Insight Into Microbial Applications for the Biodegradation of Pyrethroid Insecticides

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Pyrethroids are broad-spectrum insecticides and presence of chiral carbon differentiates among various forms of pyrethroids. Microbial approaches have emerged as a popular solution to counter pyrethroid toxicity to marine life and mammals. Bacterial and fungal strains can effectively degrade pyrethroids into non-toxic compounds. Different strains of bacteria and fungi such as *Bacillus* spp., *Raoultella ornithinolytica*, *Pseudomonas flourescens*, *Brevibacterium* sp., *Acinetobactor* sp., *Aspergillus* sp., *Candida* sp., *Trichoderma* sp., and *Candia* spp., are used for the biodegradation of pyrethroids. Hydrolysis of ester bond by enzyme esterase/carboxyl esterase is the initial step in pyrethroid biodegradation. Esterase is found in bacteria, fungi, insect and mammalian liver microsome cells that indicates its hydrolysis ability in living cells. Biodegradation pattern and detected metabolites reveal microbial consumption of pyrethroids as carbon and nitrogen source. In this review, we aim to explore pyrethroid degrading strains, enzymes and metabolites produced by microbial strains. This review paper covers in-depth knowledge of pyrethroids and recommends possible solutions to minimize their environmental toxicity.

**Keywords:** biodegradation, pyrethroids, metabolic pathway, esterase enzyme, hydrolysis

INTRODUCTION

Pyrethroids are the most commonly used global pesticides. *Chrysanthemum cinerariaefolium* flowers are the natural source of pyrethroids and allethrin was developed as the first synthetic pyrethroid insecticide in 1949 (Ensley, 2018; Gammon et al., 2019; Xu et al., 2019). Pyrethroids can be divided into two groups, type I pyrethroids containing basic cyclopropane carboxylic (e.g., allethrin) and type II pyrethroids containing cyano group (Proudfoot, 2005; Wolansky and Harrill, 2008; Chang et al., 2016; Figure 1). Presence of cyano group in type II pyrethroids enhances their insecticidal properties as compared to type I pyrethroids. All pyrethroids contain at least four stereoisomers, which exhibit different biological activities (Table 1). Pyrethroids are either marketed as racemic mixture of stereoisomers or single chemical isomer. Piperonyl butoxide acts as synergist in commercial formulation of pyrethroids and inhibits the metabolic degradation of active compounds (Bradberry et al., 2005; Fai et al., 2017). Deltamethrin is used in different countries to control malaria-spreading mosquitoes. Pyrethroids are reported to be 2250 times more toxic to insect than mammals and disrupt sodium, chloride channels (Chrustek et al., 2018). At high concentrations pyrethroids inhibit the functioning of gamma amino butyric acid (GABA) gated
chloride ion channel (Bradberry et al., 2005; Gammon et al., 2019). Pyrethroids are mainly used to control insect pests of agriculture, horticulture, forestry and household. Pyrethroids are considered comparatively safe but their extensive use makes them harmful for humans and animals (Kuivila et al., 2012; Burns and Pastoor, 2018; Bordoni et al., 2019). Previous reports have concluded their detrimental effects on non-target species including marine fish and aquatic insects (Burns and Pastoor, 2018; Lu et al., 2019). Pyrethroid toxicity biomarkers have been well documented in fish (Ullah et al., 2019). Frequent pyrethroids applications in agriculture and households can cause inappropriate effects on human growth. In humans, pyrethroids exposure leads to contaminated urine, low serum quality, and antiandrogenic activity. Bio-absorption of pyrethroids was detected in the urine samples of outdoor workers in California (Sullivan et al., 2019), which indicates the importance of this topic. In rats, the developmental of bifenthrin neurotoxicity was reported as mixed type (typeI/II) (Gammon et al., 2019) whereas non-target neurotoxicity of pyrethroids has also been investigated in zebrafish (Paravani et al., 2017; Awoyemi et al., 2019). Studies on pyrethroid residues in children diaper revealed that pyrethroid metabolites were stable on the diaper up to 72 h (Hu et al., 2004). Pyrethroid residues have been reported in dust, cloth, union suit samples, diaper, military uniform, and urine samples (Bradman et al., 2007; Proctor et al., 2003). Cyfluthrin studies on a medium pile biological samples is more reliable than environmental samples (Ghazouani et al., 2019). Toxicity studies have revealed several effects of pyrethroids on human and marine life (Table 2). Large-scale application of pyrethroids affects humans and animals. Indoor pyrethroids exposure studies revealed low levels of pyrethroids absorption in biological and environmental samples (Ghazouani et al., 2019). Measurement of absorbed daily dose (ADD) from biological samples is more reliable than environmental samples (Williams et al., 2003). Cyfluthrin studies on a medium pile of nylon carpet suggested that pyrethroids were absorbed in the surrounding surfaces and were also found in human urine samples (Williams et al., 2003; Sullivan et al., 2019). Presence of 4-fluro-3 phenoxybenzoic acid in urine samples indicated human exposure to pyrethroids