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Insights Into the Biodegradation of Lindane (γ-Hexachlorocyclohexane) Using a Microbial System

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Lindane (γ-hexachlorocyclohexane) is an organochlorine pesticide that has been widely used in agriculture over the last seven decades. The increasing residues of lindane in soil and water environments are toxic to humans and other organisms. Large-scale applications and residual toxicity in the environment require urgent lindane removal. Microbes, particularly Gram-negative bacteria, can transform lindane into non-toxic and environmentally safe metabolites. Aerobic and anaerobic microorganisms follow different metabolic pathways to degrade lindane. A variety of enzymes participate in lindane degradation pathways, including dehydrochlorinase (LinA), dehalogenase (LinB), dehydrogenase (LinC), and reductive dechlorinase (LinD). However, a limited number of reviews have been published regarding the biodegradation and bioremediation of lindane. This review summarizes the current knowledge regarding lindane-degrading microbes along with biodegradation mechanisms, metabolic pathways, and the microbial remediation of lindane-contaminated environments. The prospects of novel bioremediation technologies to provide insight between laboratory cultures and large-scale applications are also discussed. This review provides a theoretical foundation and practical basis to use lindane-degrading microorganisms for bioremediation.

Keywords: lindane, biodegradation, metabolic pathway, mechanisms, bioremediation

INTRODUCTION

Lindane (γ-hexachlorocyclohexane) is a broad-spectrum organochlorine pesticide belonging to the chlorinated hydrocarbon family. It was synthesized after the Second World War until the 1990s (Saez et al., 2015; Dominguez et al., 2018b). Four major isomers (**Figure 1**) are formed (α, β, γ, and δ) during the production of hexachlorocyclohexane (HCH), however, only the γ isomers possess insecticidal properties (Vijgen et al., 2019). For the last seven decades, lindane insecticide has been extensively used worldwide on fruits, vegetables, forest crops, animals, and on animal premises (Jung et al., 2018; Singh and Singh, 2019a). The insecticidal activity of lindane is due to its excitatory action on the nervous system (Sharma et al., 2010; Nolan et al., 2012).

FIGURE 1 | Chemical structures of four hexachlorocyclohexane (HCH) isomers.

FIGURE 2 | Migration and transformation of lindane in soil.
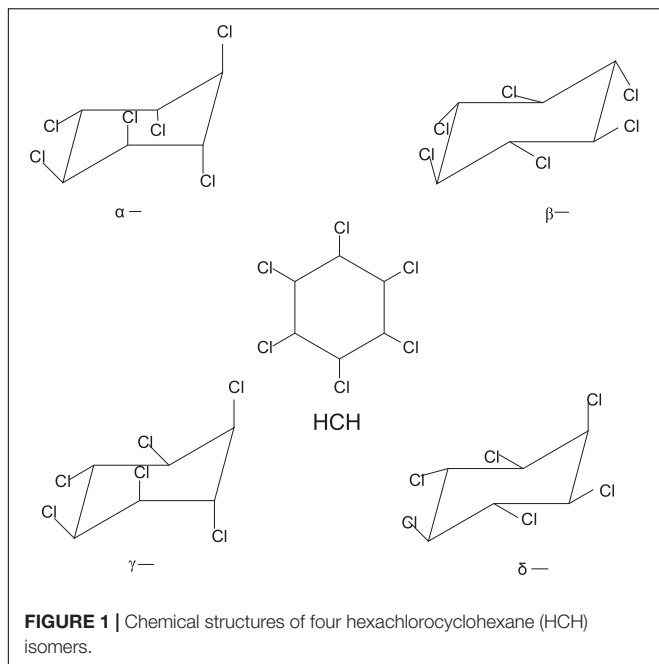
Lindane primarily acts on the γ-aminobutyric acid (GABA) receptor/chloride ionophore complex, which leads to hyperexcitation of the central nervous system (CNS) and results in paralysis, convulsions, and even death (Mladenović et al., 2010; Agrahari et al., 2019). Fractional crystallization is used for the extraction and purification of lindane from the production mixture (Padhi and Pati, 2016). Lindane production is inefficient, as the production of one ton of lindane creates approximately 8–12 tons of other waste isomers, mainly composed of α- and β-hexachlorocyclohexane (Vijgen et al., 2011).

Lindane can persist in the environment due to its high lipid solubility and chemical stability and can migrate over long distances to cause widespread contamination (Benimeli et al., 2008). The reported half-lives for lindane in soil and water were reported to be 708 and 2292 days, respectively (Beyer and Matthies, 2001). Generally, lindane soil residues enter the food chain and concentrate in the fat tissues of humans and animals causing major health hazards (Nolan et al., 2012). The lipid solubility of lindane increases its toxicity to humans and animals. Lindane has been classified as a carcinogen and endocrine disrupter, and it possesses mutagenic, genotoxic, and teratogenic effects (Markman et al., 2007; Luo et al., 2016; Muñiz et al., 2017).

