. For instance, three L-amino acid transporter (LAT) proteins (LAT1/3/4) and one (PDR11) belonging to the PDR (pleiotropic drug resistance) subfamily within the ABC (ATP-binding cassette) transporter family were confirmed to exhibit paraquat transporter activity; furthermore, transporters such as DTX6 (detoxification efflux carrier) can export/sequester paraquat inside the cell to the vacuole and apoplast, which confers stronger paraquat resistance to nearly commercial doses. In addition, the evolving perspectives in paraquat resistance research integrating big data and artificial intelligence, development of paraquat-tolerant crops, and a proposal of ryegrass (*Lolium* spp.) and/or goosegrass (*Eleusine indica*) as a model weed species for paraquat resistance studies were also briefly discussed. Further advances in elucidating the molecular mechanisms of paraquat resistance in plants, including weeds, are anticipated.

Keywords: weeds; herbicide resistance; methyl viologen; vacuole sequestration; transport; reactive oxygen species



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1. Introduction

Paraquat (N,N'-dimethyl-4,4'-bipyridinium dichloride, condensed structural formula: CH₃Cl–N–C₅H₄–C₅H₄–N–CH₃Cl), also known as methyl viologen, ranks among the top three most widely used nonselective herbicides because of its rapid action (killing green plant tissue upon contact) and its partial inactivation when in contact with soil [1,2].

Paraquat was first manufactured and marketed by Imperial Chemical Industries in the early 1960s under the trade name Gramoxone. Classified in HRAC group 22 (Legacy HRAC D and Legacy CropLife AUS Group L), paraquat functions as an oxidant that disrupts electron transfer. Specifically, it accepts electrons from ferredoxin in plant photosystem I (PSI) and transfers them to molecular oxygen, leading to the production of destructive reactive oxygen species (ROS). This results in rapid leaf wilting and necrosis—symptoms that can appear within a few hours, with sensitive plants typically dying within a couple of days [3]. Weed resistance to paraquat evolves relatively slowly compared to other herbicides (Figure 1, [4,5]), and paraquat is often used to manage weed populations that have developed resistance to other modes of action. For example, in Australia, the “double knock” strategy involves first spraying weeds with the widely used nonselective herbicide glyphosate (HRAC group 9, Legacy HRAC G and Legacy CropLife AUS Group M) followed 7–10 days later by application of paraquat before planting the crop [6]. Nonetheless, weed populations [e.g., ryegrass (*Lolium rigidum* Gaudin)] developing resistance to both glyphosate and paraquat have been reported [7,8]. So far, herbicide resistance to paraquat has been documented in 33 plant species (76 cases) worldwide (Figure 1, Table 1, [5]).

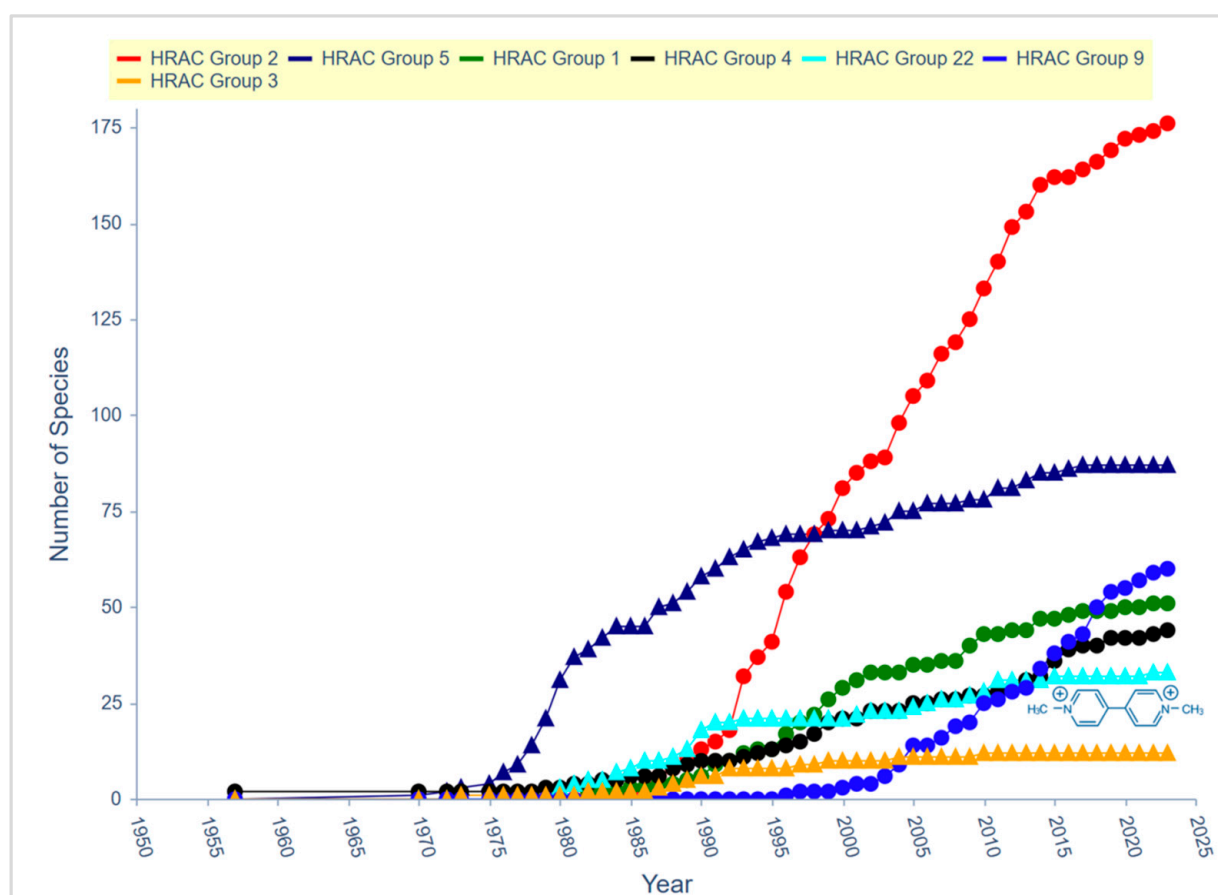


Figure 1. Chronological increase in resistant weeds globally (WeedScience.org, Ian Heap, 2025). Note: For example, diclofop-methyl and sethoxydim are in HRAC group 1 (Legacy HRAC A and Legacy AUS group K), chlorsulfuron and imazethapyr are in HRAC group 2 (Legacy HRAC B and Legacy AUS group B), trifluralin is in HRAC group 3 (Legacy HRAC K1 and Legacy AUS group D), 2,4-D is in HRAC group 4 (Legacy HRAC O and Legacy AUS group I), atrazine is in HRAC group 5 (Legacy HRAC C1 and Legacy AUS group C), glyphosate is in HRAC group 9 (Legacy HRAC G and Legacy AUS group M), and paraquat is in HRAC group 22 (Legacy HRAC D and Legacy AUS group L).

Table 1. A summary of 33 naturally evolved paraquat-resistant weedy plant species.

Scientific Name	Common Name	Resistance Level (×) (R vs. S)	LD ₅₀ (Resistant) (g ai ha ^{−1})	LD ₅₀ (Sensitive) (g ai ha ^{−1})	Possible Resistance Mechanism	Genetics	References
<i>Alopecurus japonicus</i>	Japanese Foxtail	N/A	N/A	N/A	N/A	A nuclear trait	[5]
<i>Amaranthus blitum</i> (ssp. <i>oleraceus</i>)	Livid Amaranth	N/A	N/A	N/A	N/A	N/A	[5]
<i>Arctotheca calendula</i>	Capeweed	>4	>800	<200	Reduced translocation, polyamines or a polyamine transporter	A single incompletely dominant gene	[9–11]
<i>Bidens pilosa</i>	Hairy Beggarticks	>4	>800	<200	N/A	N/A	[12,13]
<i>Convolvulus arvensis</i>	Field Bindweed	2–8	400–1200	100–300	Reduced uptake, antioxidants	N/A	[5]
<i>Conyza bonariensis</i>	Hairy Fleabane	20–300, 10–100	940 ^a , >500 ^b	N/A	Antioxidant enzymes, exclusion from its action site /sequestration	A dominant nuclear gene	[14–19]
<i>Conyza canadensis</i>	Horseweed	25–35, 160	800–3720 ^a	97–400 ^a	Antioxidants, altered transporters	Not a single major gene	[20–22]
<i>Conyza sumatrensis</i>	Sumatran Fleabane	14–39, 3.6–34	913–2468, 244–2007 ^a	54–63, 20–67 ^a	Antioxidative system, others	N/A	[23–26]
<i>Crassocephalum crepidioides</i>	Redflower Ragleaf	2.6–2.9	N/A	N/A	Antioxidant capacity	N/A	[27]
<i>Cuphea carthagenensis</i>	Tarweed Cuphea	N/A	N/A	N/A	N/A	N/A	[5]
<i>Eleusine indica</i>	Goosegrass	10–124, 3.6–30	3740, 320 ^a	30–40, 20–30 ^a	Translocation, polyamine metabolism	e.g., <i>EiKCS</i>	[28–34]
<i>Epilobium ciliatum</i>	Fringed Willowherb	N/A	N/A	N/A	N/A	N/A	[35,36]
<i>Erigeron philadelphicus</i>	Philadelphia Fleabane	>100	500 ^c	5 ^c	Paraquat movement	N/A	[37]
<i>Gamochaeta pensylvanica</i>	Pennsylvania Everlasting	N/A	N/A	N/A	N/A	N/A	[5]
<i>Hedyotis verticillata</i>	Woody Borreria	N/A	N/A	N/A	N/A	N/A	[5]
<i>Hordeum murinum</i> ssp. <i>glaucum</i>	Smooth Barley	3–40, 250	6400	25	Vacuolar sequestration, reduced uptake, translocation	A single incomplete dominant nuclear gene	[38–42]
<i>Hordeum murinum</i> ssp. <i>leporinum</i>	Hare Barley	>10	>800	57	Antioxidant enhancement, decreased translocation	A single partially dominant gene	[11,39,43–45]
<i>Ischaemum rugosum</i>	Saramollagrass	N/A	N/A	N/A	N/A	N/A	[5]
<i>Landoltia punctata</i>	Dotted Duckweed	29	148 ^d	5.1 ^d	Independent of PS electron transport	N/A	[46]
<i>Lepidium virginicum</i>	Virginia Pepperweed	10	1588–2461 ^a	191–444 ^a	N/A	N/A	[21]

Table 1. Cont.

Scientific Name	Common Name	Resistance Level (×) (R vs. S)	LD ₅₀ (Resistant) (g ai ha ^{−1})	LD ₅₀ (Sensitive) (g ai ha ^{−1})	Possible Resistance Mechanism	Genetics	References
<i>Lolium perenne</i>	Perennial Ryegrass	6	N/A	N/A	Antioxidant enhancement	N/A	[47]
<i>Lolium perenne</i> ssp. <i>multiflorum</i>	Italian Ryegrass	20.5–30	514–1780 ^a	25–59 ^a	Translocation, sequestration, reduced uptake	N/A	[48,49]
<i>Lolium rigidum</i>	Rigid Ryegrass	14–32	404–1280	30–41	Vacuolar sequestration/translocation	A single major nuclear gene	[7,50,51]
<i>Mazus fauriei</i>	Asian Mazus	N/A	N/A	N/A	N/A	N/A	[5]
<i>Mazus pumilus</i>	Japanese Mazus	4–6	150–200 ^e	10–50 ^e	Increased antioxidant capacity	N/A	[52]
<i>Mitracarpus hirtus</i>	Tropical Girdlepod	N/A	N/A	N/A	N/A	N/A	[5]
<i>Plantago lanceolata</i>	Buckhorn Plantain	2–3	785.14–1246.43	387.75	Reduced translocation	N/A	[53,54]
<i>Poa annua</i>	Annual Bluegrass	N/A	N/A	N/A	N/A	N/A	[5]
<i>Sclerochloa dura</i>	Hardgrass	N/A	N/A	N/A	N/A	N/A	[5]
<i>Solanum americanum</i>	American Black Nightshade	7–14	150–850 ^a	18–61 ^a	Reduced photosynthetic electron flow	N/A	[55,56]
<i>Solanum nigrum</i>	Black Nightshade	N/A	N/A	N/A	N/A	N/A	[5]
<i>Solanum ptycanthum</i>	Eastern Black Nightshade	N/A	N/A	N/A	N/A	N/A	[5]
<i>Vulpia bromoides</i>	Squirreltail Fescue	5–6	170	30	N/A	N/A	[57]
<i>Youngia japonica</i>	Asiatic Hawksbeard	N/A	N/A	N/A	N/A	N/A	[5]

Note: LD₅₀, herbicide rate causing 50% plant mortality; ^a, GR₅₀, herbicide rate causing 50% plant growth inhibition; ^b, herbicide rate causing 50% plant CO₂ fixation inhibition; ^c, the herbicide concentrations (μM) at which excised leaves wilt; ^d, EC₅₀, herbicide concentrations (μg L^{−1} in culture solution) cause 50% reduction in chlorophyll content; ^e, herbicide solutions (mg l^{−1}) in Petri dish causing leaf chlorophyll destruction. Resistance level R vs. S (×) was calculated by dividing LD₅₀ of resistant plants by LD₅₀ of sensitive ones.