and environmental measurements further confirmed the results (Williams et al., 2003). Studies on pyrethroid residues in children diaper revealed that pyrethroid metabolites were stable on the diaper up to 72 h (Hu et al., 2004). Pyrethroid residues have been reported in dust, cloth, union suit samples, diaper, military uniform, and urine samples (Bradman et al., 2007; Proctor et al., 2019). Pyrethroid residues in the urine samples of pregnant women have been reported from Jiangsu China and France (Qi et al., 2012; Dereumeaux et al., 2018; Kamai et al., 2019). Children in United States are more exposed to pyrethroids as compared to organic food taking children of other areas. Pyrethroid metabolite 3-phenoxybenzaldehyde was commonly found in the urine samples of exposed children (Lu et al., 2009;
| S. No. | Pyrethroids | Sample source/Study sample | Specific statement | References |
|-------|-------------|-----------------------------|-------------------|------------|
| 1     | Pyrofenofos, cypermethrin, permethrin, tefluthrin, trans-fenthiuthrin, bifenthrin, indoxacarb, acephate, and spinosyn A | Larvae of tobacco budworm, Heliothis virescens (F.) | Detection of esterase resistance/susceptibility in insect larvae | Huang and Ottea, 2004 |
| 2     | Racemic (cis-bifenthrin, fonofos, and profenofos), racemic trans-permethrin, cis-permethrin | Freshwater, invertebrates | Determination of enantioselectivity based toxicity of chiral pyrethroids | Liu et al., 2005 |
| 3     | Cyfluthrin | Human fetal astrocyte cells | Affecting growth, survival and functioning of human astrocyte cells | Mense et al., 2006 |
| 4     | Cis and trans permethrin | Human urine | Detected the presence of pyrethroid in urine | Bradman et al., 2007 |
| 5     | Cyfluthrin | Human peripheral lymphocytes | Genotoxic effect seen in the human peripheral lymphocytes due to mutation | Ila et al., 2008 |
| 6     | Type I and Type II pyrethroids | Mild poisoning sign | Hyper activity and hyper-excitability in mice and rat | Wolansky and Harrill, 2008; Wang et al., 2018 |
| 7     | Type I and Type II pyrethroids | Moderate to severe poisoning sign | Prostration, sinuous writhing, uncoordinated twitches, normothermia | Wolansky and Harrill, 2008; Wang et al., 2018 |
| 8     | Type I and Type II pyrethroids | Nearly lethal syndrome | Clonic seizures, tonic seizure, and rigors occasionally just before death | Wolansky and Harrill, 2008 |
| 9     | Cyfluthrin and beta cyfluthrin | Androgen responsive cell line, MDA-kb2 | Antiandrogenic activity was reported in presence of pyrethroids | Zhang et al., 2008 |
| 10    | α-Cyanothrin and γ-cyanothrin | Aquatic invertebrate and Fish | Single enantiomer is less toxic than racemate of pyrethroid | Giddings et al., 2009 |
| 11    | Racemic pyrethroid | Urine sample | Detection of pyrethroid intermediate 3-phenoxycyanic acid | Lu et al., 2009 |
| 12    | α-Cypermethrin | Human peripheral blood lymphocytes | High cytoxic effect at >20 µg/ml | Kocaman and Topaktaş, 2009 |
| 13    | Bifenthrin, permethrin, fenvalerate | Yeast strains | Enantioselctivity in esterogenic activity | Wang et al., 2010 |
| 14    | Deltamethrin, β-cyfluthrin, cypermethrin, permethrin, bifenthrin, esfenvalerate, α-cyanothrin, tefluthrin, fenpropatrin, resmethrin, and S-bioallethrin | Swiss-webster mice | Pyrethroid actions affect the sodium influx in cerebrocortical neurons | Cao et al., 2011 |
| 15    | Beta-cypermethrin | Soil samples | Microbial community in soil affected by the action of cypermethrin | Zhuang et al., 2011 |
| 16    | Cypermethrin and decamethrin | Brinjal fruits | It was noticed that trace quantity persist in Brinjal upto a long time | Kaur et al., 2011 |
| 17    | Lambda-cyanothrin | Developing rats | Cholinergic dysfunctions and oxidative stress is responsible for neurotoxicity in rats | Ansari et al., 2012 |
| 18    | Cypermethrin | Myrica opima | Hepatopancreas and gill have increased glycogen | Tendulkar and Kulkarni, 2012 |
| 19    | Deltamethrin | Human dopaminergic neuroblastoma SH-SY5Y cells | Oxidative stress mediated neurotoxicity | Romero et al., 2012 |
| 20    | Deltamethrin | Male BALB/c Mice | Deltamethrin inhibit the osteoclast development | Sakamoto et al., 2012 |
| 21    | Deltamethrin | Rat bone marrow cells | Testicular injury and genotoxicity due to pyrethroids when compare with biopesticide (Bacillus thuringiensis) | Ismail and Mohamed, 2012 |
| 22    | Cypermethrin | CV-1 cells (Cercopithecus aethiops monkey kidney Cells) | Cypermethrin inhibited the interaction of androgen receptor and steroid receptor coactivator-1 | Pan et al., 2012 |
| 23    | Deltamethrin | Trichogranum evanescentia, T. semiludis | Discrimination of sex pheromones affected by deltamethrin | Delpuech et al., 2012 |
| 24    | Bifenthrin | Rat adrenal phaeochromocytoma cells (PC-12) | Bilinethrin affects the antioxidant enzyme due to enantioselectivity | Lu, 2013 |
| 25    | 3-Phenoxybenzoic acid | Urine and semen samples | Pyrethroid exposure reduced semen quality | Toshima et al., 2012 |
| 26    | Pyrethroids (3-phenoxycyanic acid, 2-methyl 3-phenoxycyanic acid) | Urine samples | Chronic exposure of pyrethroids on Australian preschool childrens | Babina et al., 2012 |
TABLE 2 | Continued