In 2009, due to the environmental persistency and bioaccumulation potential, lindane, along with its α and β isomers, was included in the Stockholm Convention list of persistent organic pollutants (POPs) (Wacławek et al., 2016), and it has been banned or severely restricted. To implement the Stockholm Convention on POPs, the Ministry of Ecology and Environment of China has prohibited the production, circulation, application, import, and export of lindane since 26 March 2019 (Wang, 2019). Lindane is still being used in some developing countries for agricultural and public health purposes
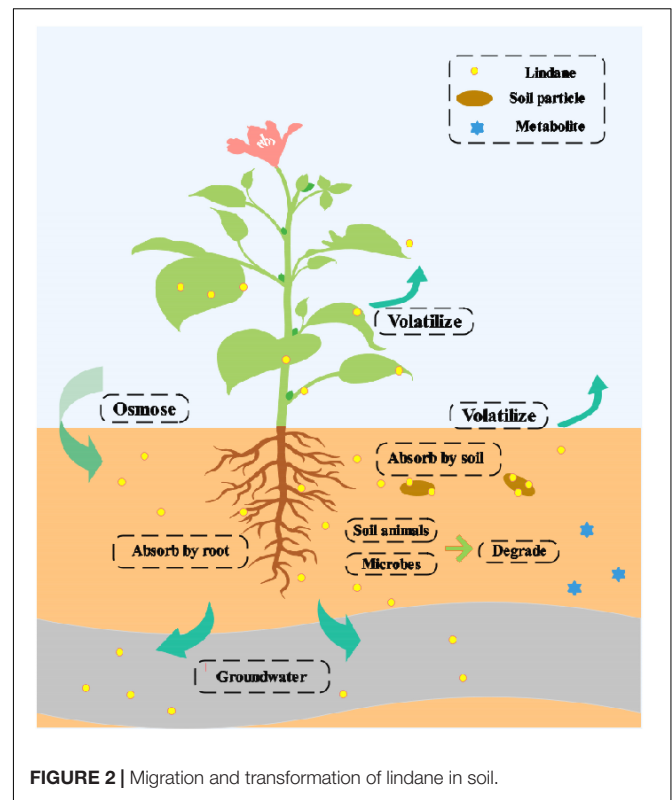
due to its low cost and versatility in pest control (Abhilash and Singh, 2010). Currently, India is the largest producer and consumer of lindane in the world (Sagar and Singh, 2011). Continuous applications and indiscriminate industrial production have led to widespread lindane contamination of soils in the country (Vankar and Ramashanker, 2011). Over the years, only a small portion of the related legal problems were addressed in the European Union (EU) or globally. Large stockpiles of lindane and its wastes are still present in the soil, which represents a large contaminant reservoir (Vijgen et al., 2019). Therefore, lindane degradation technologies must be developed to decontaminate the polluted soil and water.

The migration and transformation of lindane in the soil is presented in **Figure 2**. Several factors control the lindane distribution and fate in the fields, including (a) loss by volatilization into the atmosphere, (b) loss through surface runoff, and (c) degradation by soil microbes and animals (Lal et al., 2010; Alvarez et al., 2012; Giri et al., 2014). The natural degradation of lindane is a very slow process and varies according to the environmental conditions (Elcey and Kunhi, 2009). Currently, a variety of treatment methods are available for the removal of lindane, but these all have certain drawbacks (Nagpal and Paknikar, 2006; Nagpal et al., 2008).

Physicochemical methods, such as incineration, electro-oxidation, and microwave-induced or chemical oxidation, are not eco-friendly and require large and expensive infrastructure (Liu et al., 2015; Zhan et al., 2020). They also generate highly toxic compounds during the degradation process (Manickam et al., 2006; Usman et al., 2014; Dominguez et al., 2018a,b;

Jung et al., 2018; Huang et al., 2019). However, the microbial degradation of lindane contamination is attracting increasing attention as a less expensive and more environmentally friendly alternative to conventional treatment methods (Chen et al., 2015; Arora et al., 2017; Bajaj et al., 2017; Cycoń et al., 2017; Zhang H. et al., 2018; Bhatt et al., 2019a). The first report regarding the microbial degradation of lindane was published in 1967. Subsequently, numerous studies reported potential microorganisms for the efficient and rapid bioremediation of lindane-polluted environments (Sangwan et al., 2012; Githinji, 2015; Kumar et al., 2016). However, the literature lacks reviews regarding microbial resources and the mechanism of lindane degradation.

In this review, we emphasize the role of microbial degradation for large-scale bioremediation of lindane contamination. We compile detailed information about the microbial resources, mechanisms, and important enzymes involved in lindane degradation, and the aerobic and anaerobic metabolic pathways are also compared. Additionally, a brief account of recent lindane bioremediation methods is given. This review provides novel insights into the future of the large-scale bioremediation of lindane.

TOXICITY OF LINDANE

The extensive applications of lindane over the decades resulted in a wide distribution that affects the biota, and lindane is now considered one of the most hazardous POPs (Tsygankov et al., 2019). The chemical persistence and lipophilicity of lindane enable it to accumulate and biomagnify in food chains. On 27 October 2017, the World Health Organization published a list of carcinogens where lindane was categorized as a Group 1 carcinogen (Singh and Singh, 2019a).