Herbicide resistance mechanisms are generally classified into two categories: target-site resistance (TSR) and non-target-site resistance (NTSR). TSR occurs when structural alterations at the herbicide's binding site (such as mutations in genes encoding the target protein) reduce the herbicide's binding affinity or when the quantity of the target is changed [58]. In contrast, NTSR encompasses mechanisms that lower the amount of herbicide reaching the target site, such as reduced absorption and translocation, and increased sequestration or metabolic degradation (e.g., via cytochrome P450 monooxygenases, glutathione-S-transferase conjugation, and other enzymes) [58,59]. Enhanced detoxification can also result from a generally increased stress tolerance (i.e., higher reactive oxygen species scavenging ability) [59,60]. While resistance to many herbicides evolves either due to target-site variations or an increased ability to metabolize the herbicide into less herbicidal metabolites [61,62], in the case of paraquat, other mechanisms (such as reduced uptake and translocation and enhanced sequestration) appear to play a more significant role [4,62].

Thus, the aim of this brief review was to summarize recent studies on paraquat resistance mechanisms, with a particular focus on absorption, transport, and sequestration,

and to discuss whether these processes are indeed the primary drivers of paraquat resistance in weeds. For comprehensive background and earlier literature studies on the subject, readers may refer to previous reviews [4,62–65].

2. Suggested Paraquat Resistance Mechanisms in Plants

2.1. Target-Site Resistance Mechanisms

So far, it remains debatable whether paraquat possesses a specific binding site for electron acceptance, although ferredoxin in photosystem I has long been considered as its target [62]. Given the herbicide's strong redox potential, there is little evidence to support a TSR mechanism via specific binding-site mutations. Nevertheless, Chase et al. [66] suggested a chloroplast-based resistance mechanism involving the electron transport chain in *Solanum americanum* Mill., and Mishra and Sabat [67] reported that photosynthetic electron transport in *Hydrilla verticillata* (L.f.) Royle was insensitive to paraquat inhibition. Except for these, no clear evidence of TSR in paraquat-resistant plants has emerged. One assumption is that mutations at the target site may be lethal, which would explain the absence of isolated TSR mutants in paraquat-resistant weeds or plants [4,62]. Moreover, functional assays using intact chloroplasts isolated from resistant (R) and sensitive (S) biotypes of various weeds have shown comparable sensitivity to paraquat [14,68].

2.2. Non-Target-Site Resistance Mechanisms

2.2.1. Metabolism-Based Resistance Mechanisms

The cytochrome P450 (CYP) superfamily and related detoxification enzymes—including glutathione S-transferases (GSTs) and glycosyltransferases (GTs), play crucial roles in the metabolism and detoxification of xenobiotics such as herbicides [69–71]. Traditionally, it was anticipated that, similar to resistance against other herbicides, plants might metabolically detoxify or degrade paraquat, making this a desirable resistance strategy. However, paraquat is notably stable within plants, and metabolic degradation has not been documented in planta until very recently [61,72]. Indeed, the enhanced paraquat resistance observed in resistant biotypes of perennial ryegrass (*Lolium perenne* L.), rigid ryegrass (*L. rigidum*), and hairy horseweed (*Conyza bonariensis* L.) does not correlate with differences in paraquat metabolism [26,68,73,74]. This lack of evidence for paraquat metabolism in plants may be partly related to its rapid mode of action [62].

Interestingly, like glyphosate, paraquat can be degraded by certain soil microorganisms, an observation that has sparked interest in both genetically modified paraquat-tolerant crops and the remediation of paraquat-contaminated soils [1,48,75]. In the freshwater crustacean *Daphnia magna* Straus, a CYP enzyme (CYP360A8) has been implicated in paraquat detoxification [76]. More recently, Huang et al. [72] identified a gain-of-function *A. thaliana* mutant *pqt11D* (paraquat tolerance 11D) in which a T-DNA insertion with 35S enhancers activated the gene PQT11/CYP86A4. Overexpression of PQT11 in *A. thaliana* conferred an approximately 2-fold increase in tolerance of up to 10 µM paraquat relative to the wild type (WT), and the study further demonstrated that PQT11 facilitates the demethylation of paraquat into N-demethyl paraquat, a nontoxic metabolite, thus establishing a potentially new detoxification mechanism via plant metabolism. However, since paraquat is evidently not a natural substrate for this enzyme, its primary physiological role remains unclear. Moreover, the overall enhancement in tolerance (~1-fold increase) via PQT11 overexpression is relatively modest, especially when compared to the high-level resistance (up to ~100–300-fold, and spray solution concentration in mM) found in weeds (Table 1). It remains to be investigated how homologous CYP genes function in resistant weedy species and major crops, such as rice (*Oryza sativa* L.), wheat (*Triticum aestivum* L.), and maize (*Zea*

mays L.), and whether additional metabolic enzymes, including GSTs and GTs, contribute to paraquat degradation.

2.2.2. Enhanced Antioxidant Capacity

Reactive oxygen species (ROS), such as hydrogen peroxide (H_2O_2), the hydroxyl radical ($OH\cdot$), singlet oxygen ($^1O_2$), and superoxide (O_2^-), are highly reactive molecules produced during plant metabolism. They function as secondary messengers in numerous biological processes, including growth, development, and stress responses. However, excessive ROS can damage biomolecules (e.g., proteins, lipids, carbohydrates, DNA, and pigments) and ultimately lead to cell and plant death. Therefore, it is crucial that plants regulate ROS levels by balancing their production and scavenging. All forms of stress including herbicide application can increase ROS production [77]. Given paraquat's mode of action, it is not surprising that an enhanced antioxidant capacity (i.e., higher levels of antioxidant enzymes and/or antioxidant molecules) was implicated early in plant paraquat resistance [15,27,78]. Nevertheless, due to dramatic and constant redox cycling of paraquat in ROS production, detoxification of paraquat-generated ROS by a plant's cellular antioxidant system would be theoretically limited in conferring high levels of paraquat resistance [62].

Enhanced ROS scavenging has indeed been observed in R biotypes of several paraquat-resistant weeds, including *L. perenne*, *C. bonariensis*, Sumatran fleabane [*Conyza Sumatrensis* (Retz.) Walker], redflower ragleaf [*Crassocephalum crepidioides* (Benth.) S. Moore], and Japanese mazus (*Mazus pumilus* (Burm.f.) Steenies) when compared with S biotypes. Such paraquat-resistant plants often exhibit increased activities of antioxidant enzymes (e.g., superoxide dismutase [SOD], catalase [CAT], ascorbate peroxidase [APX], glutathione peroxidase [GPX], monodehydroascorbate reductase [MDHAR], dehydroascorbate reductase [DHAR], and glutathione reductase [GR]) and/or higher levels of non-enzymatic antioxidants (e.g., ascorbic acid, glutathione, carotenoids, and polyphenols) [15,23,27,52,78,79].

Similarly, in model plants such as *A. thaliana*, several paraquat-resistant mutants exhibited increased antioxidant activities. For example, the *gi* (gigantea) mutant could survive up to 5 μ M paraquat in growth medium at the seeding stage (versus 1 μ M lethal for WT) [80]; the *pst1* (photoautotrophic salt tolerance1) mutant showed approximately 22% seedling survival on the filter paper soaked in 30 μ M paraquat compared to 3.5% in WT [81]; the *rcd1-2* mutant (ozone-sensitive radical-induced cell death 1-2) suffered about 50% inhibition of root growth and chlorophyll content at ~0.55 μ M paraquat as compared to ~0.15 μ M in WT [82,83]; the *par2-1* mutant (paraquat-resistant 2-1; involving PAR2/GSNOR1[S-nitrosogluthathione reductase 1]/HOT5) survived 2 μ M paraquat in MS medium [84]; and the *pqt3* mutant showed over 60% seed germination with green cotyledons on MS medium containing 2 μ M paraquat, compared to just 2% in WT [85]. Additionally, *pqt3* was isolated from the same T-DNA insertion library as the transporter mutant *pqt24-1* [86]. PQT3, an E3 ubiquitin ligase, negatively regulates oxidative stress responses by ubiquitinating PRMT4b (protein methyltransferase 4b) for 26S proteasome-mediated degradation, while PRMT4b upregulates the expression of antioxidant enzymes such as APX and GPX via histone methylation under stress, thereby protecting the plant from oxidative damage [4,85]. More recently, several transgenic modifications in *A. thaliana* that enhanced paraquat resistance have been linked, at least in part, to the upregulation of antioxidant machinery, which helps maintain lower levels of ROS and reduced lipid peroxidation, such as a maize SUMO (small ubiquitin-related modifier) conjugating enzyme (ZmSCE1b) [87], and small paraquat resistance proteins (SPQ) from *A. thaliana* and *Lepidium crassifolium* (W. et K.) [88,89].

In rice, comparing a susceptible mutant line (1192-11) with a tolerant mutant line (72-16) revealed that the antioxidative effects of the ascorbate–glutathione cycle, particularly GR activity, played an essential role in paraquat tolerance [90]. Additionally, overexpression of EiKCS (β -Ketoacyl-CoA Synthase), an enzyme catalyzing a key step in fatty acid elongation derived from paraquat-resistant goosegrass (*Eleusine indica*), enhanced paraquat resistance in rice through increased antioxidant enzyme activity and the overproduction of endogenous polyamines [91]. Conceivably, any mutation or modification that improves antioxidant capacity can help plants survive paraquat stress. However, many studies attempting to engineer paraquat and associated stress tolerance via overexpression of Halliwell–Asada cycle enzymes have typically resulted in only modest increases in tolerance (generally less than 5-fold or mostly 1–3-fold) [62,92–96], even when multiple enzymes (e.g., Cu/Zn-SOD, APX, and DHAR) are coexpressed in transgenic tobacco (*Nicotiana tabacum*) [97]. Furthermore, one study found that a 50–100-fold paraquat-resistant biotype of *C. bonariensis* exhibited only moderate cross-tolerance (1.5–10-fold) to SO₂, atrazine, acifluorfen, and two experimental pyrimidinedione derivatives, while high-level (~100-fold) paraquat resistance was associated with only partial (~10-fold) cross-tolerance to diquat and no measurable cross-tolerance to morfamquat (both bipyridinium PSI herbicides like paraquat) [16,98]. These results indicate that the increased antioxidant capacities observed in weeds with very high paraquat resistance (50–100-fold or more) may not fully account for the resistance phenotype. Instead, mechanisms related to the chemical structure of paraquat, such as specific transporters that regulate herbicide uptake and sequestration, might play a more critical role [4,62].

2.2.3. Transport and Sequestration of Paraquat in Plants

In general, molecules move within plants via passive and/or active transport [99]. As a contact herbicide, paraquat's movement within a plant has traditionally been thought to be limited (i.e., confined largely to the xylem) as suggested by studies using ¹⁴C-labeled paraquat dichloride [100]. However, subsequent research showed that paraquat is more efficiently transported away from treated leaves through undamaged tissue (kept in darkness for ~24 h following treatment and then exposed to light) than through damaged tissue (kept in light immediately), and its basipetal movement under nondamaging conditions suggests that it can also traverse the symplastic route to a limited extent (Figures 2 and 3) [101,102]. In the meanwhile, it could indicate that paraquat translocation via xylem or/and phloem at commercial/field doses (much higher concentrations than in laboratory studies) would be very limited and more likely happen in the dark. Furthermore, the structural similarity between paraquat (and diquat) and certain plant polyamines implies a high likelihood of active uptake of paraquat via polyamine transport systems into plant cells through symplastic transport (Figure 3) [103,104]. For instance, studies in maize have shown that paraquat uptake into root cells and protoplasts is driven by active transport (with a K_m ~100 μ M) that is competitive with polyamines such as putrescine and cadaverine (but not spermidine) [105]. Similarly, exogenous application of polyamines on leaf discs of a *S* biotype of *Arctotheca calendula* reduced paraquat uptake and transport, thereby enhancing paraquat tolerance [58]. A recent study [106] revealed that mutations in the polyamine transporter gene PUT3 (polyamine uptake transporter) in rice confer paraquat resistance but are associated with polyamine metabolic disorders and reduced germination rates, with significant differences in growth phenotypes across rice cultivars. Ectopic expression of PUT3 restored polyamine levels and growth defects, suggesting that disrupting transporters to achieve resistance may impose negative fitness effects on crops. These properties help distinguish paraquat from other molecules with similar redox potentials, contributing to its efficacy as a PSI herbicide. Conversely, mutations that impair paraquat uptake and

transport can occur naturally or be induced, thereby reducing the herbicide's effectiveness and leading to resistance [62]. Indeed, several studies over the past decades have demonstrated that restricted uptake and movement of paraquat in R biotypes of weedy species correlate with paraquat resistance (Figure 2), and some putative transporter-related genes were proposed based on expression analysis [e.g., *CAT4* (cationic amino acid transporter 4), *PqTS1*, *PqTS2*, and *PqTS3*; Figure 3] [28,102,107–111].