| S. No. | Pyrethroids | Sample source/Study sample | Specific statement | References |
|--------|-------------|----------------------------|-------------------|------------|
| 27     | Pyrethroids mixed | Urine samples of flight attendant | Detection of pyrethroid metabolites in urine analysis | Wei et al., 2012 |
| 28     | Lambda-cyhalothrin | Liver of Oreochromis niloticus | Apoptotic and oxidative effect due to piperonyl butoxide treatment with lambda-cypermethrin | Piner and Üner, 2012 |
| 29     | Permethrin | Mice | Reproductive toxicity due to enantioselectivity of permethrin | Jin et al., 2012 |
| 30     | Bifenthrin | Sandy loam soil | Difference of half life in sterile and non-sterile soil indicated that bifenthrin persistence change microbial community | Sharma and Singh, 2012 |
| 31     | Twelve different pyrethroids | Marine animals (Dolphins) | Mother to calf transfer of pyrethroids by lactation and gestation in Dolphin | Alonso et al., 2012 |
| 32     | Thirteen different pyrethroids | Human breast milk | Analysis of pyrethroid in Brazil, Columbia and Spain by food samples to humans than transfer rate in infants | Cor ellas et al., 2012 |
| 33     | Permethrin | Consumed human food, residential exposure | Mathematical modeling of EPA that is SHEDS-multimedia model | Zartarian et al., 2012 |
| 34     | Lambda-cyhalothrin | Male mice | Reproductive and Hepatotoxicity observed | Al-Sarar et al., 2014 |
| 35     | Pyrethroids and metabolites | Urinary sample of pregnant women | Data indicated effect of pyrethroid on pregnant women that will also affect infants | Qi et al., 2012 |
| 36     | Permethrin, cyfluthrin, esfenvalerate, cypermethrin | Mammalian cells, fishes | Pyrethroids act as endocrine disruptor | Brander et al., 2016 |
| 37     | λ-Cyhalothrin, fenvalerate and permethrin | Embryo of Zebra fish (Danio rerio) | Triiodothyronine (T3) level decreased due to exposure of lambda cyhalothrin and Fenvalerate | Zhang et al., 2017 |
| 38     | Cypermethrin, deltamethrin and cychothrin | Cucumis sativus | Chlorophyll and carotenoids showed sensitive effect | Braganca et al., 2018 |
| 39     | Cypermethrin | Bacillus sp. | In vitro toxicity detected in human cell line | Sundaram et al., 2013 |
| 40     | Bifenthrin, λ-cyhalothrin, cyfluthrin, cypermethrin, cis-deltamethrin, esfenvalerate, and cis/trans permethrin | Solid food sample | Pyrethroid degradates not present in sufficient level in diet to substantially impact the adults | Birolli et al., 2016b; Morgan et al., 2018 |
| 41     | Cypermethrin | Salvator meriana (Argentine tegu) | Cypermethrin with other pesticides affect immune and endocrine system | Mestre et al., 2019 |

Dalsager et al., 2019). Presence of 3-phenoxybenzaldehyde metabolite in the semen of Japanese males suggested that their semen quality was decreased by pyrethroids (Toshima et al., 2012). Residues of organophosphorous and pyrethroids were also reported in Australian preschool children (Babina et al., 2012) and urinary concentration of pyrethroids from Queensland (Australia) pre-schoolers correlated with the age and sex (Li et al., 2019). Pyrethroids are also used to disinfect the aircrafts and presences of 3-phenoxybenzaldehyde in the urine samples of flight attendants (18–65 years old) clearly indicated pyrethroid exposure in different age groups of humans (Wei et al., 2012). Higher pyrethroids exposure was reported in farmers and consumers of northern Thailand (Hongsisong et al., 2019) and extensive studies revealed their carcinogenic potential (Navarrete-Meneses and Pérez-Vera, 2019).

