

Dehalogenase Enzyme Structure and Its Role in Degradation of Organochlorine Compounds :A Review

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Abstract: Halogenated compounds, including organochlorines, are extensively used as pesticides across agriculture and various industrial applications. These compounds persist in the environment and are toxic, posing significant challenges for remediation efforts. Detoxification strategies such as physical, chemical, and biodegradation methods have been developed to reduce their impact. Among these, biodegradation using microorganisms and their enzymes has become a preferred, environmentally friendly approach. Specifically, Haloacid dehalogenases facilitate the hydrolytic scission of carbon–halogen linkages at the C2 position of short-chain haloacids, facilitating their conversion to less toxic products. While numerous dehalogenases involved in halogenated compound degradation have been identified, detailed biochemical and structural characterizations exist for only a limited subset. This review provides a comprehensive summary of the classification, structure, catalytic mechanisms, and environmental applications of dehalogenases, highlighting their essential role in biodegrading chlorinated pollutants.

Keywords: dehalogenase; halogenated compounds; organochlorines; detoxification; biodegradation.

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1. Introduction

Pesticides—including fungicides, agricultural and domestic insecticides, and herbicides—are widely used worldwide. Among these, organophosphates and organochlorines dominate both agricultural and industrial sectors. Synthetic organophosphorus compounds (OPs) were first developed in the late 1940s and early 1950s, while chlorine-based pesticides have been utilized since the 1940s [1,2]. Halogenated organic compounds contain at least one carbon–halogen bond (Figure 1) [3]. Although over 3,800 naturally occurring halogenated organic compounds exist in the biosphere, industrial production far exceeds natural levels because of extensive use in agrochemicals, pharmaceuticals, and solvents [4]. These compounds present a substantial environmental threat because of their toxicity, persistence, and the toxicity of their degradation products [5]. A significant concern is the impact on human health. Despite their poor water solubility, these compounds are sufficiently lipophilic to

accumulate in animal adipose tissue. Their metabolic resistance leads to bioaccumulation. Multiple studies link exposure to these compounds with carcinogenic effects, including breast cancer in both laboratory animals and humans. Therefore, effective and economical pesticide detoxification methods—especially enzymatic hydrolysis—are critically important [6]. Certain bacteria can utilize halogenated compounds as their sole source of carbon and energy, thereby reducing environmental pollution [7]. These microorganisms produce dehalogenases—specialized biocatalysts that mediate the hydrolytic scission of carbon–halogen linkages within halogenated organic matrices to yield environmentally benign products. The discovery of dehalogenases dates back to Johnson, who isolated bacteria and fungi capable of growing on halogenated alkanolic acids [8]. Some microorganisms produce multiple dehalogenases, conferring survival advantages under environmental fluctuations [9]. Dehalogenases are classified based on sequence similarity, substrate specificity, optimum pH, size, subunit structure, and electrophoretic mobility under denaturing conditions. Haloacid dehalogenases from bacterial and fungal sources have received considerable attention for potential biotechnological applications, notably in bioremediation of haloacid pollutants [10,11]. Based on substrate specificity, three types of haloacid dehalogenases have been identified: dl-, d-, and l-haloacid dehalogenases [12,13]. dl-haloacid dehalogenases act on both enantiomeric forms of haloacids while demonstrating either retention or inversion of stereochemical configuration at the C2 position. By contrast, d- and l-haloacid dehalogenases are enantiomer-specific, altering the C2 configuration of the resulting hydroxyalkanoic acid [14]. Two X-ray crystal structures of mesophilic l-2-haloacid dehalogenases have been elucidated, specifically L-DEX-YL derived from *Pseudomonas* sp. YL [15] and Dh1B isolated from *Xanthobacter autotrophicus* GJ10 [16]. Both enzymes are homodimers; each subunit features a Rossmann fold core comprising six parallel β -strands, five α -helices, and a distinct four-helix bundle motif that forms the subdomain. These enzymes are classified as hydrolases (Figure 2). Additionally, the three-dimensional architecture of a putative haloacid dehalogenase, designated PH0459 and derived from the thermophilic archaeon *Pyrococcus horikoshii* OT3, has been successfully solved. Enzymes from thermophiles often demonstrate exceptional stability under harsh conditions such as elevated temperatures and organic solvents, rendering them suitable for industrial biocatalysis [17].