Figure 2. Examples of phosphor images comparing transport patterns of ¹⁴C paraquat between the susceptible (S) and resistant (R) plants of rigid ryegrass (*Lolium rigidum*), ① [50]; smooth barley (*Hordeum glaucum*), ② and ④ [74]; and hairy fleabane (*Conyza bonariensis*), ③ [14]. ① An amount of 3.5 mM containing 1.11 kBq ¹⁴C paraquat was applied as a 1 µL droplet to the middle (arrows) of expanded young leaves at the 3/4-leaf stage, and shoots were harvested 5 h (A,B), 24 h (C,D), and 48 h (E,F) following paraquat treatment. ② Plants were 1 and 2 days in a greenhouse after being sprayed with paraquat at 0.4 kg ai ha^{−1} in 106.91 L ha^{−1}. Notably, older leaves often show injury symptoms and die earlier than younger ones; whether it is due to less uptake or lower sensitivity because of less matured chloroplasts in younger leaves is unknown. ③ Drawing of autoradiogram (left), photograph (middle), and merged photo (right) of excised leaves fed a 50 µL solution of 0.064 µCi ¹⁴C paraquat (1.4 mCi mmol^{−1}) through the petiole. ④ Line drawing of autoradiography exposures from excised leaves. The leaf cut ends were immersed for 60 min in a vial containing sublethal 850 uM (methyl-¹⁴C) paraquat solution. Filed application rates for paraquat range from about 100–1100 g ai ha^{−1}, with a spray solution volume of about 50–200 L per hectare (Syngenta).

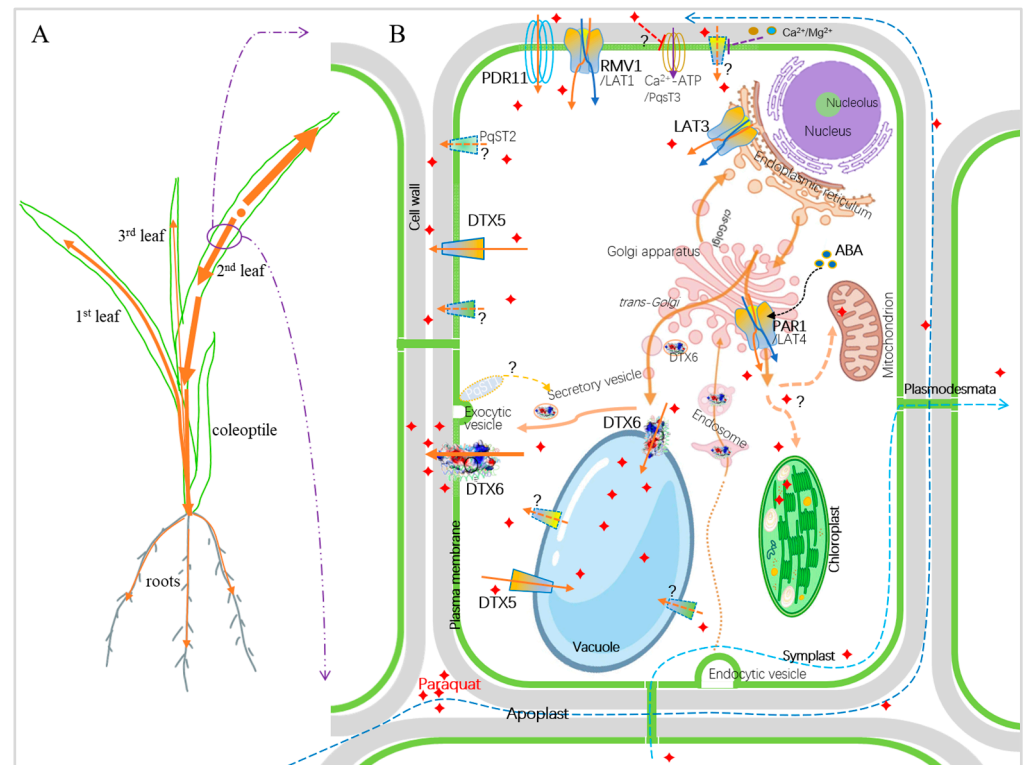


Figure 3. Schematic illustrations of the paraquat uptake/translocation at the whole plant (A) and the cellular (B) levels.

More recently, research in *A. thaliana* has begun to elucidate the molecular mechanisms of transporters involved in paraquat uptake and movement [4,104]. The first paraquat-related transporter isolated in higher plants was from *A. thaliana* about a decade ago [86]. A T-DNA insertion mutation in the *A. thaliana* locus PDR11 (pleiotropic drug resistance 11) produced a loss-of-function mutant (*pqt24-1*) that survived on MS medium containing 2 μM paraquat at the seedling stage, accompanied by an approximately 50% decrease in paraquat uptake compared to WT seedlings. *AtPDR11* encodes a plasmalemma-localized transporter that belongs to the PDR subfamily within the ABC (ATP-binding cassette) transporter family, which comprises over 130 members in *A. thaliana*. Most of the PDR members are integral membrane proteins that function as dimers to transport a wide range of substances including ions, carbohydrates, lipids, hormones, and xenobiotics [112–117]. PDR11 expression is induced by 6 μM paraquat in both roots and leaves, and it is not a polyamine carrier; its exact function and authentic substrate remain unknown (with some speculation about alkaloid substrates based on structural similarities) [86]. Interestingly, putrescine acts as a competitive inhibitor of paraquat transport in WT seedlings: in its presence (500 μM putrescine), the V_{max} remains unchanged (approximately 1.5 $\text{nM mg}^{-1} \text{h}^{-1}$), but the K_{m} increases from 237 to 498 μM . In contrast, in the *pqt24-1* mutant and another *pdr11* null mutant, both V_{max} (approximately 1.41 to 0.99 $\text{nM mg}^{-1} \text{h}^{-1}$) and K_{m} (approximately 416 to 291 μM) decrease, suggesting the existence of more than one class of active paraquat uptake transporter, some with higher paraquat affinity that are inhibited non-competitively by putrescine. Moreover, the observed equilibrium 2 h after paraquat treatment indicates that a paraquat efflux system must exist to counterbalance its import [86]. How these various importers and exporters coordinate to function as opportunistic paraquat transporters remains an intriguing question.

At the same time, T-DNA insertion mutants at the RMV1 (resistant to methyl viologen 1)/*AtLAT1* (L-amino acid transporter 1)/*AtPUT3* (polyamine uptake transporter 3) locus in *A. thaliana* exhibited increased paraquat resistance (with seedlings surviving on

MS medium containing 0.3 μM paraquat), associated with approximately a 70% decrease in paraquat uptake compared to WT. Conversely, overexpression of RMV1 resulted in paraquat (and polyamine) hypersensitivity due to increased uptake. RMV1 is a putative amino acid permease located in the plasmalemma, belonging to the LAT family within the amino acid, polyamine, and organic cation (APC) superfamily [104,118]. Subsequently, loss-of-function mutants at the *A. thaliana* locus PAR1 (paraquat resistance 1)/AtLAT4/AtPUT2, isolated from an ethyl methane sulfonate-mutagenized M₂ population based on their resistant phenotype on MS medium with 1 μM paraquat, appeared to encode a LAT-type carrier localized to the Golgi apparatus rather than the plasma membrane [119]. Although overexpression of PAR1 conferred paraquat hypersensitivity, loss of PAR1 did not alter its subcellular localization or paraquat uptake into cells. However, measurements of ¹⁴C-paraquat retention in the chloroplasts of treated seedlings suggested that PAR1 positively influences paraquat loading into chloroplasts, possibly via brefeldin-sensitive vesicle cycling. An alternative explanation is that a minor fraction of PAR1 (below the assay's detection limit) may localize to chloroplasts, as some proteins lacking a typical chloroplast transit peptide can enter the secretory pathway [120]. Additionally, more than 20 *par1* allele mutants were identified in later studies under 2 μM paraquat selection pressure [121,122], suggesting that PAR1 may be a major locus responsible for paraquat resistance in *A. thaliana* or a hotspot for resistance-conferring mutations (particularly between the 7th and 10th transmembrane domains) [4,119]). Interestingly, one study reported that abscisic acid (ABA) negatively affected the paraquat resistance of an *A. thaliana* *pqr2* mutant, where PQR2 is identical to PAR1/AtLAT4/AtPUT2 [121], while some ABC transporters (e.g., ABCG25 and ABCG40) are known to participate in ABA transport [115,123]. In rice, knock-down of a PAR1-like gene (*OsPAR1*) via RNA interference conferred paraquat resistance (with plants surviving a foliar spray of 140 μM paraquat) [119]. Moreover, disruption of three PUT genes (*OsPUT1/2/3*) using CRISPR/Cas9 resulted in even higher tolerance, and seedlings survived approximately 1–2 μM paraquat in Kimura B nutrient solution or 200 μM paraquat in a foliar spray assay on one-month-old rice plants [124]. These findings underscore the need for further investigation into the molecular mechanisms governing the transport of paraquat as a xenobiotic, including the roles of various energy-dependent and protein-structure-specified transporters with distinct subcellular localizations and the interplay between intracellular trafficking and symplastic transport.

2.2.4. Enhanced Sequestration of Paraquat in Plants

In addition to translocation, studies over the past 40 years have indicated that paraquat sequestration from the cytoplasm and target organelles (e.g., chloroplasts) into metabolically inactive compartments (such as the cell wall and vacuole) is a key mechanism of paraquat resistance in weeds [4,38,62,64]. For example, in *C. bonariensis*, high paraquat resistance (R/S up to 100-fold, ~500 μM paraquat based on a 50% reduction in leaf CO₂ fixation; Table 1) was linked to paraquat exclusion from chloroplasts via an unidentified sequestration mechanism [37]. This conclusion was based on comparisons of paraquat uptake, binding to cell walls, and the tolerance levels of chloroplasts, isolated protoplasts, and leaf sections between R and S plants [14,37,68]. Similarly, highly resistant biotypes of *L. rigidum* (R/S > 10-fold, LD₅₀ > 0.4 kg ai ha⁻¹, 13.9 mM paraquat applied) and *Hordeum glaucum* Steud. (R/S > 40-fold, LD₅₀ > 1.6 kg ai/ha, 34.5 mM paraquat at 15 °C; or R/S ~3.2-fold, LD₅₀ ~0.22 kg ai ha⁻¹, 4.7 mM paraquat at 30 °C) exhibited reduced paraquat translocation, likely due to sequestration in the vacuole or apoplast [38,39,51,102,125]. In *H. glaucum*, somewhat paradoxically, paraquat retention in the roots (from a 100 μM paraquat uptake solution) of R plants was about 7-fold (14.9 vs. 2.1 nmol g⁻¹ FW) higher than in S plants, likely due to slower efflux, particularly from the vacuolar fraction. Not to

mention the root has no chloroplasts, and the compartmentalization in the root vacuoles would effectively sequester paraquat away from leaf chloroplasts, contributing to resistance, as translocation from roots to the above-ground shoots was much lower in R than in S plants and essentially negligible [125]. A similar sequestration mechanism was observed in *Conyza canadensis* (1 kg ai ha⁻¹, 500 µM paraquat applied), where a significant portion of the applied paraquat was retained in the vacuole and cytosol, limiting chloroplastic accumulation and conferring resistance [111]. Specifically, the maximum paraquat content in the chloroplasts of R plants was lower than in S plants (~9%), remaining at about 5–6% 1 h after treatment (HAT) and decreasing to 5% 4 HAT. Interestingly, paraquat levels in both chloroplasts and mitochondria became undetectable 24 h or a month after treatment, while intracellular paraquat content remained high (~2 nmol/g FW, mostly in the cytosol and vacuole) in R biotypes, which is somewhat counterintuitive. Additionally, the authors suggested that CAT4, a member of the CAT family in the APC superfamily, was likely involved in intracellular paraquat transport, thereby enhancing resistance in the R biotype of *C. canadensis*, based on an analysis of differentially expressed sequence tags (ESTs) [111]. It was hypothesized that a CAT-type transporter, rather than an ABC-type, could be involved in paraquat uptake into the vacuoles [62,126].