Macrophages are immune cells that play important role in pathogen removal from the cells. It was observed that β-cypermethrin and cyhalothrin treatment decreased phagocytic activity and nitric oxide production in macrophage cells (He et al., 2019). No activity was detected at low concentration of cyhalothrin whereas macrophage activity was blocked at higher concentration. Direct effect of cyhalothrin on macrophage cells is due to the activity of sodium ion membrane channels whereas activity of hypothalamus pituitary adrenal axis caused indirect effects in rats (Righi and Palermo-Neto, 2005; He et al., 2019). Different levels of pyrethroid toxicity in freshwater invertebrates Ceriodaphnia dubia and Daphnia magna is due to a selective enantiomer in racemate (Liu et al., 2005). Comparative study of cyfluthrin and chlorpyrifos toxicity in human fetal astrocytes (star shaped glial cells in the brain and spinal cord) revealed that cyfluthrin exerts more toxic effects on survival, growth and proper functioning of human peripheral lymphocytes, and induces apoptosis (Mense et al., 2006; Segura et al., 2018). Cyfluthrin and chlorpyrifos over express pro-inflammatory mediators, and cyfluthrin can cause mutation to change chromosome number (Mense et al., 2006; Muzinic et al., 2018). Genotoxic and cytotoxic effects of cyfluthrin were detected by Salmonella/mammalian microsome mutagenicity test, chromosomal aberration, chromatid exchange, and micronucleus formation in cultured human peripheral blood lymphocytes in vitro (Ila et al., 2008; Chalap et al., 2018). Pyrethroid genotoxicity demands for their restricted use around children, elderly people, and pregnant women (Kocaman and Topaktaş, 2009).
Pyrethroids are neurotoxic pesticides and affect neurotransmitters (Gammon et al., 2019). Effect of low acute oral dose of pyrethroids has been investigated in small rodents. Neurobehavioral study suggested that pyrethroids block sodium chloride and GABA channels, which inhibit transfer of neurotransmitters between cells (Cao et al., 2011; Richardson et al., 2019). Permethrin was reported against Laccophilus minutus (Touylia et al., 2019) and in humans it is absorbed through dermal and non-dietary entry points (Nakagawa et al., 2019). Cypermethrin, allethrin, cis/trans permethrin and deltamethrin modified the strength and behavior of tested organisms, whereas decreased grip strength was noted after pyrethrum, cypermethrin, bifenthrin, β-cyfluthrin, deltamethrin, S-bioallethrin, and permethrin treatments. A coordination study of deltamethrin and α-cypermethrin with rotarod revealed that the compound with α-α and ε-ε group enhanced acoustic evoked startle response amplitude whereas opposite effect was observed without α-ε group. Intensity of tremor and sensory response is rarely explored against pyrethroids (Wolansky and Harrill, 2008). Ansari et al. (2012) reported that long term exposure of α-cypermethrin produces harmful neurochemical endpoints that cause behavioral variations in rats.

Antidiagnostic activity of cyfluthrin and β-cyfluthrin in a carcinogenic cell line MDA-kb2 has also been reported (Zhang et al., 2008). Bifenthrin evokes various toxicological effects in different human cells by modifying homeostasis and cell viability in human prostate cancer cells (Chien et al., 2019). Bifenthrin acts as endocrine disrupting chemical by inhibiting the expression of glucocorticoid and estrogen receptor (Ligocki et al., 2019). 5-Dihydrotestosterone induced androgen receptor activity was blocked by pyrethroids in MDA-kb2 cells and considered as moderate antidiagnostic (Zhang et al., 2008). Giddings et al. (2009) compared the effect of γ-cyhalothrin and λ-cyhalothrin, and suggested that the single active enantiomer (isomer) causes more toxicity than racemic mixture of both pyrethroids in marine fish and invertebrates (Giddings et al., 2009). Lambda-cyhalothrin and fenvalerate decreased triiodothyronine (T3) in the embryo of Zebrafish (Danio rerio) (Awoyemi et al., 2019). Due to specific binding between ERα receptor and pyrethroid isomer, synthetic pyrethroids act as estrogenic endocrine disrupting compounds (Wang et al., 2010; Lauretta et al., 2019).