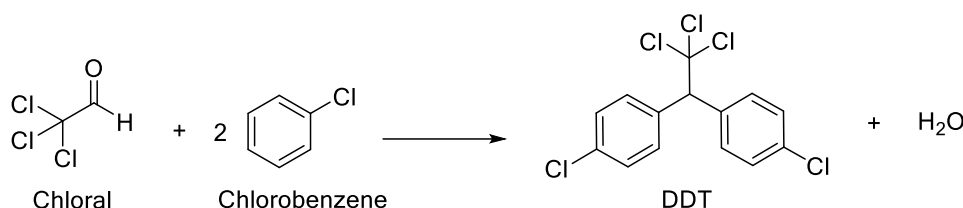


Figure 1. The chemical process that produces DDT.

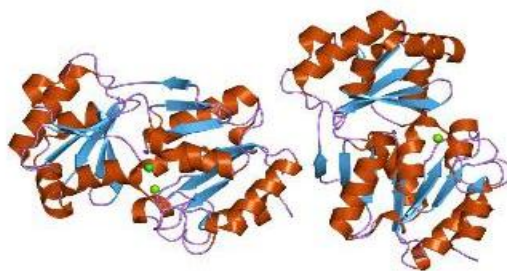


Figure 2. Hydrolase structure.

The genome of *Sulfolobus tokodaii*—a crenarchaeote isolated in 1983 from the Beppu hot spring in Kyushu, Japan—has been sequenced. This organism thrives optimally at 80°C in sulfur-rich, acidic environments and oxidizes hydrogen sulfide to sulfate [18]. This review briefly discusses the impact of organochlorines on human health and explores enzymatic strategies for their detoxification [19].

2. The Risk of Using Organochlorine Pesticides to Human Health

Producing safe food for human consumption is a global priority, making the health risks associated with organochlorine pesticides (OCPs) a major concern. OCPs, including compounds such as DDT, endosulfan, and chlordane, have been extensively used to protect crops but pose considerable ecotoxicological and public health risks due to their chemical stability and environmental persistence [20].

2.1. Chemical stability and environmental persistence.

OCPs possess strong carbon–chlorine bonds that confer both chemical stability and resistance to metabolic degradation. This stability leads to their long-term persistence, bioaccumulation, and biomagnification throughout the food chain, resulting in sustained environmental contamination [21].

2.2. Health hazards.

2.2.1. Acute and chronic toxic effects.

Short-term exposure to OCPs can cause symptoms including headache, vomiting, skin rashes, respiratory distress, and convulsions. Prolonged exposure may suppress immune and reproductive systems, induce neurological damage, and, in severe cases, lead to mortality [22].

2.2.2. Endocrine disruption.

OCPs act as endocrine-disrupting chemicals (EDCs), interfering with hormone signaling pathways such as thyroid function, estrogen, androgen, and steroid biosynthesis. Even at low doses, they can cause reproductive abnormalities, disrupt sexual behaviors, and alter bone development by disrupting thyroid hormone regulation. These chemicals may mimic or block natural hormones, adversely affecting both wildlife and human development.

2.2.3. Carcinogenicity.

Extensive research links OCP exposure to increased risks of various cancers, including breast, pancreatic, liver, skin, and hematological malignancies. Elevated OCP residues are often detected in blood samples from cancer patients compared to healthy individuals, with compounds such as DDT and endosulfan strongly associated with breast cancer.

2.2.4. Neurotoxicity and Genotoxicity.

OCPs can impair nervous system function and brain health and have been shown to cause genetic damage in developing fetuses, possibly leading to neurological and developmental disorders. Chronic exposure can disrupt neurotransmitter balance and contribute to neuroendocrine dysfunction [20].