In, *L. rigidum*, paraquat-treated protoplasts of R plants retained 2–3 times more paraquat than those of S plants, indirectly suggesting enhanced vacuolar accumulation [47]. In *L. multiflorum*, paraquat movement was largely restricted to the treated leaf in R biotypes, while it was translocated 20 times more efficiently in S plants [74]. In *Plantago lanceolata* (R/S ~3-fold, LD₅₀ ~0.69 kg ai ha⁻¹, 6.7 mM paraquat applied), reduced paraquat translocation, presumably due to sequestration, appears to be the main resistance mechanism in the R biotype [53]. The involvement of tonoplast-localized polyamine uptake transporters (PUTs) in vacuolar sequestration was proposed, though molecular validation is still needed [74]. Collectively, these findings strongly suggest that transporters mediating paraquat sequestration into the vacuole and apoplast play a critical role in reducing paraquat availability at the site of action, thereby contributing to resistance in weedy species. However, direct evidence for membrane transporters enabling paraquat transport in weeds has not been established.

Very recently, a genetic screen in *A. thaliana* for paraquat-tolerant mutants identified *pqt15-D* (paraquat tolerance 15-D), which exhibited resistance up to 80 times greater than the WT. This mutation affects the PQT15 gene, which encodes the transporter Detoxification Efflux Carrier 6 (DTX6). The dominant gain-of-function mutation introduces a G311E substitution (glycine to glutamic acid) in the substrate tunnel of DTX6 (DTX6-D), which increases its negative charge and likely enhances its binding affinity and efflux activity toward positively charged molecules, particularly paraquat. Functional studies confirmed DTX6's role as a key efflux transporter for paraquat. Plants with disrupted DTX6 (*dtx6*) exhibited reduced paraquat tolerance, while those overexpressing the gene showed increased tolerance (1 mM paraquat for WT DTX6 or 4 mM for mutant DTX6-D). DTX6 is primarily localized to the plasma membrane and endomembranes, supporting its role in exporting paraquat from cells [122]. As a member of the MATE (multidrug and toxic compound extrusion) family, DTX6 uses membrane potential gradients to facilitate the transport of substances, typically as antiporters via H⁺ exchange [127,128]. Protoplast studies further demonstrated that DTX6-overexpressing cells exported about 125% more paraquat than WT cells. Notably, an independent study also identified the same G311E mutation for DTX6 in the *A. thaliana* semidominant mutant (*rtp1*) [129]. Further structural and functional analysis revealed that the charge property of residue 311 is critical for paraquat binding affinity and plant resistance, and it suggested that DTX6 is involved in a dynamic endomembrane trafficking pathway from the Golgi body to the vacuole

and plasma membrane, where it facilitates paraquat exocytosis and vacuolar sequestration [130]. These findings align with the broader mechanism of paraquat sequestration into metabolically inactive compartments such as the vacuole and cell wall.

Meanwhile, DTX5 (At2g04090), a homolog of DTX6 and previously identified as a negative regulator of plant disease resistance [96], shares 91.3% amino acid sequence identity with DTX6 (At2g04100) and exhibits functional redundancy, suggesting that other similar transporters may also contribute to paraquat sequestration [122]. DTX/MATE subfamily genes are highly conserved across plants, animals, and microorganisms, performing diverse roles, including resistance to various toxins [131–133]. The *A. thaliana* genome alone contains over 50 DTX members [134]. A comprehensive homology search, phylogenetic analysis, and protein structure simulation across species would provide further insight into the sequestration mechanism for paraquat resistance, especially since DTX6 is preferentially expressed in roots, with very low expression levels in leaves (more relevant to paraquat resistance following foliar application in field practices). Additionally, it has been suggested that DTX6 functions similarly to the bacterial membrane protein PqrA from *Ochrobactrum anthropi*, which exports toxic compounds and confers paraquat resistance when expressed heterologously in *Escherichia coli* [135] and in tobacco plants [110]. These studies collectively propose a common efflux transporter mechanism for paraquat resistance, with sequestration likely serving as the major model for paraquat resistance in plants (Figure 3). However, further functional genomics and genetic studies are needed to investigate if this mechanism endows paraquat resistance in weedy plants.

In the dark (Figure 3A), paraquat can move in both acropetal and basipetal ways. When paraquat is applied to the middle of a fully expanded second leaf of a grass plant (orange dot), most of the herbicide moves (orange arrows) upward toward the leaf tips. A smaller portion is translocated downward through the leaf blade, sheath, and stem, reaching the crown (the junction nodes between the shoot and the root). From the crown, a minor amount continues to the roots, while more paraquat moves upward into the first (old) leaf and only a small amount reaches the third (young) leaf. As shown in the right part of the figure (Figure 3B), Ca^{2+} , Mg^{2+} , and La^{3+} all caused a progressive inhibition of the saturable component of paraquat uptake (influx across the plasmalemma), indicating a driving force of the gradient for electrochemical potential of paraquat across the plasmalemma. Paraquat showed a reciprocal interaction by inhibiting Ca^{2+} influx into plant cells [136]. Three LAT proteins (LAT1/RMV1/PUT3, LAT3/PUT1, and LAT4/PAR1/PUT2) exhibit both polyamine (blue arrow) and paraquat (orange arrow) transporter activity and paraquat [104,118]. The plasma membrane-localized LAT1/RMV1 is one of the primary routes of paraquat entering cells. PDR11/PQT24 also takes part in transporting paraquat across the plasma membrane [86]. LAT4/PAR1 is involved in the paraquat accumulation in the chloroplast, possibly through the Golgi-mediated pathway [119]. Paraquat inside the cell is exported/sequestered to the vacuole and apoplast by efflux transporters such as DTX6/PQT15/RTP1, which is localized in a dynamic endomembrane trafficking pathway from the Golgi body to the vacuole and to the plasma membrane. DTX5 functions similar and redundant to DTX6 [122,129]. PqST1 shares high homology with SYP121 (syntaxin of plants 121)/PEN1 encoding a SNARE (Soluble N-ethylmaleimide-sensitive factor attachment protein receptor) superfamily protein involved in the transport of secretory vesicles at the plasma membrane. PqST2 is a homolog of MDR1/ABCB1 (ABC transporter B family) that encodes a paraquat efflux transporter in human and mice [28]. Arrows made up of solid blue and orange lines indicate experimentally demonstrated polyamine and paraquat transport pathway, respectively. Unconfirmed paraquat transporters and transport routes are indicated by dashed lines and question marks.

3. Perspectives of Paraquat and Paraquat Resistance Research in Plants

As a once widely used herbicide, paraquat now faces an uncertain future because of a confluence of factors, such as its inherent high toxicity to humans and animals, growing environmental concerns, increasing herbicide resistance, and, thus, bans in many countries (Table S1) [137–139]. In the United States, paraquat is not completely banned but is classified as a restricted-use pesticide, usable only by licensed applicators and prohibited on golf courses and other recreational areas by the Environmental Protection Agency (EPA). The estimated use of paraquat in U.S. agriculture, as mapped by the U.S. Geological Survey, reached 4500 tons in 2018, over nine times the usage reported in 1974 [140,141]. Although its use in North America is predicted to increase, campaigns to ban paraquat continue worldwide, especially in developed countries such as the United States and Australia. For instance, over 50 U.S. lawmakers have called on the EPA to ban paraquat because of its links to Parkinson's disease and other health risks [142]. In Australia, the Australian Pesticides and Veterinary Medicines Authority (APVMA) has proposed restricting many current high-rate applications—such as reducing the maximum annual paraquat use in vineyards from 800 g to 45 g ai ha^{−1}—when the risks to the environment or the short-term poisoning risk cannot be adequately mitigated [143,144]. At a lower paraquat rate, weed control effectiveness is likely to be greatly reduced. In time, developed countries may phase out paraquat despite potential increases in cropping costs and declines in farm profits [143], and some studies suggest that agriculture without paraquat is feasible without a loss in productivity [145]. By contrast, the cheap and popular paraquat will likely remain widely available in many developing countries. In response, some manufacturers have developed new formulations, such as granular and gel forms, in an attempt to reduce mishandling risks and meet regulatory requirements. Syngenta, for example, claims that its new gel formulation, which incorporates a gelling agent, can improve survival by approximately 30% after ingestion [146]. More recently, Peng et al. [147] discovered a paraquat pro-herbicide, dienediamine, which is the “reduced” form of paraquat that converts back to paraquat under natural sunlight and ambient conditions, offering a potential, safer alternative for sustainable agriculture globally.

Genetically modified (GM) crops engineered for herbicide resistance have been widely adopted since the 1990s as part of integrated weed control strategies, most notably through the use of glyphosate or glufosinate combined with resistant crop varieties such as soybean, maize, cotton, and canola [148,149]. Notably, there are also claims that GM crops have exacerbated the risk of selecting for herbicide resistance, which is complex, with evidence suggesting both positive and negative impacts. Nevertheless, GM crops are more sustainable as a component of more broadly integrated weed management systems [5,150]. Early studies investigating paraquat resistance inheritance found that a single major gene was responsible for naturally evolved paraquat resistance in various weeds (Table 1), which makes GM crops for paraquat resistance be very feasible. However, due to limited understanding of the molecular mechanisms, early attempts to engineer paraquat tolerance in plants via gene overexpression or knockout yielded only modest resistance (typically a less than 5-fold increase and tolerance to less than 10 µM paraquat) [62]. With an increasing understanding of the molecular mechanisms of paraquat resistance in plants, particularly *A. thaliana*, more genetic loci are now available for developing paraquat-resistant plants. For example, rice plants with RNA interference targeting *OsPAR1* exhibit high resistance and survive 140 µM paraquat under field spray conditions [119]. One-month-old rice plants with CRISPR/Cas9-targeted mutagenesis of *OsPUT1/2/3* survive up to 200 µM paraquat in a foliar spray condition [124]. Even more promising, a recent study in *A. thaliana* demonstrated that overexpression of *DTX6D*, a transporter involved in paraquat sequestration, conferred strong resistance to nearly commercial doses of paraquat up to 4 mM [122]. How-

ever, because DTX6 mediates sequestration of paraquat into both the apoplast and vacuole and more paraquat could be compartmented in cells and last for a long period [47,111,125], there is thus a major concern about paraquat residues accumulating in plant tissues, raising food safety issues. Therefore, while combining genes for nonoverlapping resistance mechanisms is an attractive strategy, developing crops that can metabolize paraquat into nontoxic compounds would be the ideal solution [72], a goal that remains distant. With advances in instrumentation, techniques, multi-omics data and large-scale AI (artificial intelligence)-assisted protein structure prediction and docking [151–154], revisiting earlier studies on high-level paraquat resistance for possible metabolic mechanisms, particularly in cases where uptake and translocation are not the primary causes [155], could yield significant breakthroughs.

Considering that *A. thaliana* is generally very sensitive to paraquat, it may not be the best model for identifying genes that confer high-level paraquat resistance, particularly at the metabolic level [4]. In-depth molecular studies are needed not only in model plants like *A. thaliana* but also in crop plants such as rice, wheat, and maize, as well as in highly resistant weedy species (e.g., various ryegrass species), particularly when considering the large resistance-level discrepancy between model plants and weeds [62]. Ryegrass (mainly *L. rigidum* and *L. perenne*), which is often used as a forage crop or turfgrass and is more closely related to major cereal crops [156,157], and for which quality genome resources and transformation/gene editing systems are now available [158–161], could serve as a good model weedy plant for herbicide resistance studies, including paraquat. One possible disadvantage could be its high outcrossing rate, which could make genetic analysis challenging. Considering this, goosegrass (*Eleusine indica*) could be a good alternative, which is primarily a self-pollinating diploid species with an ability to produce a large number of seeds. Like *Lolium rigidum*, it has been reported to be highly resistant to multi-herbicides, including paraquat [5]. Its small (~500 Mb) and readily available high-quality genome data and efficient agrobacterium-mediated genetic transformation system further make *Eleusine indica* a promising choice [29,162,163].