Lindane is the most acutely toxic HCH isomer that affects the central nervous system and endocrine system. Lindane is attributed to various adverse health effects in humans, including immunosuppressive, oxidative, proinflammatory, carcinogenic, neurotoxic, and hormone-disruption effects, and even convulsions and death (Vega et al., 2016). The first evidence of death by lindane toxicity was reported in 1953 (Nolan et al., 2012). Due to the lipophilicity, lindane can infiltrate and accumulate in the brain, human breast milk, and other organs that are rich in fat. Epidemiological and agricultural health studies reported that lindane exposure could be associated with the cancers of the breast, prostate, lung, stomach, colon, rectum, and bladder (Jayaraj et al., 2016; Abolhassani et al., 2019; Mortazavi et al., 2019).

Broad applications of lindane pose serious threats to the environment. Once released, lindane can disseminate to all environmental compartments. Compared with other organochlorine pesticides, lindane is ubiquitous due to the high water solubility and volatility (Zhang et al., 2010). Lindane has a strong adsorption tendency in organic materials; therefore, it is long-lived and can be transported for long-ranges in the environment (Vega et al., 2016). Lindane contaminants have leached underground for decades, polluting both the surface water and groundwater (Weber et al., 2013). Lindane is a threat to a wide range of environments as it bioaccumulates in microorganisms, invertebrates, fish, birds, and mammals (Vijgen et al., 2018) and threatens human health through the food chain. The microbial community structure has a unique response to pesticide pollution, and recent research found that microbial diversity, richness, and structure undergo changes with lindane concentration (Sun et al., 2019).

POTENTIAL MICROORGANISMS IN LINDANE DEGRADATION

The bacterial degradation of lindane and other xenobiotics are widely reported (Chen et al., 2012, 2013; Yang et al., 2018; Zhang H. et al., 2018; Bhatt et al., 2020c). Bacterial cells use organic pollutants as a sole source of carbon and nitrogen (Chen et al., 2011, 2014; Zhan et al., 2018b; Lin et al., 2020). Currently, a number of lindane-degrading bacterial strains have been screened, enriched, and domesticated (**Table 1**), including *Microbacterium* (Singh and Singh, 2019b), *Paracoccus* (Sahoo et al., 2019), *Achromobacter* (Singh and Singh, 2019a), *Burkholderia* (Kumar, 2018), *Rhodococcus* (Egorova et al., 2017), *Chromohalobacter* (Bajaj et al., 2017), *Kocuria* (Kumar et al., 2016), *Staphylococcus* (Kumar et al., 2016), *Streptomyces* (Sineli et al., 2016), *Arthrobacter* (De Paolis et al., 2013), *Azotobacter* (Anupama and Paul, 2009), *Sphingomonas* (Manickam et al., 2008), *Xanthomonas* (Manickam et al., 2010), *Pseudomonas* (Kumar et al., 2011), *Pseudoarthrobacter* (Nagpal and Paknikar, 2006), *Klebsiella* (Nagpal and Paknikar, 2006), *Pleurotus* (Dritsa and Rigas, 2013), *Fusarium* (Sagar and Singh, 2011), and *Actinobacteria* (Cuozzo et al., 2017).

Bacteria play a pivotal role in lindane biodegradation through chemical and physical interactions that lead to structural changes or complete degradation of the target molecule. Different bacteria were reported to degrade lindane at different rates. Singh and Singh (2019b) isolated and identified rhizospheric bacteria *Microbacterium* spp. strain P27 from *Phragmites karka*, which effectively degraded 82.7% lindane (50 mg·L^{-1}) in 15 days and promoted plant growth as well. Sahoo et al. (2019) isolated *Paracoccus* sp. NITDBR1 from the agricultural fields of Manipur, which efficiently degraded 90% lindane (100 mg·L^{-1}) in 8 days by using it as the sole source of carbon for its growth. Kumar (2018) isolated and characterized *Burkholderia* spp. strain IPL04 from a contaminated site by an enrichment culture method, which degraded 98% lindane in 8 days. The bacterial degradation of lindane has been extensively studied, however, only a few bacteria are known to completely mineralize lindane.

Fungal biodegradation is also considered an environment friendly approach for the detoxification of POPs in comparison with the traditional physical and chemical methods (Saez et al., 2018). Several studies reported the fungal degradation of lindane (Guillén-Jiménez et al., 2012; Salam et al., 2013; Kaur and Kaur, 2016). Fungi have extracellular enzymes that are relatively non-specific to the substrate and possess strong activity. These

TABLE 1 | Lindane degradation by various microorganisms.