2.3. Food chain and environmental impact.

OCP residues persist in soil, water, and crops, bioaccumulating in plant tissues and magnifying through the food chain, ultimately affecting ruminants and humans [20]. These pesticides can cause significant ecological disturbances, including disruptions in ecosystem health and animal population declines [23,24].

Table 1. WHO classification of toxicity. WHO classification of toxicity. Source: Adapted from World Health Organization (WHO) Recommended Classification of Pesticides by Hazard [26].

WHO hazard class	LD ₅₀ (Oral, rat, mg/kg)	Description
Ia	≤5 (solids), ≤20 (liquids)	Extremely hazardous
Ib	5–50 (solids), 20–200 (liquids)	Highly hazardous
II	50–500 (solids), 200–2,000 (liquids)	Moderately hazardous
III	>500 (solids), >2,000 (liquids)	Slightly hazardous

According to the World Health Organization (WHO) classification of pesticide toxicity (Table 1), a significant proportion of organochlorine pesticides (OCPs) are categorized as Class I (Extremely Hazardous) or Class II (Highly Hazardous). These classifications underscore the severe toxicological risks these compounds pose to human health, even at minimal exposure levels. Consequently, the persistence of OCPs in the environment requires rigorous management strategies and advanced remediation techniques to mitigate their long-term ecological and public health impacts [25–28].

These classifications reflect the severe toxic effects these compounds can exert on humans even at low exposure levels, indicating their significant risk profile and emphasizing the need for careful management and remediation [25–28].

3. Degradation of Chlorinated Aromatic Compounds

A diverse array of halogenated aromatics, spanning chlorobenzenes, chlorobenzoates, chlorophenols, chloroanilines, hexachlorobenzene, polychlorinated biphenyls (PCBs), chloronitrophenols, chloroaminophenols, and atrazine, are major environmental pollutants. These compounds are extensively used in dyes, pharmaceuticals, pesticides, and various industrial products [29–35]. The strength and stability of their carbon–chlorine bonds make them highly persistent in the environment, thus requiring effective degradation strategies.

3.1. Dechlorination mechanisms proceed via two main pathways.

3.1.1. Spontaneous chemical dechlorination.

Spontaneous chemical dechlorination typically proceeds through the breakdown of unstable intermediates generated during unrelated enzymatic processes. A notable example is the degradation of γ -Hexachlorocyclohexane, where chlorohydroquinone-1,2-dioxygenase catalyzes ring cleavage to produce an acyl chloride intermediate. This intermediate spontaneously converts to maleylacetate, releasing hydrogen chloride (HCl) in the process. Similarly, chlorobenzoic acids are metabolized into chlorocatechols, which undergo a modified ortho-cleavage pathway. In this pathway, spontaneous dehalogenation occurs as a natural consequence of the metabolism of ring-cleaved products [36–45].

3.1.2. Enzymatic dechlorination.

Specific enzymes mediate enzymatic dechlorination by targeting the carbon–chlorine bond through three primary mechanisms: hydrolytic, reductive, and oxygenolytic dehalogenation. Hydrolytic dehalogenation involves the substitution of a chlorine atom with a hydroxyl group derived from water, as illustrated in Figure 3 [36]. In contrast, reductive dehalogenation entails the replacement of chlorine with hydrogen. Oxygenolytic dehalogenation replaces chlorine with a hydroxyl group containing oxygen sourced from molecular O₂ [36]. This latter mechanism is further subdivided into monooxygenase-type dehalogenases, which incorporate a single oxygen atom, and dioxygenase-type dehalogenases, which incorporate two oxygen atoms during the dechlorination reaction [46].