Damage of β-cypermethrin to soil microbial communities is less as compared to marine life (Zhuang et al., 2011). Bifenthrin affects microbial community in sandy loam soil and pyrethroids are generally considered as a threat to marine life (Sharma and Singh, 2012). Cypermethrin and deltamethrin residues were reported in Brinjal fruits which can be reduced by washing and boiling before cooking (Kaur et al., 2011). Deltamethrin induced shift of soil microorganisms was reported with cabbage plants after 30 days of treatment (Braganca et al., 2019). Pyrethroids are highly toxic to aquatic organisms such as fish, shrimp, crab and shellfish. Effects of γ-cyhalothrin and modulator piperonyl butoxide were observed in fish Oreochromis niloticus. Study revealed that λ-cyhalothrin causes oxidative stress in the liver of O. niloticus and stress was further increased in the presence of piperonyl butoxide (Piner and Üner, 2012; Giddings et al., 2019). Pyrethroids transform into solid, liquid and gas phase and enter in food chains to pose high health risk. Pyrethroids accumulated in sediment are major source of aquatic toxicity (Tang et al., 2018). Toxicity of type I and type II pyrethroids was assessed in embryo of Zebrfish (D. rerio) that depicted different mechanistic effects of pyrethroids and their instability in marine environment (Awoyemi et al., 2019). Pyrethroids toxicity to red blood cells and brain cells is associated with physiological changes and DNA damage in fish (Paravani et al., 2019; Ullah et al., 2019).

Cypermethrin stress decreased total glycogen content in different organs/tissues of Marica opima and affected its metabolic activity (Tendulkar and Kulkarni, 2012). Oxidative stress produced by deltamethrin is one of the major mechanism of neurotoxicity (Romero et al., 2012). Deltamethrin inhibits the differentiation of osteoclast by regulating nuclear factor of activated T-cells cytoplasmic-1 (NFATc-1) and oxygenase-1 which is an important regulatory protein (Sakamoto et al., 2012). Deltamethrin is more hazardous than biopesticide (Bacillus thuringiensis) and has been reported to cause testicular injury in rats and affect sex pheromones (Delpuech et al., 2012; Ismail and Mohamed, 2012). Cypermethrin inhibits the androgen receptor (AR) activity by disrupting AR-SRC1 (steroid receptor coactivator-1) interaction (Pan et al., 2012). Toxicity of pyrethroids (cis-bifenthrin) is enantioselective in nature and particular degrading enzymes are more expressive. These previous studies provide detailed knowledge of chiral chemical toxicity at molecular level (Lu, 2013). High pesticide exposure leads to acute pesticide poisoning and damages central nervous system (CNS) (Starks et al., 2012).

Permethrin and its four chiral isomers caused severe histopathological testicular damage in mice at 100 mg/kg by decreasing testis weight and concentration of testosterone hormone (Jin et al., 2012). These pesticides have been noted to transfer from mother to calf in dolphins via gestation and lactation pathways (Alonso et al., 2012; Kondo et al., 2019). Studies conducted in Brazil, Columbia and Spain reported the presence of pyrethroids in human breast milk at concentrations of about 1.45–24.2 ng/gm lw (Corcellas et al., 2012).

Zartarian et al. (2012) studied the effects of permethrin in 3–5 years old children. Stochastic human exposure and dose stimulation model (SHEDS) for multimedia multi-pathway chemicals is commonly known as multimedia computer based method developed by environmental protection agency (EPA) for the study of toxic chemicals (Zartarian et al., 2012). Lambda-cypermethrin has been reported to cause reproductive toxicity, hepatotoxicity, splenotoxicity, and nephrotoxicity in male mice (Starks et al., 2012). Effect of pyrethroids on different fish suggested that highly lipophilic pyrethroids accumulate in sediments and organisms. These compounds also act as endocrine disruptor and block the hormonal signaling in aquatic animals and mammals (Brander et al., 2016).

A study of cypermethrin, deltamethrin, and cyhalothrin phytotoxicity on Cucumis sativus showed that these insecticides affected the production of chlorophyll and carotenoids in plants (Braganca et al., 2018). The study on cypermethrin biodegradation and metabolites detection in tomato, cabbage, rape, pepper, and cucumber revealed its rapid dissipation in
plants. Enatioselective degradation was observed in pepper and cucumber (Yao et al., 2018).