Species	Microorganism	Concentration of lindane	Degradation rate	Sources	References
Bacteria	*Microbacterium* sp. P27	50 mg/L	82.7% in 15 days	*Phragmites karka*	Singh and Singh, 2019b
	Paracoccus sp. NITDBR1	100 mg/L	90% in 8 days	Agricultural field	Sahoo et al., 2019
	Achromobacter sp. strain A3	50 mg/L	88.7% in 15 days	*Acorus calamus*	Singh and Singh, 2019a
	Burkholderia sp. IPL04	100 mg/L	98% in 8 days	Soil	Kumar, 2018
	Rhodococcus wratislaviensis Ch628	200 mg/L	32.3% in 5 days	Soil	Egorova et al., 2017
	Chromohalobacter sp. LD2	50 mg/L	89.6% in 7 days	Soil	Bajaj et al., 2017
	Kocuria sp. DAB-1Y	10 mg/L	94% in 8 days	Soil	Kumar et al., 2016
	Staphylococcus sp. DAB-1W	10 mg/L	98% in 8 days	Soil	Kumar et al., 2016
	Streptomyces sp. M7	1.66 mg/L	45% in 7 days	Sediment	Sineli et al., 2016
	Arthrobacte fluorescens	100 mg/L	40% in 72 h	Soil	De Paolis et al., 2013
	Arthrobacter giacomelloi	100 mg/L	56% in 72 h	Soil	De Paolis et al., 2013
	Azotobacter chroococcum	10 mg/L	Almost complete in 6 days	Farm fields	Anupama and Paul, 2009
	Sphingomonas sp. NM05	100 mg/L	90% in 7 days	Soil	Manickam et al., 2008
	Xanthomonas sp. ICH12	100 mg/L	100% in 8 days	Soil	Manickam et al., 2010
	Pseudomonas aeruginosa ITRC5	2 mg/kg of soil	76% in 15 days	Soil	Kumar et al., 2011
	Microbacterium sp. ITRC1	200 mg/kg of soil	96% in 28 days	Soil	Manickam et al., 2006
	Pseudoarthrobacter sp.	5 mg/L	50.7% in 7 days	Soil	Nagpal and Paknikar, 2006
	Pseudomonas sp.	5 mg/L	52.2% in 7 days	Soil	Nagpal and Paknikar, 2006
	Klebsiella sp.	5 mg/L	51.2% in 7 days	Soil	Nagpal and Paknikar, 2006
	Arthrobacter citreus B1-100	100 mg/L	100% in 8 h	Soil	Datta et al., 2000
Fungi	*Ganoderma lucidum* GL-2	4 mg/L	75.5% in 28 days		Kaur and Kaur, 2016
	Pleurotus ostreatus	2.03 mg/L		Rotten wood	Dritsa and Rigas, 2013
	Fusarium verticilliodes AT-100	50 mg/L	30% in 7 days	Leaves	Guillén-Jiménez et al., 2012
	Rhodotorula sp. VITJzN03	600 mg/L	100% in 10 days	Soil	Salam et al., 2013
	Fusarium poae	100 mg/L	56.7% in 10 days	Soil	Sagar and Singh, 2011
	Fusarium solani	100 mg/L	59.4% in 10 days	Soil	Sagar and Singh, 2011
	Conidiobolous 03-1-56	5 mg/L	100% in 5 days	Soil	Nagpal et al., 2008
	Bjendera audusta	100 mg/kg of soil	69.1% in 30 days	Soil	Quintero et al., 2007
	Cyathus bulleri,	5 μM	97% in 28 days		Singh and Kuhad, 2000

enzymes catalyze a wide range of reactions to break down lindane, and this might be induced by nutritional constraints (Nagpal et al., 2008).

The ligninolytic extracellular enzyme activity of white rot fungi efficiently degrades lindane. The soil environmental conditions (temperature, moisture content, and C/N ratio) and the presence of other microorganisms can affect the biodegradation activity of fungi (Kaur and Kaur, 2016). Kaur and Kaur (2016) reported 75.50% lindane degradation on the 28th day with the white rot fungus *Ganoderma lucidum* GL-2 strain grown in liquid-state fermentation. Guillén-Jiménez et al. (2012) isolated a non-white-rot fungus *Fusarium verticillioides* AT-100 from the leaves of *Agave tequilana* using an enrichment technique and then used lindane as the sole source of carbon and energy. This was the first report of lindane degradation by *F. verticillioides* to produce benzoic acid derivatives. *Rhodotorula* VITJzN03 was isolated from a sorghum cultivation field, and mineralized 100% lindane

within 10 days at an initial concentration of 600 mg·L^{-1} (Salam et al., 2013).

MICROBIAL METABOLIC PATHWAY OF LINDANE DEGRADATION

Microbial metabolism can effectively degrade lindane through producing extracellular and intracellular enzymes that directly transform lindane into less toxic and non-toxic compounds (Alvarez et al., 2012). Lindane can be biodegraded under both aerobic and anaerobic conditions, however, it is generally mineralized only under aerobic conditions.

Aerobic Degradation

Several aerobic microorganisms are known to degrade lindane, and the aerobic degradation pathway of lindane was extensively studied in *Sphingobium japonicum* UT26 (Nagata et al., 2007).

UT26 uses lindane as a sole source of carbon and energy under aerobic conditions. Many studies found that the degradation pathways of other aerobic lindane degrading strains are the same or very similar to those in UT26. The main reactions that occur during microbial degradation of lindane include dehydrogenation, dechlorination, hydroxylation, dehydrochlorination, and mineralization (Cuozzo et al., 2017). The proposed aerobic biodegradation pathways of lindane are summarized in **Figure 3**. The key reaction during microbial degradation of lindane is the removal of the chlorine atom (Lal et al., 2006).