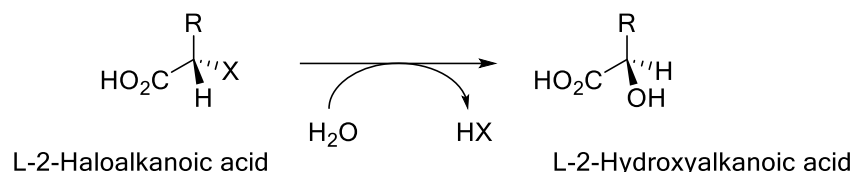


Figure 3. Hydrolysis reaction catalyzed by L-2-dehalogenase. Note: This figure is original and created by the authors for this review.

3.2. Chlorobenzoyl-CoA dehalogenase.

4-Chlorobenzoyl-CoA dehalogenase is one of the most extensively studied enzymes catalyzing hydrolytic dehalogenation reactions. This enzyme catalyzes the hydrolytic transformation of 4-chlorobenzoyl-CoA into its 4-hydroxy counterpart concomitant with chloride liberation (Figure 4a). It plays a crucial role in 4-chlorobenzoate degradation and is found in several diverse microbial degraders, notably *Burkholderia* sp. CBS3 (previously classified as *Pseudomonas* sp. CBS3), alongside *Arthrobacter* sp. 4-CB1 and strain TM-1 [47–49]. The catalytic mechanism proceeds via the formation of a covalent aryl-enzyme intermediate through nucleophilic aromatic substitution (Figure 4b) [50]. Initially, the enolate anion of the thioester bond in 4-chlorobenzoyl-CoA binds to the enzyme, forming a transient enzyme-substrate complex that generates a partial positive charge on the chlorinated carbon, thereby facilitating nucleophilic assault by the conserved aspartate residue at position 145 (Asp145) [51,52]. Asp145 attacks the C(4) position of the benzoyl ring, resulting in the formation of a Meisenheimer intermediate (σ-complex), which subsequently liberates chloride and forms the covalent aryl-enzyme intermediate.

The catalytic cycle concludes with hydrolytic cleavage of the aryl-enzyme intermediate, facilitated by a water molecule activated through histidine at position 90 (His90), yielding 4-hydroxybenzoyl-CoA and regenerating the free enzyme. Structural studies reveal that the 4-chlorobenzoyl-CoA dehalogenase from strain CBS3 is a homotrimer [51–54]. Each subunit comprises two distinct domains: an N-terminal domain containing 10 β-strands arranged in two nearly perpendicular layers flanked by α-helices, and a C-terminal domain consisting of three amphiphilic α-helices responsible for trimerization [51–54]. The N-terminal region of every monomer interacts with the C-terminal segment of an adjacent subunit through a cation, likely a calcium ion.

Crystallographic data confirm the catalytic roles of Asp145 in stabilizing and forming the Meisenheimer complex, and His90 as the general base facilitating the hydrolysis step. In *Arthrobacter* strains 4-CB1 and TM-1, 4-chlorobenzoyl-CoA dehalogenase exists as a homotetramer, with subunits of approximately 33 kDa each. The enzyme molecular weight for

the 4-CB1 isolate registers at approximately 116 kDa, exhibiting an optimal pH of 8.1 and an isoelectric point (pI) of 6.1, whereas the TM-1 variant displays a molecular mass near 131 kDa with an optimum pH of 8.0 and a pI of 6.42; furthermore, the N-terminal sequence of the 4-CB1 enzyme shares 30% identity with its *Burkholderia* sp. CBS3 counterpart and is distinguished from the TM-1 strain by the inclusion of extra alanine and valine residues [47,54].