**PYRETHROID-DEGRADING MICROORGANISMS AND THEIR DEGRADATION CHARACTERISTICS**

Many studies have confirmed that bacteria and fungi are capable of degrading pyrethroids in liquid cultures or soils (Table 3). Microorganisms can degrade pyrethroids by using either directly as a source of carbon or co-metabolically (Biroli et al., 2016b; Cycoń and Piotrowska-Seget, 2016; Chen and Zhan, 2019). *Acidomonas* sp. degraded more than 70% of allethrin in 72 h as carbon and nitrogen source (Paingankar et al., 2005). *Micrococcus* sp. strain CPN1 has been reported to biodegrade and completely mineralize cypermethrin through enzymatic cleavage of ester bond (Tallur et al., 2008; Zhao et al., 2015). Pyrethroid degrading bacterium *Sphingobium* sp. JZ-2 was isolated and characterized from amended sludge of pyrethroid manufacturing wastewater. Strain JZ-2 efficiently degraded cypermethrin, bifenthrin, and fenvalerate. Novel pyrethroid hydrolase purified from the cell extract was strongly inhibited by different ions (Ag⁺, Cu²⁺, Hg²⁺, and Zn²⁺) (Guo et al., 2009). *Serratia* sp. strain JC1 and JCN13 efficiently biodegraded beta-cypermethrin due to their higher hydrophobicity. Strain JC1 degraded 92% beta-cypermethrin within 10 days whereas strain JCN13 degraded 89% within 4 days. Growth conditions for better biodegradation were also optimized through response surface methodology (RSM) and Box-Behnken design (Zhang et al., 2010). Pyrethroid degrading bacterium *Raoultella ornithinolytica* ZK4 was isolated from the soil samples of a pesticide plant and it degraded lambda-cyhalothrin and deltamethrin (Zhang et al., 2019). Recently 3-phenoxybenzoic acid and other pyrethroids were degraded (96.37%) within 72 h of treatment by using *Klebsiella pneumoniae* strain BPBA052 (Tang et al., 2019).

Aerobic and anaerobic soil biodegradation of pyrethroid etofenprox was investigated in the rice fields of California. 3-Phenoxybenzoic acid, a hydrolytic product of ester bond cleavage was not detected in any sample. Microbial population in a flooded soil (anaerobic) played role in conversion and dissipation of etofenprox (Vasquez et al., 2011; Furihata et al., 2019). β-Cyfluthrin is commonly used by Indian farmers at Indian Agriculture Research Institute Delhi for controlling *Lepidopteran* pests of *Solanaceae* crops. To degrade its soil residues, *Pseudomonas stutzeri* was isolated, and identified using enrichment culture technique and intermediate metabolites were confirmed according to the previous reported pathway (Saikia et al., 2005; Biroli et al., 2019). Cyfluthrin degradation by bacterium *Photobacterium ganghwaense* was confirmed by comparative metabolomics (Wang et al., 2019). Pyrethroid degradation capability of *Ochrobacterium tritici* strain pyd1 is dependent upon the molecular structure of synthetic pyrethroids (Wang et al., 2011). Strain pyd-1 effectively degraded both, cis and trans isomers at the same rate. Detailed metabolic pathway of fenpropatrin biodegradation through strain pyd-1 was also identified. Specific enzyme activities of pyrethroid hydrolase, 3-phenoxybenzaldehyde (PBD) dehydrogenase, 3-phenoxybenzoic acid (PBA) hydroxylase, 4-hydroxy-PBA dioxygenase, and p-hydroquinone hydroxylase have been studied in relation to pyrethroid fenpropatrin (Dehmel et al., 1995; Wang et al., 2011; Luo et al., 2019). *Pseudomonas pseudaoalcigenes* strain POB310 has been reported for the degradation of 3- and 4-carboxyphenyl ethers (Dehmel et al., 1995). A genetically engineered strain of *Pseudomonas putida* also degraded other pesticides similar to pyrethroids (Gong et al., 2018). Anaerobic bacterium *Clostridium* strain ZP3 isolated from the mixed wastewater and sludge samples degraded higher concentrations of fenpropathrin by co-metabolic activity and was used to analyze complex redox reaction in fenpropathrin biodegradation (Zhang S. et al., 2011; Zhao et al., 2016). Co-metabolic biodegradation of β-cypermethrin was explored with *Bacillus licheniformis* B-1 (Zhao et al., 2019). *Pseudomonas aeruginosa* CH7 degraded 90% of beta-cypermethrin by isomerization within 12 days. Bio-surfactant (rhamnolipid) promotes the adsorption and hydrophobicity of chemical compounds (Zhang C. et al., 2011). Neustonic and epiphytic bacteria and their mixed cultures were noted to similarly degrade deltamethrin (Kalwasinska et al., 2011). Chen et al. (2012d) also validated the cypermethrin biodegradation through *Bacillus cereus* ZH-3 and *S. aureus* HP-S-01 cells.