In this pathway, lindane is converted to 1,2,4-trichlorobenzene (1,2,4-TCB), 2,5-dichlorophenol (2,5-DCP), and 2,5-dichlorohydroquinone (2,5-DCHQ) by the enzymatic activities of dehydrochlorinase (LinA), halidohydrolase (LinB), and dehydrogenase (LinC). The degradation of lindane to 2,5-DCHQ is referred to as an upstream pathway, which is further metabolized through the downstream pathway (Endo et al., 2005). 2,5-DCHQ is converted to β-ketoadipate by reductive dechlorinase (LinD), ring-cleavage dioxygenase (LinE), and maleylacetate reductase (LinF). Researchers documented β-ketoadipate as a marker metabolite for the degradation of aromatic ring-containing compounds. The intermediate β-ketoadipate is further converted to succinyl-coenzyme A (CoA) and acetyl-CoA by succinyl-CoA: 3-oxoadipate CoA transferase (LinGH) and β-ketoadipyl CoA thiolase (LinJ). Both of these compounds are metabolized in the tricarboxylic acid (TCA) cycle (Nagata et al., 2007; Camacho-Pérez et al., 2012). In addition, other studies reported that lindane can be metabolized by microorganisms to produce pentachlorocyclohexene (PCCH), 3,4,5,6-tetrachloro-1-cyclohexene (TCCH), pentachlorobenzene (PCB), or trichlorobenzene (TCB) (Geueke et al., 2013; Cuozzo et al., 2017).

Anaerobic Degradation

Several studies reported that the microbial anaerobic degradation of lindane is different from aerobic degradation (Endo et al., 2005; Bashir et al., 2018). Dichloro-elimination and dehydrochlorination appear to be the main processes during the transformation of lindane via tetrachlorocyclohexene (TCCH) into lower chlorinated products under the anoxic conditions of aquifer sediments (Lal et al., 2010). There are two different descriptions of the microbial anaerobic degradation pathways of lindane (**Figure 4**). Some studies proposed that the degradation proceeds through two dichloroeliminations, resulting in the formation of 3,4,5,6-tetrachloro-1-cyclohexene (γ-TCCH) followed by 5,6-dichlorocyclohexa-1,2-diene. Chlorobenzene is then produced by a dehydrochlorination reaction (Saez et al., 2017). Another anaerobic degradation pathway produces pentachlorocyclohexene (PCCH) followed by 1,2-dichlorobenzene (1,2-DCB) and 1,3-dichlorobenzene (1,3-DCB) (Quintero et al., 2005a,b). Anaerobic bacteria from the sediments and pure cultures of sulfate-reducing bacteria influenced lindane dehalogenation resulting in the accumulation of final products, such as monochlorobenzene and benzene (Camacho-Pérez et al., 2012).

FUNCTIONAL ENZYMES INVOLVED IN LINDANE DEGRADATION

Dehalogenases are the key enzymes that degrade various halogenated compounds through cleavage of the carbon chlorine stable bond (Lal et al., 2010). Lindane has six chlorine atoms per molecule and dechlorination is a significant step in its degradation. As shown in **Figure 3**, the biodegradation of lindane requires the participation of various enzymes. The dehalogenases that degrade lindane are dehydrochlorinase (LinA), dehalogenase (LinB), and reductive dechlorinase (LinD) (Nagata et al., 2007). Dehydrogenase (LinC), ring cleavage oxygenase (LinE), and maleylacetate reductase (LinF), which catalyze the dechlorination of substrates, can also be generally categorized as dehalogenases (Lal et al., 2006).

In general, LinA, LinB, and LinC are upstream pathway enzymes of lindane degradation. LinA is a homotetrameric protein with a molecular mass of 16.5 kDa (Nanasato et al., 2016). LinA belongs to the dehydrohalogenase class of enzymes, which can eliminate HCl from a substrate molecule to form a double bond (Cuozzo et al., 2017). LinA mediates the first two dehydrochlorination steps of lindane (Manickam et al., 2008). Additionally, LinA does not require cofactors to catalyze its activity and thus is a unique dehydrogenase enzyme that distinguishes between the two previously reported dehydrochlorinases (dichlorodiphenyltrichloroethane (DDT) dehydrochlorinase and 3-chloro-D-alanine dehydrochlorinase).

Unlike LinA, LinB is a monomeric 32 kDa protein located in the periplasm of sphingomonads (Geueke et al., 2013). LinB is a haloalkane dehalogenase of the α/β-hydrolase family and possesses relatively broad substrate specificity (Janssen, 2004). LinB is a key enzyme for lindane degradation in soil and catalyzes dehalogenation through a hydrolytic mechanism. LinB is responsible for the hydrolytic dechlorination of 1,3,4,6-tetrachloro-1,4-cyclohexadiene (1,4-TCDN) to 2,5-dichloro-2,5-cyclohexadiene-1,4-diol (2,5-DDOL) during the aerobic degradation pathway of lindane (Jan et al., 2005). LinB was found to be involved in the degradation of β- and δ-HCH up to different levels.