One particularly interesting phenomenon is the temperature-dependent paraquat resistance observed in some weed species, including ryegrass. Whether this is due to additional stress at high temperatures (given that they are C₃ plants that grow optimally under cool conditions), the temperature dependence of biochemical processes, altered membrane function/stability, differences in transporter activity, protein trafficking, or other mechanisms requires further detailed investigation [39,43,50,102]. Notably, expression of a cyanobacterial *desA* gene (encoding $\Delta 12$ acyl-lipid desaturase) in potato (*Solanum tuberosum*) improved tolerance to oxidative stress induced by paraquat, attributed to better maintenance of cell membrane structure and function [164]. Additionally, the long-distance translocation of paraquat is light-dependent, which makes the paraquat resistance mechanism more intriguing and warrants further study as well [59,108].

In conclusion, although paraquat remains a valuable tool for some farmers, its long-term future as a herbicide is bleak, which would diminish the value of research on paraquat resistance mechanisms to some degree. Like many herbicides, paraquat has contributed to the growing problem of herbicide resistance in weeds. Over the past decades, progress has been made in understanding the mechanisms of plant paraquat resistance, particularly various transporters related to paraquat uptake and transport in model plants like *A. thaliana* in the last decade; however, the molecular basis of paraquat resistance in field-evolved resistant weedy species remain elusive. For example, findings also suggest that transporters mediating paraquat's sequestration into the vacuole and apoplast are critical for resistance in weedy species, yet direct evidence for these membrane transporters in weeds is still lacking. With the advent of new techniques such as large-scale multi-omics

and AI-assisted protein structure prediction and docking focusing on transporters and metabolic enzymes (e.g., cytochrome P450 monooxygenases, glutathione-S-transferase, glycosyltransferase, and other enzymes), further breakthroughs in elucidating the molecular mechanisms underlying weeds' paraquat resistance appear promising.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/agriculture15121288/s1>, Table S1.

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References

1. Bromilow, R.H. Paraquat and sustainable agriculture. *Pest Manag. Sci.* **2004**, *60*, 340–349. [[CrossRef](#)] [[PubMed](#)]
2. Syngenta. Paraquat. Available online: <https://www.syngenta.com/media/paraquat-in-the-media> (accessed on 7 February 2025).
3. Shaner, D.L. *Herbicide Handbook*; Weed Science Society of America: Lawrence, KS, USA, 2014.
4. Nazish, T.; Huang, Y.-J.; Zhang, J.; Xia, J.-Q.; Alfatih, A.; Luo, C.; Cai, X.-T.; Xi, J.; Xu, P.; Xiang, C.-B. Understanding paraquat resistance mechanisms in *Arabidopsis thaliana* to facilitate the development of paraquat-resistant crops. *Plant Commun.* **2022**, *3*, 100321. [[CrossRef](#)] [[PubMed](#)]
5. Heap, I. The International Herbicide-Resistant Weed Database. 2025. Available online: <http://www.weedscience.org/> (accessed on 1 March 2025).
6. Borger, C.P.; Hashem, A. Evaluating the double knockdown technique: Sequence, application interval, and annual ryegrass growth stage. *Aust. J. Agric. Res.* **2007**, *58*, 265–271. [[CrossRef](#)]
7. Yu, Q.; Cairns, A.; Powles, S. Glyphosate, paraquat and ACCase multiple herbicide resistance evolved in a *Lolium rigidum* biotype. *Planta* **2007**, *225*, 499–513. [[CrossRef](#)] [[PubMed](#)]
8. Jalaludin, A.; Yu, Q.; Powles, S. Multiple resistance across glufosinate, glyphosate, paraquat and ACCase-inhibiting herbicides in an *Eleusine indica* population. *Weed Res.* **2015**, *55*, 82–89. [[CrossRef](#)]
9. Soar, C.; Preston, C.; Karotam, J.; Powles, S.B. Polyamines can inhibit paraquat toxicity and translocation in the broadleaf weed *Arctotheca calendula*. *Pestic. Biochem. Physiol.* **2004**, *80*, 94–105. [[CrossRef](#)]
10. Soar, C.; Karotam, J.; Preston, C.; Powles, S.B. Reduced paraquat translocation in paraquat resistant *Arctotheca calendula* (L.) Levyns is a consequence of the primary resistance mechanism, not the cause. *Pestic. Biochem. Physiol.* **2003**, *76*, 91–98. [[CrossRef](#)]
11. Purba, E.; Preston, C.; Powles, S.B. Inheritance of Bipyrindyl Herbicide Resistance in *Arctotheca calendula* and *Hordeum leporinum*. *Theor. Appl. Genet.* **1993**, *87*, 598–602. [[CrossRef](#)]
12. Njoroge, J.M. Tolerance of *Bidens pilosa* L. and *Parthenium hysterophorus* L. to paraquat (Gramoxone) in Kenya coffee. *Kenya Coffee-Coffee Board Kenya Mon. Bull.* **1991**, *56*, 651.
13. Addow, A. Evaluation of Black Jack (*Bidens pilosa* L.) Resistance to Paraquat. Master's Thesis, University of Nairobi, Nairobi, Kenya, 1996.
14. Fuerst, E.P.; Nakatani, H.Y.; Dodge, A.D.; Penner, D.; Arntzen, C.J. Paraquat Resistance in *Conyza*. *Plant Physiol.* **1985**, *77*, 984–989. [[CrossRef](#)]
15. Shaaltiel, Y.; Gressel, J. Multienzyme oxygen radical detoxifying system correlated with paraquat resistance in *Conyza bonariensis*. *Pestic. Biochem. Physiol.* **1986**, *26*, 22–28. [[CrossRef](#)]
16. Shaaltiel, Y.; Chua, N.H.; Gepstein, S.; Gressel, J. Dominant pleiotropy controls enzymes co-segregating with paraquat resistance in *Conyza bonariensis*. *Theor. Appl. Genet.* **1988**, *75*, 850–856. [[CrossRef](#)]
17. Amsellem, Z.; Jansen, M.; Driesenaar, A.; Gressel, J. Developmental Variability of Photooxidative Stress Tolerance in Paraquat-Resistant *Conyza*. *Plant Physiol.* **1993**, *103*, 1097–1106. [[CrossRef](#)] [[PubMed](#)]

18. Palma-Bautista, C.; Vázquez-García, J.G.; Domínguez-Valenzuela, J.A.; Mendes, K.F.; de la Cruz, R.A.; Torra, J.; De Prado, R. Non-Target-Site Resistance Mechanisms Endow Multiple Herbicide Resistance to Five Mechanisms of Action in *Conyza bonariensis*. *J. Agric. Food Chem.* **2021**, *69*, 14792–14801. [\[CrossRef\]](#)
19. Qasem, J.R. Chemical control and herbicide resistance of hairy fleabane (*Erigeron bonariensis* L.) in Jordan. *PLoS ONE* **2023**, *18*, e0263154. [\[CrossRef\]](#)
20. Pölös, E.; Mikulás, J.; Szigeti, Z.; Matkovics, B.; Hai, D.Q.; Párducz, Á.; Lehoczki, E. Paraquat and Atrazine Co-Resistance in *Conyza canadensis* (L.) Cronq. *Pestic. Biochem. Physiol.* **1988**, *30*, 142–154. [\[CrossRef\]](#)
21. Smisek, A.; Doucet, C.; Jones, M.; Weaver, S. Paraquat resistance in horseweed (*Conyza canadensis*) and Virginia pepperweed (*Lepidium virginicum*) from Essex County, Ontario. *Weed Sci.* **1998**, *46*, 200–204. [\[CrossRef\]](#)
22. Hickmott, H.; Tardif, F.J.; Laforest, M.; Rajcan, I.; Meloche, S.; Thibodeau, A.; Bedal, E.; Page, E.R. Transgressive segregation and the inheritance of paraquat resistance in horseweed (*Erigeron canadensis*). *Weed Sci.* **2025**, *73*, e2. [\[CrossRef\]](#)
23. Chiang, Y.J.; Wu, Y.X.; Chiang, M.Y.; Wang, C.Y. Role of antioxidative system in paraquat resistance of tall fleabane (*Conyza sumatrensis*). *Weed Sci.* **2008**, *56*, 350–355. [\[CrossRef\]](#)
24. Zobiole, L.; Pereira, V.; Albrecht, A.; Rubin, R.; Adegas, F.; Albrecht, L. Paraquat Resistance of Sumatran Fleabane (*Conyza sumatrensis*). *Planta Daninha* **2019**, *37*, e019183264. [\[CrossRef\]](#)
25. Albrecht, A.J.P.; Thomazini, G.; Albrecht, L.P.; Pires, A.; Lorenzetti, J.B.; Danilussi, M.T.Y.; Silva, A.F.M.; Adegas, F.S. *Conyza sumatrensis* Resistant to Paraquat, Glyphosate and Chlorimuron: Confirmation and Monitoring the First Case of Multiple Resistance in Paraguay. *Agriculture* **2020**, *10*, 582. [\[CrossRef\]](#)
26. Leal, J.F.L.; Souza, A.d.S.; Borella, J.; Araujo, A.L.S.; Langaro, A.C.; Chapeta, A.C.; Amorim, E.S.; Silva, G.S.; Morran, S.; Zobiole, L.H.S.; et al. Sumatran fleabane (*Conyza sumatrensis*) resistant to PSI-inhibiting herbicides and physiological responses to paraquat. *Weed Sci.* **2022**, *70*, 46–54. [\[CrossRef\]](#)
27. Ismail, B.S.; Chuah, T.S.; Salmijah, S.; Hussin, K.H. Role of superoxide dismutase and peroxidase activities in paraquat-resistant redflower ragleaf (*Crassocephalum crepidioides* (Benth.) S. Moore). *Aust. J. Agric. Res.* **2001**, *52*, 583–586. [\[CrossRef\]](#)
28. Luo, Q.; Wei, J.; Dong, Z.; Shen, X.; Chen, Y.; Gupta, D. Differences of endogenous polyamines and putative genes associated with paraquat resistance in goosegrass (*Eleusine indica* L.). *PLoS ONE* **2019**, *14*, e0216513. [\[CrossRef\]](#)
29. Luo, Q.; Chen, S.; Nian, H.; Ma, Q.; Ding, Y.; Hao, Q.; Wei, J.; Patel, J.D.; McElroy, J.S.; Liu, Y.; et al. Establishment of an efficient agrobacterium-mediated genetic transformation system to enhance the tolerance of the paraquat stress in engineering goosegrass (*Eleusine indica* L.). *Int. J. Mol. Sci.* **2023**, *24*, 6629. [\[CrossRef\]](#)
30. Buker, R.S.; Steed, S.T.; Stall, W.M. Confirmation and control of a paraquat-tolerant goosegrass (*Eleusine indica*) biotype. *Weed Technol.* **2002**, *16*, 309–313. [\[CrossRef\]](#)
31. Seng, C.T.; VAN Lun, L.; San, C.T.; BIN Sahid, I. Initial report of glufosinate and paraquat multiple resistance that evolved in a biotype of goosegrass (*Eleusine indica*) in Malaysia. *Weed Biol. Manag.* **2010**, *10*, 229–233. [\[CrossRef\]](#)
32. McElroy, J.S.; Harris, J.R.; Price, A.; Harkess, A.; Li, X. Identification of a paraquat-resistant goosegrass (*Eleusine indica*) population from a central Alabama vegetable production field. *Weed Sci.* **2021**, *69*, 648–652. [\[CrossRef\]](#)
33. Napitupulu, B.S.; Purba, E. Fitness of paraquat resistant and susceptible biotypes population of goosegrass (*Eleusine indica* (L.) Gaetrn.). *IOP Conf. Ser. Earth Environ. Sci.* **2021**, *810*, 012050. [\[CrossRef\]](#)
34. Vázquez-García, J.G.; la Cruz, R.A.-D.; Rojano-Delgado, A.M.; Palma-Bautista, C.; Vasconcelos, J.M.d.P.; De Prado, R. Multiple Herbicide Resistance Evolution: The Case of *Eleusine indica* in Brazil. *J. Agric. Food Chem.* **2021**, *69*, 1197–1205. [\[CrossRef\]](#)
35. Diaz, M.A.; De Prado, R.; Paul, R.N.; Smeda, R.J. Identification of paraquat and atrazine resistance in populations of *Epilobium ciliatum*. In Proceedings of the 50th International Symposium on Crop Protection, Ghent, Belgium, 5 May 1998; Volume 50, pp. 795–797.
36. Tahmasebi, B.K.; La Cruz, R.A.-D.; Alcántara, E.; Torra, J.; Valenzuela, J.A.D.; Cruz-Hipólito, H.E.; Rojano-Delgado, A.M.; De Prado, R. Multiple Resistance Evolution in Bipyrldylium-Resistant *Epilobium ciliatum* After Recurrent Selection. *Front. Plant Sci.* **2018**, *9*, 695. [\[CrossRef\]](#) [\[PubMed\]](#)
37. Tanaka, Y.; Chisaka, H.; Saka, H. Movement of Paraquat in Resistant and Susceptible Biotypes of *Erigeron-Philadelphicus* and *Erigeron-Canadensis*. *Physiol. Plant.* **1986**, *66*, 605–608. [\[CrossRef\]](#)
38. Bishop, T.; Powles, S.B.; Cornic, G. Mechanism of Paraquat Resistance in *Hordeum-Glaucum*. 2. Paraquat Uptake and Translocation. *Aust. J. Plant Physiol.* **1987**, *14*, 539–547. [\[CrossRef\]](#)
39. Purba, E.; Preston, C.; Powles, S.B. The mechanism of resistance to paraquat is strongly temperature-dependent in resistant *Hordeum-leporinum* Link and *H-glaucum* steud. *Planta* **1995**, *196*, 464–468. [\[CrossRef\]](#)
40. Powles, S.B. Appearance of a Biotype of the Weed, *Hordeum glaucum* Steud, Resistant to the Herbicide Paraquat. *Weed Res.* **1986**, *26*, 167–172. [\[CrossRef\]](#)
41. Islam, A.; Powles, S.B. Inheritance of resistance to paraquat in barley grass *Hordeum glaucum* steud. *Weed Res.* **1988**, *28*, 393–397. [\[CrossRef\]](#)