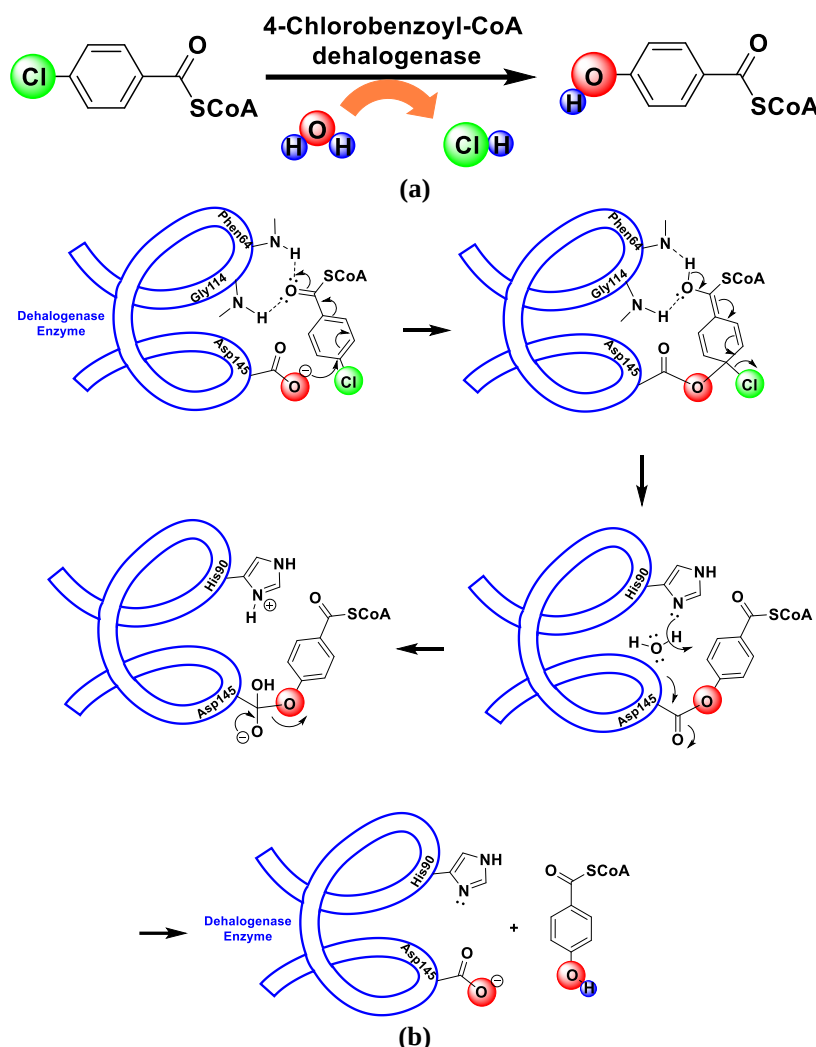


Figure 4. Hydrolytic dehalogenation. (a) Conversion of 4-chlorobenzoyl-CoA to 4-hydroxybenzoyl-CoA with the release of chloride ion by a 4-chlorobenzoyl-CoA dehalogenase; (b) Mechanism of 4-chlorobenzoyl-CoA dehalogenase.

4. Generalized Catalytic Mechanisms for L-2-Haloacid Dehalogenases.

The most extensively characterized L-2-haloacid dehalogenases include the L-DEX enzyme from *Pseudomonas* sp. YL and DhIB derived from *Xanthobacter autotrophicus* GJ10, both of which have been crystallized and whose catalytic mechanisms are well characterized [55,56]. These biocatalysts facilitate the hydrolytic scission of carbon–halogen linkages through similar mechanisms, described by the reaction:



where R denotes hydrogen or an alkyl group, and X is a halogen atom.

Structural comparisons show conserved hydrophobic interactions among the monomers of *Sulfolobus tokodaii* haloacid dehalogenases and the bacterial enzymes L-DEX-YL and

DhlB. Notably, L-DEX-YL features additional hydrogen bonding between the α -helix 2 regions of each subunit. In contrast, DhlB possesses an extra dimerization domain composed of two antiparallel α -helices forming hydrophobic contacts with α -helices 2 and 3 of the adjacent subdomain upon dimerization.

5. Catalytically Important Residues in l-Specific Dehalogenases

Specific conserved amino acid residues are essential for the catalytic activity of l-2-haloacid dehalogenases. These residues have been identified and structurally characterized in *Pseudomonas* sp. YL l-DEX, *X. autotrophicus* GJ10 DhlB, *Burkholderia cepacia* MBA4 DehIVa, and *S. tokodaii* L-HAD [15,56-59].