Less is currently known about the third upstream pathway enzyme LinC or any other downstream pathway proteins. LinC (28 kDa) is considered a 2,5-DDOL dehydrogenase in the short-chain alcohol dehydrogenase family (Rinku et al., 2005). A general catalytic mechanism explained that hydride transfer from the substrate to NAD⁻ forms NADPH and a reduced product [the conversion of 2,5-DDOL to 2,5-dichlorohydroquinone (2,5-DCHQ)]. LinD (38.4 kDa), LinE (36.0 kDa), LinF (38.0 kDa), and LinR (33.6 kDa) (a transcriptional regulator) are associated with the downstream lindane degradation pathway (Lal et al., 2010). In *S. japonicum* UT26, LinD and LinE were induced by LinR in the presence of 2,5-DCHQ, chlorohydroquinone (CHQ) and hydroquinone (HQ) (Keisuke et al., 2002). As the degradation of lindane can lead to different intermediate compounds, we must also consider key enzymes for the further degradation of commonly reported lindane

FIGURE 3 | Aerobic degradation pathways of lindane.
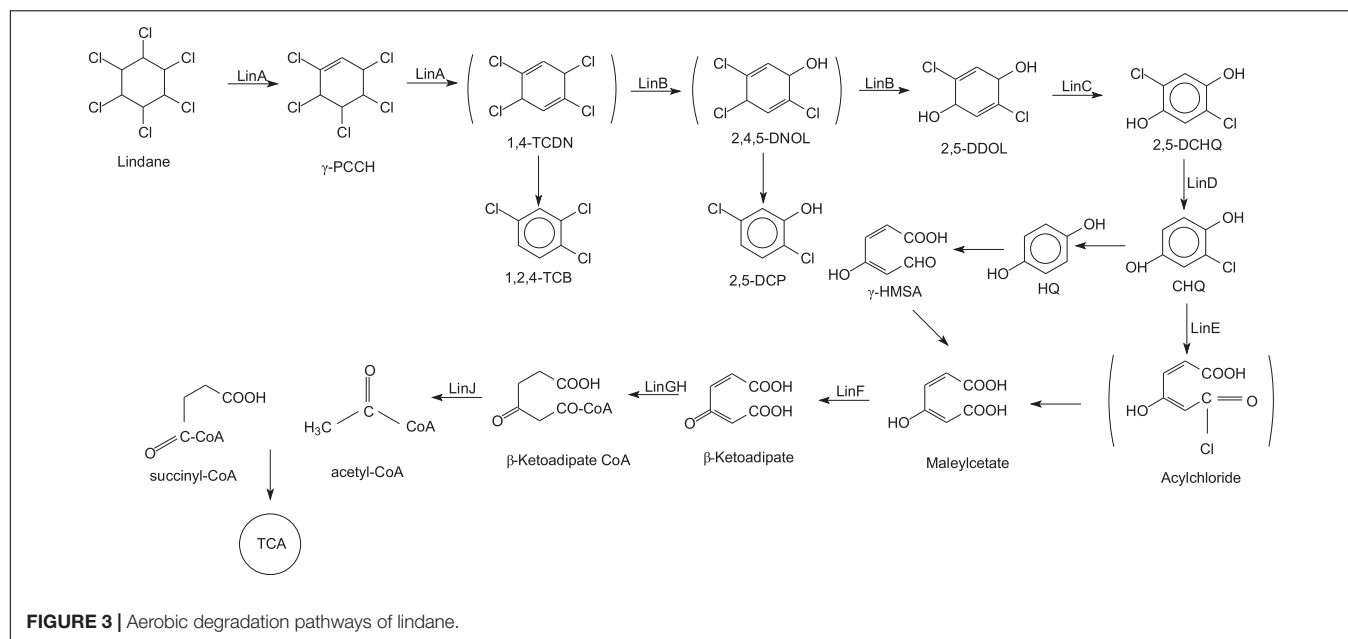
metabolites. To further understand the mechanisms of lindane biodegradation, it is necessary to explore further key enzymes of lindane degradation.

BIOREMEDIATION OF LINDANE-CONTAMINATED ENVIRONMENTS

Lindane is an organochlorine pesticide that is highly persistent in the environment due to frequent crop spraying, field applications, accidental spills, domestic wastes, industrial effluents, and garbage dumping (Singh and Singh, 2019b). Lindane residues permeate through the soil surface to the groundwater and cause the extensive pollution of aquatic ecosystems. Lindane accumulation has been reported worldwide and is very toxic to the environment, humans, and animals (Pamela et al., 2011). Therefore, urgent consideration and management of the problem is necessary. Bioremediation is the most promising biotechnological approach to clean polluted environments (Egorova et al., 2017; Zhang J. et al., 2018; Bhatt et al., 2020a). The bacterial strains isolated from sponges demonstrate robustness in lindane degradation. Bacteria associated with the sponge *Hymeniacidon perlevis* were found to be suitable for lindane degradation. The bacteria isolated belong to *Mameliella phaeodactyli*, *Pseudovibrio ascidiaceicola*, *Oceanicaulis stylophorae*, *Ruegeria atlantica,* and other uncharacterized genera (Loredana et al., 2017). For lindane bioremediation in samples collected from different polluted sites, researchers applied novel techniques (Asemoloye et al., 2017; Salam et al., 2017; Wang et al., 2019). Pure cultures, microbial consortium, nanobiotechnology, and plant–microbe interactions are discussed below along with their successful outcomes.