42. Powles, S.B.; Tucker, E.S.; Morgan, T.R. Eradication of Paraquat-Resistant *Hordeum glaucum* Steud. by Prevention of Seed Production for 3 Years. *Weed Res.* **1992**, *32*, 207–211. [\[CrossRef\]](#)
43. Preston, C.; Soar, C.J.; Hidayat, I.; Greenfield, K.M.; Powles, S.B. Differential translocation of paraquat in paraquat-resistant populations of *Hordeum leporinum*. *Weed Res.* **2005**, *45*, 289–295. [\[CrossRef\]](#)
44. Tucker, E.S.; Powles, S.B. A Biotype of Hare Barley (*Hordeum leporinum*) Resistant to Paraquat and Diquat. *Weed Sci.* **1991**, *39*, 159–162. [\[CrossRef\]](#)
45. Purba, E.; Preston, C.; Powles, S.B. Growth and competitiveness of paraquat-resistant and -susceptible biotypes of *Hordeum leporinum*. *Weed Res.* **1996**, *36*, 311–317. [\[CrossRef\]](#)
46. Koschnick, T.J.; Haller, W.T.; Glasgow, L. Documentation of landoltia (*Landoltia punctata*) resistance to diquat. *Weed Sci.* **2006**, *54*, 615–619. [\[CrossRef\]](#)
47. Yu, Q.; Huang, S.; Powles, S. Direct measurement of paraquat in leaf protoplasts indicates vacuolar paraquat sequestration as a resistance mechanism in *Lolium rigidum*. *Pestic. Biochem. Physiol.* **2010**, *98*, 104–109. [\[CrossRef\]](#)
48. Van Eerd, L.L.; Hoagland, R.E.; Zablotowicz, R.M.; Hall, J.C. Pesticide metabolism in plants and microorganisms. *Weed Sci.* **2003**, *51*, 472–495. [\[CrossRef\]](#)
49. Tehranchian, P.; Nandula, V.; Jugulam, M.; Putta, K.; Jasieniuk, M. Multiple resistance to glyphosate, paraquat and ACCase-inhibiting herbicides in Italian ryegrass populations from California: Confirmation and mechanisms of resistance. *Pest Manag. Sci.* **2018**, *74*, 868–877. [\[CrossRef\]](#)
50. Yu, Q.; Cairns, A.; Powles, S.B. Paraquat resistance in a population of *Lolium rigidum*. *Funct. Plant Biol.* **2004**, *31*, 247–254. [\[CrossRef\]](#)
51. Yu, Q.; Han, H.; Nguyen, L.; Forster, J.W.; Powles, S.B. Paraquat resistance in a *Lolium rigidum* population is governed by one major nuclear gene. *Theor. Appl. Genet.* **2009**, *118*, 1601–1608. [\[CrossRef\]](#)
52. Tsuji, K.; Hosokawa, M.; Morita, S.; Miura, R.; Tominaga, T.; Kudsk, P. Resistance to paraquat in *Mazus pumilus*. *Weed Res.* **2013**, *53*, 176–182. [\[CrossRef\]](#)
53. Ndou, V.; Kotze, D.; Marjanovic-Painter, B.; Phiri, E.E.; Pieterse, P.J.; Sonopo, M.S. Reduced Translocation Confers Paraquat Resistance in *Plantago lanceolata*. *Agronomy* **2024**, *14*, 977. [\[CrossRef\]](#)
54. Ndou, V.; Eksteen, F.; Phiri, E.; Pieterse, P.J. First report of glyphosate and paraquat resistance in two *Plantago* biotypes. *South Afr. J. Plant Soil* **2021**, *38*, 134–139. [\[CrossRef\]](#)
55. Bewick, T.A.; Kostewicz, S.R.; Stall, W.M.; Shilling, D.G.; Smith, K. Interaction of Cupric Hydroxide, Paraquat, and Biotype of American Black Nightshade (*Solanum americanum*). *Weed Sci.* **1990**, *38*, 634–638. [\[CrossRef\]](#)
56. Chase, C.A.; Bewick, T.A.; Shilling, D.G. Differential photosynthetic electron transport and oxidative stress in paraquat-resistant and sensitive biotypes of *Solanum americanum*. *Pestic. Biochem. Physiol.* **1998**, *60*, 83–90. [\[CrossRef\]](#)
57. Purba, E.; Preston, C.; Powles, S.B. Paraquat Resistance in a Biotype of *Vulpia bromoides* (L.) S.F. Gray. *Weed Res.* **1993**, *33*, 409–413. [\[CrossRef\]](#)
58. Gaines, T.A.; Duke, S.O.; Morran, S.; Rigon, C.A.G.; Tranel, P.J.; Küpper, A.; Dayan, F.E. Mechanisms of evolved herbicide resistance. *J. Biol. Chem.* **2020**, *295*, 10307–10330. [\[CrossRef\]](#) [\[PubMed\]](#)
59. Ghanizadeh, H.; Harrington, K.C. Non-target Site Mechanisms of Resistance to Herbicides. *Crit. Rev. Plant Sci.* **2017**, *36*, 24–34. [\[CrossRef\]](#)
60. Perotti, V.E.; Larran, A.S.; Palmieri, V.E.; Martinatto, A.K.; Permingeat, H.R. Herbicide resistant weeds: A call to integrate conventional agricultural practices, molecular biology knowledge and new technologies. *Plant Sci.* **2020**, *290*, 110255. [\[CrossRef\]](#)
61. Powles, S.B.; Yu, Q. Evolution in Action: Plants Resistant to Herbicides. *Annu. Rev. Plant Biol.* **2010**, *61*, 317–347. [\[CrossRef\]](#)
62. Hawkes, T.R. Mechanisms of resistance to paraquat in plants. *Pest Manag. Sci.* **2014**, *70*, 1316–1323. [\[CrossRef\]](#)
63. Fuerst, E.P.; Vaughn, K.C. Mechanisms of Paraquat Resistance. *Weed Technol.* **1990**, *4*, 150–156. [\[CrossRef\]](#)
64. Hart, J.J.; Di Tomaso, J.M. Sequestration and Oxygen Radical Detoxification as Mechanisms of Paraquat Resistance. *Weed Sci.* **1994**, *42*, 277–284. [\[CrossRef\]](#)
65. Preston, C. Resistance to Photosystem I Disrupting Herbicides. In *Herbicide Resistance in Plants, Biology and Biochemistry*; Powles, S.B., Ed.; CRC Press: Boca Raton, FL, USA, 1994; pp. 61–82.
66. Chase, C.A.; Bewick, T.A.; Shilling, D.G. Characterization of paraquat resistance in *Solanum americanum* Mill. II: Evidence for a chloroplast mechanism. *Pestic. Biochem. Physiol.* **1998**, *60*, 23–30. [\[CrossRef\]](#)
67. Mishra, S.; Sabat, S. Photosynthetic Electron-Transport in *Hydrilla verticillata* (L.) is Insensitive to Methylviologen (Paraquat) Inhibition. *Biochem. Biophys. Res. Commun.* **1995**, *212*, 132–137. [\[CrossRef\]](#) [\[PubMed\]](#)
68. Norman, M.; Fuerst, E.; Smeda, R.; Vaughn, K. Evaluation of Paraquat Resistance Mechanisms in *Conyza*. *Pestic. Biochem. Physiol.* **1993**, *46*, 236–249. [\[CrossRef\]](#)
69. Dixon, D.P.; Laphorn, A.; Edwards, R. Plant glutathione transferases. *Genome Biol.* **2002**, *3*, reviews3004. [\[CrossRef\]](#) [\[PubMed\]](#)
70. Hansen, C.C.; Nelson, D.R.; Möller, B.L.; Werck-Reichhart, D. Plant cytochrome P450 plasticity and evolution. *Mol. Plant* **2021**, *14*, 1244–1265. [\[CrossRef\]](#)