*Ochrobactrum anthropi* strain YZ-1 is quite potent to degrade pyrethroids. Role of bacterial esterase PytZ (606 bp) in biodegradation without any cofactor has been confirmed (Zhai et al., 2012). Pyrethroid hydrolase of molecular weight 53 KDa was purified and characterized from *A. niger* strain ZD11. Pyrethroid activity was not detected in the presence of glucose and it indicates that pyrethroid hydrolase only expresses in fungus after pyrethroid stress. Optimum pH for *A. niger* was found to be lower than *B. cereus* (7.3) whereas the optimum temperature was comparatively higher (45°C) as compared to *B. cereus* strain SM3 (37°C). Enzyme activity inhibition by thiol modifying enzyme (PCMB) p-chloromercuribenzoate suggested that sulphydryl group was involved in the catalytic center of enzyme (Liang et al., 2005). Cypermethrin reportedly caused toxicity to human hepatocarcinoma cell line H4H7 (Sundaram et al., 2013). *Bacillus* sp. helps to biodegrade cypermethrin in soil microcosm and *B. cereus* MTCC 1305 has been reported to biodegrade fenvalerate (Selvam et al., 2013). Pyrethroid toxicity and biodegradation efficiency of *Pseudomonas viridiflava* has also been thoroughly investigated (Selvam et al., 2013; Thatheyus and Selvam, 2013). Two strains of *S. marcescens* Del-I and Del-2, enhanced the disappearance of cypermethrin (Cycoń et al., 2014). Application of ammonium nitrate as external nitrogen at the rate of 122.1 kg/ha⁻¹ increased cypermethrin degradation by 80% (Xie et al., 2008). External nitrogen might accelerate microbial metabolism in lag phase.

Metabolic and ecological potential of fungi makes them suitable for bioremediation and waste treatment (Harms et al., 2011). Cell free extracts of fungi are known to effectively degrade chlorpyrifos and pyrethroids (Yu et al., 2006). β-Cyhalothrin degradation by different fungi has been reported including *Trichoderma viridae* strain 5-2, *Trichoderma viridae* strain 2211,
### TABLE 3 | Pyrethroid degrading microorganisms and their optimized conditions in lab/field.