Pure Cultures

Considering the vast amount of lindane used and the residues in the environment, attempts were made in the past to use pure cultures for the decontamination of lindane. As previously described, a large number of microorganisms with lindane degradation capacity were isolated and characterized (**Table 1**). Several studies described the application of a single microorganism for the bioremediation of lindane-contaminated soil (Aparicio et al., 2015; Salam et al., 2017). *Streptomyces* sp. M7 exhibited strong versatility, showing the ability to bioremediate lindane contaminated soil samples at several physicochemical conditions (Aparicio et al., 2015).

The ascomycetous yeast strain *Candida* VITJzN04 has the ability to degrade 78% of lindane in garden soils (lindane ~100 mg/kg) within 30 days (Salam et al., 2017). The traditional microbial methods are based on the culture dependent approach (Zhan et al., 2018a; Bhatt et al., 2020b). However, the ability of a single microorganism to degrade lindane is influenced not only by its genetic properties but also by the environmental conditions, such as the pH, temperature, concentration of lindane, etc. (Feng et al., 2020).

Microbial Consortium

A microbial consortium performs better than axenic cultures due to robustness in metabolic function (Bhatt et al., 2019b). A mixed community of microorganisms can alleviate the metabolic limitations of a single population (Shong et al., 2012). In nature, microorganisms coexist as part of microbial consortia where multiple populations carry out complex chemical and physiological functions for the survival of the community (Polti et al., 2014). Natural and artificial microbial consortia are of great significance for the degradation and removal of lindane. Murthy and Manonmani (2007) developed a microbial consortium against lindane and optimized the degradation

FIGURE 4 | Anaerobic degradation pathways of lindane.
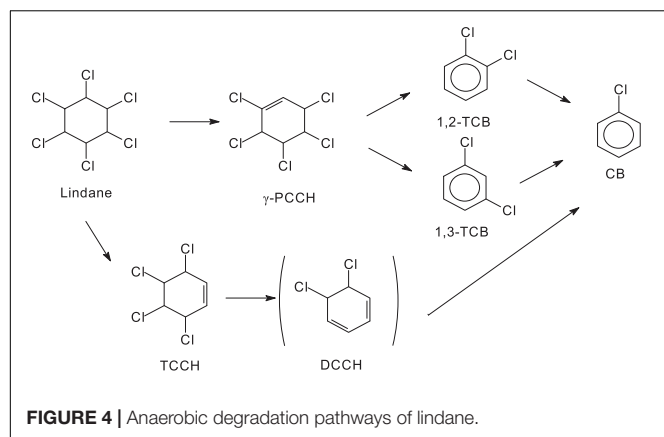
conditions. The consortium rapidly degraded all concentrations of lindane up to 25 mg/L.

Saez et al. (2015) evaluated the influence of a *Streptomyces* consortium on lindane degradation in liquid and slurry systems. An actinobacteria consortium was stable and removed 97% of the lindane. Aparicio et al. (2017) established the optimal biological and physicochemical parameters to simultaneously remove lindane and Cr (VI) from the soil with an actinobacteria consortium of *Streptomyces* sp. M7, MC1, and A5 and *Amycolatopsis tucumanensis* AB0. An actinobacteria consortium was found to be superior for the degradation of lindane from a contaminated environment.

Kumar et al. (2017) conducted a bath culture degradation analysis and reported the enhanced codegradation of chlorpyrifos and lindane with two or more strains. Elcey and Kunhi (2009) isolated a lindane-degrading consortium from a sugarcane field. The consortium mineralized 300 μg/mL of lindane after 108 h of acclimation in the presence of a substrate, and no apparent accumulation of intermediary metabolites was observed.

Microbial consortiums communicated with each other via the mechanism known as quorum sensing (Ye et al., 2019, 2020). Due to this communication in the lindane-contaminated sites, the metabolic burden is divided into various members and the consortium perform complex functions. In nature, microbes coexists as communities that are affected by the local environmental conditions. Mixed microbial cultures may compete for the same resources in nature, however, they can cross feed with each other and live symbiotically with a single carbon source (Mas et al., 2016). The pesticides are degraded by the microbial consortium, which shares the metabolic labor during the degradation (Billet et al., 2019). A consortium of *Streptomyces* was able to efficiently degrade various chlorinated pesticides (Fuentes et al., 2013). A bacterial consortium (10 bacterial strains) was able to simultaneously degrade organophosphorous and organochlorine pesticides within 24 h (Abraham et al., 2014).

Nanobiotechnology

Currently, an integrated nanobiotechnological approach for the treatment of pesticides is gaining popularity as a novel and effective technology. Over the past decade, studies investigated the combination of nanoscale inorganic particles and microbial

cells in the degradation of chlorinated hydrocarbons (Wang and Tseng, 2009). These studies proposed reductive dechlorination of lindane by nanoparticles followed by oxidative degradation of metabolites by the microbial cells. Salam and Das (2015) evaluated the effect of an embedded bio-nano hybrid system using nanoscale zinc oxide (n-ZnO) and the lindane-degrading yeast *Candida* VITJzN04 for lindane degradation. The bio-nano hybrid degraded lindane more effectively than the native yeasts and completely removed lindane within 3 days.