71. Gharabli, H.; Della Gala, V.; Welner, D.H. The function of UDP-glycosyltransferases in plants and their possible use in crop protection. *Biotechnol. Adv.* **2023**, *67*, 108182. [\[CrossRef\]](#)
72. Huang, Y.J.; Huang, Y.P.; Xia, J.Q.; Fu, Z.P.; Chen, Y.F.; Huang, Y.P.; Ma, A.; Hou, W.T.; Chen, Y.X.; Qi, X.; et al. *AtPQT11*, a P450 enzyme, detoxifies paraquat via N-demethylation. *J. Genet. Genom.* **2022**, *49*, 1169–1173. [\[CrossRef\]](#)
73. Harvey, B.M.R.; Muldoon, J.; Harper, D.B. Mechanism of paraquat tolerance in perennial ryegrass. *Plant Cell Environ.* **1978**, *1*, 203–209. [\[CrossRef\]](#)
74. Brunharo, C.A.C.G.; Hanson, B.D. Vacuolar Sequestration of Paraquat Is Involved in the Resistance Mechanism in *Lolium perenne* L. spp. *multiflorum*. *Front. Plant Sci.* **2017**, *8*, 1485. [\[CrossRef\]](#)
75. Huang, Y.; Zhan, H.; Bhatt, P.; Chen, S. Paraquat Degradation from Contaminated Environments: Current Achievements and Perspectives. *Front. Microbiol.* **2019**, *10*, 1754. [\[CrossRef\]](#)
76. Religia, P.; Nguyen, N.D.; Nong, Q.D.; Matsuur, T.; Kato, Y.; Watanabe, H. Mutation of the Cytochrome P450 CYP360A8 Gene Increases Sensitivity to Paraquat in *Daphnia magna*. *Environ. Toxicol. Chem.* **2021**, *40*, 1279–1288. [\[CrossRef\]](#)
77. Mittler, R.; Zandalinas, S.I.; Fichman, Y.; Van Breusegem, F. Reactive oxygen species signalling in plant stress responses. *Nat. Rev. Mol. Cell Biol.* **2022**, *23*, 663–679. [\[CrossRef\]](#) [\[PubMed\]](#)
78. Harper, D.B.; Harvey, B.M.R. Mechanism of paraquat tolerance in perennial ryegrass II. Role of superoxide dismutase, catalase and peroxidase. *Plant Cell Environ.* **1978**, *1*, 211–215. [\[CrossRef\]](#)
79. Pereira, V.G.C.; Carbonari, C.A.; Silva, M.A.; Costa, R.N.; Krenchinski, F.H.; Bevilacqua, N.C.; Velini, E.D. The role of the antioxidant system and the photosynthetic behavior of paraquat-resistant *Conyza sumatrensis* in Brazil. *J. Environ. Sci. Health. Part. B Pestic. Food Contam. Agric. Wastes* **2023**, *58*, 80–89. [\[CrossRef\]](#) [\[PubMed\]](#)
80. Kurepa, J.; Smalle, J.; Va, M.; Montagu, N.; Inzé, D. Oxidative stress tolerance and longevity in *Arabidopsis*: The late-flowering mutant *gigantea* is tolerant to paraquat. *Plant J.* **1998**, *14*, 759–764. [\[CrossRef\]](#)
81. Tsugane, K.; Kobayashi, K.; Niwa, Y.; Ohba, Y.; Wada, K.; Kobayashi, H. A recessive *Arabidopsis* mutant that grows photoautotrophically under salt stress shows enhanced active oxygen detoxification. *Plant Cell* **1999**, *11*, 1195–1206. [\[CrossRef\]](#)
82. Fujibe, T.; Saji, H.; Arakawa, K.; Yabe, N.; Takeuchi, Y.; Yamamoto, K.T. A methyl viologen-resistant mutant of *Arabidopsis*, which is allelic to ozone-sensitive *rcd1*, is tolerant to supplemental ultraviolet-B irradiation. *Plant Physiol.* **2004**, *134*, 275–285. [\[CrossRef\]](#)
83. Sipari, N.; Lihavainen, J.; Keinänen, M. Metabolite Profiling of Paraquat Tolerant *Arabidopsis thaliana* Radical-induced Cell Death1 (*rcd1*)-A Mediator of Antioxidant Defence Mechanisms. *Antioxidants* **2022**, *11*, 2034. [\[CrossRef\]](#)
84. Chen, R.; Sun, S.; Wang, C.; Li, Y.; Liang, Y.; An, F.; Li, C.; Dong, H.; Yang, X.; Zhang, J.; et al. The *Arabidopsis Paraquat Resistant2* gene encodes an S-nitrosoglutathione reductase that is a key regulator of cell death. *Cell Res.* **2009**, *19*, 1377–1387. [\[CrossRef\]](#)
85. Luo, C.; Cai, X.-T.; Du, J.; Zhao, T.-L.; Wang, P.-F.; Zhao, P.-X.; Liu, R.; Xie, Q.; Cao, X.-F.; Xiang, C.-B.; et al. Paraquat Tolerance3 is an E3 Ligase That Switches off Activated Oxidative Response by Targeting Histone-Modifying Protein Methyltransferase4b. *PLoS Genet.* **2016**, *12*, e1006332. [\[CrossRef\]](#)
86. Xi, J.; Xu, P.; Xiang, C.B. Loss of AtPDR11, a plasma membrane-localized ABC transporter, confers paraquat tolerance in *Arabidopsis thaliana*. *Plant J.* **2012**, *69*, 782–791. [\[CrossRef\]](#)
87. Wang, H.; Xu, D.; Zhu, X.; Wang, M.; Xia, Z. The maize SUMO conjugating enzyme ZmSCE1b protects plants from paraquat toxicity. *Ecotoxicol. Environ. Saf.* **2021**, *211*, 111909. [\[CrossRef\]](#) [\[PubMed\]](#)
88. Rigó, G.; Valkai, I.; Faragó, D.; Kiss, E.; Van Houdt, S.; Van de Steene, N.; Hannah, M.A.; Szabados, L. Gene mining in halophytes: Functional identification of stress tolerance genes in *Lepidium crassifolium*. *Plant Cell Environ.* **2016**, *39*, 2074–2084. [\[CrossRef\]](#) [\[PubMed\]](#)
89. Faragó, D.; Zsigmond, L.; Benyó, D.; Alcazar, R.; Rigó, G.; Ayaydin, F.; Rabilu, S.A.; Hunyadi-Gulyás, É.; Szabados, L. Small paraquat resistance proteins modulate paraquat and ABA responses and confer drought tolerance to overexpressing *Arabidopsis* plants. *Plant Cell Environ.* **2022**, *45*, 1985–2003. [\[CrossRef\]](#) [\[PubMed\]](#)
90. Tseng, T.-Y.; Ou, J.-F.; Wang, C.-Y. Role of the Ascorbate-Glutathione Cycle in Paraquat Tolerance of Rice. *Weed Sci.* **2013**, *61*, 361–373. [\[CrossRef\]](#)
91. Luo, Q.; Chen, S.; Zhu, J.; Ye, L.; Hall, N.D.; Basak, S.; McElroy, J.S.; Chen, Y. Overexpression of *EiKCS* confers paraquat-resistance in rice (*Oryza sativa* L.) by promoting the polyamine pathway. *Pest Manag. Sci.* **2022**, *78*, 246–262. [\[CrossRef\]](#)
92. Broadbent, P.; Creissen, G.; Kular, B.; Wellburn, A.; Mullineaux, P. Mullineaux. Oxidative Stress Responses in Transgenic Tobacco Containing Altered Levels of Glutathione-Reductase Activity. *Plant J.* **1995**, *8*, 247–255. [\[CrossRef\]](#)
93. Kwon, S.Y.; Jeong, Y.J.; Lee, H.S.; Kim, J.S.; Cho, K.Y.; Allen, R.D.; Kwak, S.S. Enhanced tolerances of transgenic tobacco plants expressing both superoxide dismutase and ascorbate peroxidase in chloroplasts against methyl viologen-mediated oxidative stress. *Plant Cell Environ.* **2002**, *25*, 873–882. [\[CrossRef\]](#)
94. Kwon, S.-Y.; Choi, S.-M.; Ahn, Y.-O.; Lee, H.-S.; Lee, H.-B.; Park, Y.-M.; Kwak, S.-S. Enhanced stress-tolerance of transgenic tobacco plants expressing a human dehydroascorbate reductase gene. *J. Plant Physiol.* **2003**, *160*, 347–353. [\[CrossRef\]](#)

95. Murgia, I.; Tarantino, D.; Vannini, C.; Bracale, M.; Carravieri, S.; Soave, C. *Arabidopsis thaliana* plants overexpressing thylakoidal ascorbate peroxidase show increased resistance to Paraquat-induced photooxidative stress and to nitric oxide-induced cell death. *Plant J.* **2004**, *38*, 940–953. [\[CrossRef\]](#)
96. Yoshimura, K.; Miyao, K.; Gaber, A.; Takeda, T.; Kanaboshi, H.; Miyasaka, H.; Shigeoka, S. Enhancement of stress tolerance in transgenic tobacco plants overexpressing *Chlamydomonas* glutathione peroxidase in chloroplasts or cytosol. *Plant J.* **2004**, *37*, 21–33. [\[CrossRef\]](#)
97. Lee, Y.-P.; Kim, S.-H.; Bang, J.-W.; Lee, H.-S.; Kwak, S.-S.; Kwon, S.-Y. Enhanced tolerance to oxidative stress in transgenic tobacco plants expressing three antioxidant enzymes in chloroplasts. *Plant Cell Rep.* **2007**, *26*, 591–598. [\[CrossRef\]](#) [\[PubMed\]](#)
98. Vaughn, K.C.; Vaughan, M.A.; Camilleri, P. Lack of Cross-Resistance of Paraquat-Resistant Hairy Fleabane (*Conyza bonariensis*) to Other Toxic Oxygen Generators Indicates Enzymatic Protection is Not the Resistance Mechanism. *Weed Sci.* **1989**, *37*, 5–11. [\[CrossRef\]](#)
99. Taiz, L.; Zeiger, E.; Møller, I.M.; Murphy, A. *Plant Physiology and Development*; Sinauer Associates: Sunderland, MA, USA, 2015.
100. Slade, P.; Bell, E.G. Movement of Paraquat in Plants. *Weed Res.* **1966**, *6*, 267–274. [\[CrossRef\]](#)
101. Putnam, A.R.; Ries, S.K. Factors Influencing Phytotoxicity and Movement of Paraquat in Quackgrass. *Weed Sci.* **1968**, *16*, 80–83. [\[CrossRef\]](#)
102. Lasat, M.M.; Ditomaso, J.M.; Hart, J.J.; Kochian, L.V. Resistance to paraquat in *Hordeum glaucum* is temperature dependent and not associated with enhanced apoplasmic binding. *Weed Res.* **1996**, *36*, 303–309. [\[CrossRef\]](#)
103. Hart, J.J.; DiTomaso, J.M.; Linscott, D.L.; Kochian, L.V. Transport interactions between paraquat and polyamines in roots of intact maize seedlings. *Plant Physiol.* **1992**, *99*, 1400–1405. [\[CrossRef\]](#)
104. Fujita, M.; Shinozaki, K. Identification of Polyamine Transporters in Plants: Paraquat Transport Provides Crucial Clues. *Plant Cell Physiol.* **2014**, *55*, 855–861. [\[CrossRef\]](#)
105. Hart, J.J.; DiTomaso, J.M.; Kochian, L.V. Characterization of paraquat transport in protoplasts from maize (*Zea mays* L.) suspension cells. *Plant Physiol.* **1993**, *103*, 963–969. [\[CrossRef\]](#)
106. Jared, B.F.; Fitzpatrick, T.B. Paraquat resistance mutations have differential effects on plant fitness in two rice cultivars. *Biochem. J.* **2025**, *482*, 401–412.
107. Vaughn, K.C.; Fuerst, E. Structural and physiological studies of paraquat-resistant *Conyza*. *Pestic. Biochem. Physiol.* **1985**, *24*, 86–94. [\[CrossRef\]](#)
108. Preston, C.; Holtum, J.A.M.; Powles, S.B. On the mechanism of resistance to paraquat in *Hordeum glaucum* and *H. leporinum*—Delayed inhibition of photosynthetic o₂ evolution after paraquat application. *Plant Physiol.* **1992**, *100*, 630–636. [\[CrossRef\]](#) [\[PubMed\]](#)
109. Norman, M.; Smeda, R.; Vaughn, K.; Fuerst, E. Differential movement of paraquat in resistant and sensitive biotypes of *Conyza*. *Pestic. Biochem. Physiol.* **1994**, *50*, 31–42. [\[CrossRef\]](#)
110. Jo, J.; Won, S.-H.; Son, D.; Lee, B.-H. Paraquat resistance of transgenic tobacco plants over-expressing the *Ochrobactrum anthropi pqrA* gene. *Biotechnol. Lett.* **2004**, *26*, 1391–1396. [\[CrossRef\]](#) [\[PubMed\]](#)
111. Jóri, B.; Soós, V.; Szegő, D.; Páldi, E.; Szigeti, Z.; Rácz, I.; Lásztity, D. Role of transporters in paraquat resistance of horseweed *Conyza canadensis* (L.) Cronq. *Pestic. Biochem. Physiol.* **2007**, *88*, 57–65. [\[CrossRef\]](#)
112. Brûle, S.V.D.; Müller, A.; Fleming, A.J.; Smart, C.C. The ABC transporter SpTUR2 confers resistance to the antifungal diterpene sclareol. *Plant J.* **2002**, *30*, 649–662. [\[CrossRef\]](#)
113. Schulz, B.; Kolukisaglu, H. Genomics of plant ABC transporters: The alphabet of photosynthetic life forms or just holes in membranes? *Febs Lett.* **2006**, *580*, 1010–1016. [\[CrossRef\]](#)
114. Kim, D.Y.; Bovet, L.; Maeshima, M.; Martinoia, E.; Lee, Y. The ABC transporter AtPDR8 is a cadmium extrusion pump conferring heavy metal resistance. *Plant J.* **2007**, *50*, 207–218. [\[CrossRef\]](#)
115. Kang, J.; Hwang, J.-U.; Lee, M.; Kim, Y.-Y.; Assmann, S.M.; Martinoia, E.; Lee, Y. PDR-type ABC transporter mediates cellular uptake of the phytohormone abscisic acid. *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 2355–2360. [\[CrossRef\]](#)
116. Song, W.; Maeda, H.; DellaPenna, D. Mutations of the ER to plastid lipid transporters TGD1, 2, 3 and 4 and the ER oleate desaturase FAD2 suppress the low temperature-induced phenotype of *Arabidopsis* tocopherol-deficient mutant *vte2*. *Plant J.* **2010**, *62*, 1004–1018. [\[CrossRef\]](#)
117. Panzeri, D.; Cassani, E.; Doria, E.; Tagliabue, G.; Forti, L.; Campion, B.; Bollini, R.; Brearley, C.A.; Pilu, R.; Nielsen, E.; et al. A defective ABC transporter of the MRP family, responsible for the bean *lpa1* mutation, affects the regulation of the phytic acid pathway, reduces seed myo-inositol and alters ABA sensitivity. *New Phytol.* **2011**, *191*, 70–83. [\[CrossRef\]](#)
118. Fujita, M.; Fujita, Y.; Iuchi, S.; Yamada, K.; Kobayashi, Y.; Urano, K.; Kobayashi, M.; Yamaguchi-Shinozaki, K.; Shinozaki, K. Natural variation in a polyamine transporter determines paraquat tolerance in *Arabidopsis*. *Proc. Natl. Acad. Sci. USA* **2012**, *109*, 6343–6347. [\[CrossRef\]](#) [\[PubMed\]](#)
119. Li, J.; Mu, J.; Bai, J.; Fu, F.; Zou, T.; An, F.; Zhang, J.; Jing, H.; Wang, Q.; Li, Z.; et al. Paraquat Resistant1, a Golgi-Localized Putative Transporter Protein, is Involved in Intracellular Transport of Paraquat. *Plant Physiol.* **2013**, *162*, 470–483. [\[CrossRef\]](#) [\[PubMed\]](#)