Ichiyama *et al.* [58] conducted site-directed mutagenesis, replacing conserved charged and polar residues (except the N-terminal methionine) in l-DEX and tested the mutant enzymes against l-2-chloropropionic acid. Mutations at Asp10, Asp180, Arg41, Lys151, Ser175, Ser118, Thr14, Tyr157, and Asn177 caused substantial loss of activity without affecting the overall protein structure, indicating these residues are critical for catalysis.

Asp10 acts as the catalytic nucleophile. Replacement with Asn did not completely abolish activity, possibly due to deamidation back to Asp or partial activity of Asn as a nucleophile; however, substitution by Ala, Gly, or Glu completely inactivated the enzyme [56].

The catalytic residues identified in l-DEX are conserved in DhlB [16] and DehIVa [58], as supported by crystal structures and reaction intermediate analyses. However, site-directed mutagenesis for these latter enzymes remains to be done.

6. Classification of Haloacid Dehalogenases

Haloacid dehalogenases are primarily classified based on their substrate specificity and the stereochemical configuration of their reaction products. Slater and colleagues proposed a four-class system: Class 1L enzymes are specific for l-2-haloalkanoic acids and produce d-2-hydroxyalkanoic acids; Class 1D enzymes act on d-2-haloalkanoic acids to yield l-2-hydroxyalkanoic acids; Class 2I (Inversion-type) enzymes dehalogenate both enantiomers with an inversion of stereochemistry; and Class 2R (Retention-type) enzymes act on both enantiomers while retaining their original configuration. However, relying solely on substrate specificity can be misleading when assessing evolutionary relationships—for instance, *Rhizobium* sp. RC1 DehL targets L-2-chloropropionate, yet its gene sequence diverges significantly from other bacterial dehalogenases with similar specificity, suggesting it belongs to a distinct evolutionary group [60].

However, substrate specificity alone may be misleading for evolutionary relationships. For instance, *Rhizobium* sp. RC1 DehL targets L-2-chloropropionate, but its gene sequence substantially diverges from other bacterial dehalogenases with similar substrate specificity, suggesting it belongs to a novel group [60].

Sequence analyses also show that *Moraxella* sp. dehH1 [61], encoding fluoroacetate dehalogenase H-I, clusters with haloalkane dehalogenase genes such as dhlA (*X. autotrophicus*), dhaA (*Rhodococcus rhodochrous*), and linB (*Pseudomonas paucimobilis*), indicating an additional functional group of haloalkanoic acid dehalogenases [62,63].

Bhandari *et al.* [64] developed a molecular phylogenetic classification using degenerate PCR primers to amplify group I and group II dehalogenases. Group II enzymes are stereoselective, dehalogenating L- but not D-2-chloropropionate, while group I includes non-

stereoselective and D-2-chloropropionate-specific dehalogenases. This classification has been widely adopted and facilitates evolutionary and functional studies [64,65].

Although most known dehalogenases target the α -carbon (C2) of haloalkanoic acids, enzymes capable of dehalogenating the β -halo-substituted alkanoic acids have been identified. For example, Mesri *et al.* [68] reported 2-chloropropionate dehalogenase activity with minor activity against 3-chloropropionate in crude extracts of *Pseudomonas putida* PP3. Recently, research has focused more on enzymes targeting the β -carbon halogen substituents of chloroalkanoic acids [66-69].

6.1. L-2-haloacid dehalogenases from different organisms.

L-stereospecific haloacid dehalogenases are produced by many organisms, likely because the majority of naturally occurring halogenated organic compounds are predominantly in the L-configuration [70]. Numerous genes encoding these enzymes have been sequenced (summarized in Table 2) [67,71].

Most characterized dehalogenases originate from proteobacterial species; however, Gram-positive bacteria such as *Rhodococcus* species also degrade haloacids [72]. The Gram-positive bacterium *Staphylococcus* sp., for example, produces a haloalkanoic acid dehalogenase, particularly when present in soils containing fluoroacetate-producing plants.