Singh et al. (2013) used an integrated nano biotechnique to combine stabilized Pd/Fe (0) bimetallic nanoparticles [carboxymethyl cellulose (CMC)-Pd/Fe (0)] with *Sphingomonas* spp. strain NM05 for lindane degradation in contaminated soil. Their study signifies the potential efficacy of an integrated technique as an effective alternative remedial tool for lindane-contaminated soils. The embedded bio-nano hybrid system can be applied as an effective remediation method for the treatment of lindane-contaminated soils and wastewaters.

Plant–Microbe Association

Plants also possess a remarkable ability to remove or immobilize various environmental pollutants (Asemoloye et al., 2017). A unique chemical communication occurs between plants and their rhizospheric microbes that can be used to repair the polluted environment. In the plant–microbe relationship, plants provide habitats and nutrients for their associated bacteria. These bacteria can provide the plant with improved stress resistance, growth, and degradation of environmental pollutants (Singh and Singh, 2019b). Therefore, plant–microbe-associated bioremediation techniques were reported as cost-efficient and eco-friendly methods of cleaning polluted sites.

Sainz et al. (2010) investigated the effects of lindane pollution on vegetables and the associated arbuscular mycorrhiza. Their research indicated that the fungus increases the plant's tolerance toward the toxic effects of soil conditions. Becerra-Castro et al. (2013) inoculated substrates seeded with *Cytisus striatus*, *Rhodococcus erythropolis* ET54b, and *Sphingomonas* sp. D4. The results showed that the inoculation of *C. striatus* with a combination of bacterial strains is a promising approach for the remediation of lindane-contaminated sites. Asemoloye et al. (2017) isolated five dominant fungal strains from an aged lindane polluted site. Lindane degradation in polluted soil was reported to be more effective in response to the combined actions of plant roots and fungi. However, the plant–microbe association bioremediation technique for lindane degradation is still in the primary stages. There is a need for large-scale and in-depth evaluation of bioremediation protocols, as they may be useful for the remediation of lindane-polluted soils.

Novel Technologies

Traditional technologies, such as pure cultures, lack widespread application due to the low remediation capacity and sensitivity to environmental conditions. Therefore, based on the limitations of traditional technology and the modern molecular biology technology, some novel technologies that are considered to be highly efficient, eco-friendly, and promising tools were proposed to remediate the contaminated sites, for instance, metagenomics,

genetic engineering, and enzyme engineering. With the development of new techniques, including metagenomics and genetic engineering, it becomes easy to explore new microorganisms and genes/enzymes, and these can be deployed in bioremediation programs (Kumar and Pannu, 2018).

One novel approach to enzyme immobilization is based on the entrapment of magnetic nanoparticles via epoxy cross-linking. This technique can be employed to improve the activity of pollutant degradation bacteria, fungi, or heterologous-expressed enzymes (Iype et al., 2017; Gangola et al., 2018). Recent high throughput techniques can be used to explore key functional strains from the pesticide degradation microbial community and fulfill the gap between laboratory cultures and large-scale applications (Chen et al., 2019).

Omics-based technologies provided insights into pesticide degradation (Bhatt, 2019). Advancements in next generation sequencing provide a huge amount of microbial data in the form of nucleotides and protein sequences that are deposited in various online databases (NCBI, DDBJ, Uniprot, PDB, etc.) (Bhatt and Barh, 2018). The data from the omics-based approaches can be used for the identification of novel genes and enzymes and molecular docking studies (Bhatt, 2018). These databases are also helpful for the classification of novel lindane-degrading microbes and phylogenetic analysis.

Microbial systems biology is another recent tool to study the lindane-degrading microbes and their physiology in a contaminated environment (Bhatt, 2019). The systems biology of pesticide-degrading microbial cells is helpful for understanding the detailed metabolic pathways, lindane residues in the soil/water system and their effect on other living systems. Using this tool, we can analyze the overall biomagnification due to lindane in the environment (Bhatt et al., 2019b). Systems biology tools are also helpful to design the synthetic microbial consortium for the rapid removal of lindane from soil and water bodies. With the development of modern science and technology, new technologies will continue to be developed and applied for *in situ* and *ex situ* remediation-based environmental management programs.

CONCLUSION AND FUTURE PERSPECTIVES

Lindane, a persistent organochlorine pollutant, has become a major environmental problem around the world. Biodegradation based on the catabolic activity of pesticide-degrading microorganisms has emerged as the most cost effective, eco-friendly, and promising strategy to eliminate environmental lindane residues. The research mainly focused on the screening of lindane-degrading strains and the analysis of degradation products under laboratory conditions. A few studies reported the degradation mechanisms and practical applications of specific strains. Given the health hazards and the environmental impact of lindane, the microbial degradation-based bioremediation methods and associated technologies should be widely developed and applied. Increasing the information available regarding degradation pathways with regulatory genes and enzymes will help with the development of novel remediation technologies. Moreover, advanced molecular approaches, enzyme engineering, and emerging materials will provide better tools for the remediation of harmful pollutants.

AUTHOR CONTRIBUTIONS

SC conceived the presented idea. WZ contributed to the writing and prepared figures and table. ZL, SP, PB, and SC participated in revising the manuscript. All authors approved it for publication.

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