120. Liu, J.; Chen, H.; Liu, L.; Meng, X.; Liu, Q.; Ye, Q.; Wen, J.; Wang, T.; Dong, J. A cargo sorting receptor mediates chloroplast protein trafficking through the secretory pathway. *Plant Cell* **2024**, *36*, 3770–3786. [CrossRef] [PubMed]
121. Dong, S.; Hu, H.; Wang, Y.; Xu, Z.; Zha, Y.; Cai, X.; Peng, L.; Feng, S. A *pqr2* mutant encodes a defective polyamine transporter and is negatively affected by ABA for paraquat resistance in *Arabidopsis thaliana*. *J. Plant Res.* **2016**, *129*, 899–907. [CrossRef]
122. Xia, J.-Q.; Nazish, T.; Javaid, A.; Ali, M.; Liu, Q.-Q.; Wang, L.; Zhang, Z.-Y.; Zhang, Z.-S.; Huang, Y.-J.; Wu, J.; et al. A gain-of-function mutation of the MATE family transporter DTX6 confers paraquat resistance in *Arabidopsis*. *Mol. Plant* **2021**, *14*, 2126–2133. [CrossRef]
123. Kuromori, T.; Sugimoto, E.; Shinozaki, K. *Arabidopsis* mutants of *AtABCG22*, an ABC transporter gene, increase water transpiration and drought susceptibility. *Plant J.* **2011**, *67*, 885–894. [CrossRef]
124. Lyu, Y.-S.; Cao, L.-M.; Huang, W.-Q.; Liu, J.-X.; Lu, H.-P. Disruption of three polyamine uptake transporter genes in rice by CRISPR/Cas9 gene editing confers tolerance to herbicide paraquat. *Abiotech* **2022**, *3*, 140–145. [CrossRef]
125. Lasat, M.M.; DiTomaso, J.M.; Hart, J.J.; Kochian, L.V. Evidence for vacuolar sequestration of paraquat in roots of a paraquat-resistant *Hordeum glaucum* biotype. *Physiol. Plant.* **1997**, *99*, 255–262. [CrossRef]
126. Mornet, C.; Mondory, C.; Gaillard, C.; Martinoia, E. Transport of paraquat and polyamines across the vacuolar membrane of barley mesophyll cells. *Plant Physiol. Biochem.* **1997**, *35*, 589–594.
127. Tanaka, Y.; Hipolito, C.J.; Maturana, A.D.; Ito, K.; Kuroda, T.; Higuchi, T.; Katoh, T.; Kato, H.E.; Hattori, M.; Kumazaki, K.; et al. Structural basis for the drug extrusion mechanism by a MATE multidrug transporter. *Nature* **2013**, *496*, 247–251. [CrossRef]
128. Lu, M. Structures of multidrug and toxic compound extrusion transporters and their mechanistic implications. *Channels* **2016**, *10*, 88–100. [CrossRef] [PubMed]
129. Lv, Z.; Zhao, M.; Wang, W.; Wang, Q.; Huang, M.; Li, C.; Lian, Q.; Xia, J.; Qi, J.; Xiang, C.; et al. Changing Gly311 to an acidic amino acid in the MATE family protein DTX6 enhances *Arabidopsis* resistance to the dihydropyridine herbicides. *Mol. Plant* **2021**, *14*, 2115–2125. [CrossRef] [PubMed]
130. Sun, X.; Gilroy, E.M.; Chini, A.; Nurnberg, P.L.; Hein, I.; Lacomme, C.; Birch, P.R.J.; Hussain, A.; Yun, B.-W.; Loake, G.J. ADS1 encodes a MATE-transporter that negatively regulates plant disease resistance. *New Phytol.* **2011**, *192*, 471–482. [CrossRef] [PubMed]
131. Li, L.; He, Z.; Pandey, G.K.; Tsuchiya, T.; Luan, S. Functional cloning and characterization of a plant efflux carrier for multidrug and heavy metal detoxification. *J. Biol. Chem.* **2002**, *277*, 5360–5368. [CrossRef]
132. Omote, H.; Hiasa, M.; Matsumoto, T.; Otsuka, M.; Moriyama, Y. The MATE proteins as fundamental transporters of metabolic and xenobiotic organic cations. *Trends Pharmacol. Sci.* **2006**, *27*, 587–593. [CrossRef]
133. Dobritsch, M.; Lübken, T.; Eschen-Lippold, L.; Gorzolka, K.; Blum, E.; Matern, A.; Marillonnet, S.; Böttcher, C.; Dräger, B.; Rosahl, S. MATE Transporter-Dependent Export of Hydroxycinnamic Acid Amides. *Plant Cell* **2016**, *28*, 583–596. [CrossRef]
134. Takanashi, K.; Shitan, N.; Yazaki, K. The multidrug and toxic compound extrusion (MATE) family in plants. *Plant Biotechnol.* **2014**, *31*, 417–430. [CrossRef]
135. Won, S.-H.; Lee, B.-H.; Lee, H.-S.; Jo, J. An *Ochrobactrum anthropi* gene conferring paraquat resistance to the heterologous host *Escherichia coli*. *Biochem. Biophys. Res. Commun.* **2001**, *285*, 885–890. [CrossRef]
136. Norman, M.A.; Fuerst, E. Interactions of cations with paraquat in leaf sections of resistant and sensitive biotypes of *Conyza bonariensis*. *Pestic. Biochem. Physiol.* **1997**, *57*, 181–191. [CrossRef]
137. Copping, L.G. Paraquat: Boon or Bane? *Outlooks Pest. Manag.* **2004**, *15*, 258. [CrossRef]
138. Dinham, B. Why paraquat should be banned. *Outlooks Pest. Manag.* **2004**, *15*, 268. [CrossRef]
139. Utyasheva, L.; Amarasinghe, P.; Eddleston, M. Paraquat at 63—the story of a controversial herbicide and its regulations: It is time to put people and public health first when regulating paraquat. *Res. Sq.* **2024**. [CrossRef]
140. EPA. *Pesticide Usage Survey of Agricultural, Governmental, and Industrial Sectors in the United States*; EPA: Washington, DC, USA, 1974.
141. USGS. *2018: Estimated Agricultural Use for Paraquat*; USGS: Reston, VA, USA, 2018.
142. Casar, G. Casar Leads 46 Members of Congress to Demand EPA Bans Use of Paraquat to Protect Public Health. 2024. Available online: <https://casar.house.gov/media/press-releases/news-casar-leads-46-members-congress-demand-epa-bans-use-paraquat-protect#:~:text=Golfers%20are%20already%20protected,%20farmworkers,U.S.%20to%20protect%20public%20health> (accessed on 12 June 2025).
143. Walsh, A.; Kingwell, R. Economic implications of the loss of glyphosate and paraquat on Australian mixed enterprise farms. *Agric. Syst.* **2021**, *193*, 103207. [CrossRef]
144. APVMA. *Understanding the Proposed Regulatory Decision for Paraquat*; APVMA: Armidale, NSW, Australia, 2024.
145. Stuart, A.M.; Merfield, C.N.; Horgan, F.G.; Willis, S.; Watts, M.A.; Ramírez-Muñoz, F.; Jorge Sanchez, U.; Utyasheva, L.; Eddleston, M.; Davis, M.L.; et al. Agriculture without paraquat is feasible without loss of productivity—lessons learned from phasing out a highly hazardous herbicide. *Environ. Sci. Pollut. Res. Int.* **2023**, *30*, 16984–17008. [CrossRef]
146. Watts, M. *Paraquat: Pesticide Action Network Asia and the Pacific (PANAP)*; Pesticide Action Network Asia and the Pacific: Penang, Malaysia, 2010.

147. Peng, H.; Zhao, D.; Tang, W.; Peng, A. Dienediamine: A safe surrogate for the herbicide paraquat. *Mol. Plant* **2023**, *16*, 1962–1975. [\[CrossRef\]](#)
148. Brookes, G. Weed control changes and genetically modified herbicide tolerant crops in the USA 1996–2012. *GM Crops Food* **2014**, *5*, 321–332. [\[CrossRef\]](#)
149. Brookes, G. Genetically Modified (GM) Crop Use 1996–2020: Environmental Impacts Associated with Pesticide Use Change. *GM Crops Food* **2022**, *13*, 262–289. [\[CrossRef\]](#)
150. Gage, K.L.; Krausz, R.F.; Walters, S.A. Emerging Challenges for Weed Management in Herbicide-Resistant Crops. *Agriculture* **2019**, *9*, 180. [\[CrossRef\]](#)
151. Subramanian, I.; Verma, S.; Kumar, S.; Jere, A.; Anamika, K. 2020: Multi-omics Data Integration, Interpretation, and Its Application. *Bioinform. Biol. Insights* **2020**, *14*, 1177932219899051. [\[CrossRef\]](#)
152. Xia, J.Q.; Liu, Q.Q.; Xiang, C.B. (14) C-paraquat Efflux Assay in *Arabidopsis* Mesophyll Protoplasts. *Bio Protoc.* **2022**, *12*, e4512. [\[CrossRef\]](#)
153. Zhao, M.; Wang, Q.; Shi, M.; Sun, Z.; Tang, H.; Ge, X. Determination of Paraquat in *Arabidopsis* Tissues and Protoplasts by UHPLC-MS/MS. *Int. J. Mol. Sci.* **2023**, *13*, e4642. [\[CrossRef\]](#) [\[PubMed\]](#)
154. Michels, J.; Bandrupalli, R.; Akbari, A.A.; Le, T.; Xiao, H.; Li, J.; Hom, E.F.Y. Natural Language Processing Methods for the Study of Protein–Ligand Interactions. *J. Chem. Inf. Model.* **2025**, *65*, 2191–2213. [\[CrossRef\]](#) [\[PubMed\]](#)
155. Carroll, E.W.; Schwarz, O.J.; Hickok, L.G. Biochemical Studies of Paraquat-Tolerant Mutants of the Fern *Ceratopteris richardii* 1. *Plant Physiol.* **1988**, *87*, 651–654. [\[CrossRef\]](#) [\[PubMed\]](#)
156. Wilkins, P. Breeding perennial ryegrass for agriculture. *Euphytica* **1991**, *52*, 201–214. [\[CrossRef\]](#)
157. Griffith, S.; Chastain, T. Physiology and growth of ryegrass. *Ecol. Prod. Manag. Lolium Forage USA* **1997**, *24*, 15–28.
158. Nagy, I.; Veeckman, E.; Liu, C.; Van Bel, M.; Vandepoele, K.; Jensen, C.S.; Ruttink, T.; Asp, T. Chromosome-scale assembly and annotation of the perennial ryegrass genome. *BMC Genom.* **2022**, *23*, 505. [\[CrossRef\]](#)
159. Paril, J.; Pandey, G.; Barnett, E.M.; Rane, R.V.; Court, L.; Walsh, T.; Fournier-Level, A. Rounding up the annual ryegrass genome: High-quality reference genome of *Lolium rigidum*. *Front. Genet.* **2022**, *13*, 1012694. [\[CrossRef\]](#)
160. Chen, Y.; Kölliker, R.; Mascher, M.; Copetti, D.; Himmelbach, A.; Stein, N.; Studer, B. An improved chromosome-level genome assembly of perennial ryegrass (*Lolium perenne* L.). *Gigabyte* **2024**, *2024*, 112. [\[CrossRef\]](#)
161. Chen, Y.; Kiesbauer, J.; Copetti, D.; Frei, D.; Frey, J.E.; Grieder, C.; Koelliker, R.; Studer, B. Chromosome-level haplotype-resolved genome assembly provides insights into the highly heterozygous genome of Italian ryegrass (*Lolium multiflorum* Lam.). *bioRxiv* **2024**. [\[CrossRef\]](#)
162. Zhang, C.; Johnson, N.A.; Hall, N.; Tian, X.; Yu, Q.; Patterson, E.L. Subtelomeric 5-enolpyruvylshikimate-3-phosphate synthase copy number variation confers glyphosate resistance in *Eleusine indica*. *Nat. Commun.* **2023**, *14*, 4865. [\[CrossRef\]](#)
163. Lee, S.; Kim, C. Chromosome-scale genome assembly of Korean goosegrass (*Eleusine indica*). *Sci. Data* **2025**, *12*, 156. [\[CrossRef\]](#)
164. Demin, I.N.; Naraikina, N.V.; Tsedendambaev, V.D.; Moshkov, I.E.; Trunova, T.I. Integration of the Cyanobacterial *DesA* Gene for $\Delta 12$ -Acyl-Lipid Desaturase Improves Potato Tolerance to Paraquat-Induced Oxidative Stress. *Russ. J. Plant Physiol.* **2011**, *58*, 660–666. [\[CrossRef\]](#)

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