The thermophilic archaeon *Sulfolobus tokodaii* strain 7, isolated from the Beppu hot spring in Kyushu, Japan, in 1983, carries the L-specific dehalogenase L-HAD. This acidophilic archaeon grows optimally at 80°C, and its genome has been fully sequenced, facilitating the identification of L-HAD. L-HAD displays maximal activity at 60°C, retains enzymatic function across a wide pH range of 4 to 10, and remains fully active after incubation at 70°C for 4 hours [73,74].

Table 2. L-2-Haloacid dehalogenases from different organisms.

Dehalogenase	Organism	NCBI accession no.	References
DehL	Rhizobium sp. RC1	CAA63794.1	[15]
HadL	P. putida AJ1	M81841.1	[36,37]
DhlB	X. autotrophicus GJ10	M81691.1	[38]
DehH109	P. putida 109	D17523.1	[39]
HehIVa	B. cepacia MBA4	X66249.1	[40]
H-II	Moraxella sp. B	D90423.1	[41]
L-DEX	Pseudomonas sp. YL	S74078.1	[42]
DehII	P. putida PP3	AJ133462.1	[16]
DehCI	Pseudomonas sp. CBS3	M62908.1	[43]
DehCII	Pseudomonas sp. CBS3	M62909.1	[43]
L-HAD	Sulfolobus tokodaii 7	NC_003106.2	[13]

Table 2. L-2-Haloacid dehalogenases from different organisms. Note: Data compiled from various sources as cited in the references.

7. Modification and Immobilization of Enzymes

Enzymes are biocatalysts that catalyze reactions efficiently under mild conditions with high stereospecificity and enantioselectivity, while minimizing unwanted side reactions. They have versatile applications in organic synthesis, brewing, food processing, medicine, and various industrial fields. However, enzymes often have limited mechanical and storage stability, limiting their reusability and continuous use in industrial processes.

To overcome these limitations, protein modification and immobilization techniques have emerged as effective strategies to enhance enzyme stability and enable continuous, automated use in industrial production. Immobilization can modulate enzyme properties and

performance depending on the method applied. Proper immobilization generally improves enzyme stability and, in some cases, catalytic activity; however, unsuitable strategies can cause enzyme inactivation or reduced stability.

Physical immobilization methods, such as adsorption and entrapment, are straightforward but are prone to enzyme leakage during operation. In contrast, covalent immobilization through multipoint chemical binding minimizes enzyme leaching and significantly enhances chemical stability, albeit sometimes at the expense of catalytic activity [75]. Additionally, immobilization may create a favorable microenvironment for enzymes and prevent multilayer enzyme packing, resulting in improved specific activity in certain cases [76].

The orientation of the enzyme upon immobilization is critical for preserving activity. If a substrate is large and the enzyme's active site is oriented toward the support surface, steric hindrance may reduce substrate access and enzymatic efficiency [77]. Moreover, interactions involving specific enzyme regions during immobilization can induce structural alterations leading to inactivation [78].

Site-specific modification via peptide tag fusion is a promising approach to preserve enzyme activity and reduce the risk of inactivation caused by chemical immobilization. This method enables selective, site-specific protein modification through co-expressed enzymes, both *in vivo* and *in vitro* [79].

Haloacid dehalogenases, which belong to the L-2-Haloacid Dehalogenase (L-2-HAD) superfamily, show significant potential in pharmaceutical synthesis, chemical industry, and bioremediation of contaminated environments. These enzymes are valued for their high catalytic efficiency, stereoselectivity, thermostability, and broad pH tolerance. The monomeric globin ST2570 from *Sulfolobus tokodaii* strain 7 is an excellent model enzyme for evaluating site-specific covalent immobilization techniques [80-86].

8. Active Site

The enzyme's active site lies at the interface between its two domains. The amino acid residues from the core domain form the base of the catalytic cavity, with the subdomain covering the top. In *S. tokodaii* dehalogenase, the proposed active site comprises Asp7, Ala8, Phe9, Arg23, Leu27, Phe42, Leu94, Ser95, Asn96, Gly97, Lys128, Asn152, Phe154, and Asp155. Compared to homologous enzymes *DhlB* and *L-DEX-YL*, the only difference is the substitution of Phe9 in *S. tokodaii* with a tyrosine residue [87].

Mutagenesis studies on *L-DEX-YL* have highlighted several key residues, whose mutation results in decreased enzymatic activity. Sequence alignments suggest that corresponding residues in *S. tokodaii* dehalogenase include Asp7, Thr11, Arg23, Ser95, Lys128, Tyr134, Ser150, Asn152, and Asp155. These residues are fully conserved in *DhlB* and mostly conserved in *PH0459*.

Previous investigations of ester intermediate complexes of *L-DEX-YL* identified Ser118 as a key residue binding the substrate's carboxyl group, alongside main-chain nitrogens of Leu11 and Tyr12. In *DhlB*, these roles are played by Ser114, Ala9, and Tyr10. *S. tokodaii* dehalogenase Ser95 aligns with these conserved serine residues, implying a similar function, supported by main-chain residues Ile8 and Phe9.

Crystallographic analyses of the enzyme purified under orthorhombic conditions revealed an inorganic phosphate molecule occupying the substrate carboxyl-binding site, derived from the 50 mM phosphate in the gel filtration buffer. In another crystal form purified

in Tris–HCl buffer and crystallized in monoclinic form, additional electron density corresponds to a ligand containing six non-hydrogen atoms. The carboxylate moiety of this ligand interacts similarly to phosphate in the other form, resembling the covalent intermediates observed in other haloacid dehalogenases (e.g., PDB codes 1QQ7 and 1QQ5) [56].

9. Conclusion

Dehalogenases have been identified across a broad spectrum of bacteria, with many enzymes sequenced and thoroughly characterized regarding substrate specificity and kinetic parameters. These biocatalysts hydrolytically cleave carbon–halogen bonds in recalcitrant organohalides, converting them into environmentally benign products.

L-2-haloacid dehalogenases belong to the expansive haloacid dehalogenase (HAD) superfamily (Pfam PF00702), characterized by a fully conserved aspartic acid residue essential for catalytic activity. This superfamily also includes related enzymes such as ATPases, epoxide hydrolases, and distinct classes of phosphatases.

Overall, owing to their high catalytic efficiency, broad substrate spectrum, and robust enzymatic activity, l-2-haloacid dehalogenases represent a promising tool for effective biodegradation and bioremediation of halogenated environmental pollutants.

Author Contributions

Conceptualization, A.C. and F.M.; methodology, A.C. and N.G.; software, H.M.; validation, A.C., N.G. and A.H.C.; formal analysis, F.M. and H.M.; investigation, F.M. and A.H.C.; resources, A.C.; data curation, N.G. and A.H.C.; writing—original draft preparation, F.M. and A.H.C.; writing—review and editing, A.C., N.G., H.M. and A.H.C.; visualization, H.M. and A.H.C.; supervision, A.C.; project administration, A.C. All authors have read and agreed to the published version of the manuscript.

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Informed Consent Statement

Not applicable.

Data Availability Statement

No new data were created or analyzed in this study. Data sharing **does not apply** to this article as no datasets were generated or analyzed during the current study.

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Conflicts of Interest

The authors declare no conflict of interest.

Abbreviations

The following abbreviations are used in this manuscript:

Abbreviation	Definition
OCPs	Organochlorine Pesticides
EDCs	Endocrine-Disrupting Chemicals
PCBs	Polychlorinated Biphenyls
WHO	World Health Organization
L-DEX	L-2-Haloacid Dehalogenase
DhlB	Dehalogenase B from <i>Xanthobacter autotrophicus</i>
HAD	Haloacid Dehalogenase Superfamily
PDB	Protein Data Bank
IRB	Institutional Review Board

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