| S. No | Bacteria/Fungi/Insect/Other | Pyrethroid used | Standard condition for growth | Specific statement | References |
|-------|-----------------------------|----------------|-------------------------------|--------------------|------------|
| 1     | *Bacillus cereus*, *Pseudomonas fluorescense*, and *Achromobacter sp.* | Permethrin, deltamethrin, fastac, fenvalerate, and fluvalinate | pH-7.0, Temp-30°C, Tween,80 to maintain relatively insoluble compound in solution | 3-Phenoxybenzoic acid was the major product, Permethrin transformed rapidly as compared to others | Maloney et al., 1988 |
| 2     | *Pseudomonas sp. ET1* | 3-Phenoxybenzoate | pH-7.2, Temp-30°C | Phenoxy substituted benzyl aldehyde was metabolized whereas benzyl alcohol, benzene, phenol, and aniline were not | Topiw and Akhtar, 1991 |
| 3     | *Trichoderma viridae*, *Trichoderma fasciculare*, *Aspergillus niger*, and *Phanerochaete chrysosporium* | Beta-cyfluthrin | pH-6.5°C, czapek dox medium was used | Cleavage of ether linkage result in metabolites formation. That is confirmed by NMR analysis | Saikia and Gopal, 2004; Deng et al., 2015 |
| 4     | *Acidomonas sp.* | Allethrin | pH-7.0, Temp-37°C with minimal salt medium | Allethrin is metabolized by hydrolytic pathway followed by dehydrogenation and oxidation | Paingankar et al., 2005 |
| 5     | *Pseudomonas stutzeri S1* | Beta-cyfluthrin | pH-7.0, Temp-28°C, Minimal salt media | Strain able to degrade the beta-cyfluthrin | Saikia et al., 2005 |
| 6     | *Aspergillus niger* ZD11 | Trans-permethrin, cis-permethrin, cypermethrin, fenvalerate, and deltamethrin | pH-6.8, Temp-30°C, Minimal salt media | Novel pyrethroid hydrolase having the potential of wide range of pyrethroid degradation | Liang et al., 2005; Deng et al., 2015 |
| 7     | *Micrococcus sp.* CPN1 | Cypermethrin | pH-7.0, Temp-28°C, Minimal salt medium at 150 rpm | Presence of 3-phenoxybenzoate, protocatechucate, and phenol were investigated | Tallur et al., 2008 |
| 8     | *Bacillus sp.* | Cypermethrin | pH-7.0, Temp-30°C, Rpm-110 | 3-Phenoxybenzaldehyde and other metabolites of the pathway | Bhatt et al., 2016b, 2019b |
| 9     | *Sphingobium sp.* JZ-2 | Fenpropathrin, cypermethrin, permethrin, cyhalothrin, deltamethrin, fenvalerate, and bifenthrin | pH-7.0, Temp-30°C, Luria Bertani medium | 3-Phenoxybenzaldehyde, 2,2,3,3-tetramethylcyclopropanecarboxylic acid, 3-phenoxybenzoic acid, 3-phenoxybenzaldehyde, 3-phenoxybenzaldehyde, protocatechuate, and catechol | Guo et al., 2009 |
| 10    | *Serratia spp.* | Beta-cypermethrin | pH-6-9, Temp-20–38°C | 3-Phenoxybenzaldehyde, 3-phenoxybenzaldehyde, 3-phenoxybenzaldehyde, 3-phenoxybenzaldehyde, 3-phenoxybenzaldehyde, 3-phenoxybenzaldehyde, 3-phenoxybenzaldehyde, 3-phenoxybenzaldehyde, and p-hydroquinone | Zhang et al., 2010 |
| 11    | *Ochrobactrum tritici* pyd-1 | Cis and trans permethrin, fenpropatrin | Luria Bertani medium, Temp-30°C | 2,2,3,3-Tetramethylcyclopropanecarboxylic acid, 3-phenoxybenzaldehyde, 3-phenoxybenzaldehyde, 3-phenoxybenzaldehyde, protocatechuate, and p-hydroquinone | Wang et al., 2011 |
| 12    | *Clostridium sp.* ZP3 | Fenpropatrin | pH-7.5, Temp-35°C | Benzyl alcohol, benzenemethanol, and 3,3-diethylamphethamine | Zhang S. et al., 2011 |
| 13    | *Pseudomonas aeruginosa* CH7 | Beta-cypermethrin | pH-6-9, Temp-25–35°C | Biosurfactant production increased beta-cypermethrin degradation | Zhang C. et al., 2011 |
| 14    | Neustonic and epiphytic bacteria | Deltamethrin | pH-7.0, Temp-20°C, Minimal salt medium | Bacteria reduced the initial concentration of cypermethrin | Kalwasinska et al., 2011 |
| 15    | *Bacillus cereus* MTCC19305 | Fenvalerate | pH-6-7.4 | HPLC analysis showed 500 ppm fenvalerate degradation by the bacterium | Selvam et al., 2013 |
| 16    | *Pseudomonas viridoflava* | Fenvalerate | pH-6.2-7.0 | HPLC analysis showed the pyrethroid is degraded with different peak areas | Selvam et al., 2013 |
| 17    | *Serratia marcescens* | Deltamethrin | No data | 3-Phenoxybenzaldehyde and peaks of other metabolites | Cyreri et al., 2014 |

(Continued)
| S. No | Bacteria/Fungi/Insect/Other               | Pyrethroid used                                                                 | Standard condition for growth | Specific statement                                                                 | References |
|-------|-----------------------------------------|---------------------------------------------------------------------------------|-------------------------------|-----------------------------------------------------------------------------------|------------|
| 18    | Acinetobactor calcoaceticus Mcm5        | Cypermethrin, bifenthrin, cyhalothrin, and deltamethrin                         | pH-7.0 Temp-30°C              | All the pyrethroid degraded by the bacterial strain Mcm5                         | Akbar et al., 2015b |
| 19    | Azoracus indogens Hz5                   | Cypermethrin                                                                    | pH-7.0 Temp-30°C              | 70% cypermethrin degradation after 144 h                                          | Burns and Pastoor, 2018 |
| 20    | Bacillus sp. SG2                        | Cypermethrin                                                                    | pH-7.0 Temp-32°C              | 82% cypermethrin degraded after 15 days of experiment                            | Bhatt et al., 2016b, 2019a |
| 21    | Bacillus sp. DG-02                      | Fenpropathrin, cypermethrin, cyfluthrin, lambda-cyhalothrin, deltamethrin, permethrin, and bifenthrin | pH-7.5 Temp-30°C              | Different biodegradation patterns followed with distinct concentration           | Chen et al., 2012b, 2014 |
| 22    | Bacillus amyoliquifaciens AP01          | Cypermethrin                                                                    | pH-7.0 Temp-30°C              | Approximately 45% cypermethrin degradation observed in 5 days                 | Lee et al., 2016 |
| 23    | Bacillus megaterium Jcm2 Brevibacillus parabreviis Jcm4 | Cypermethrin, bifenthrin, cyhalothrin, and deltamethrin                         | pH-7.0 Temp-30°C              | Maximum 89% degradation obtained in cypermethrin                               | Akbar et al., 2015a |
| 24    | Brevibacterium aureus DG-12             | Cyfluthrin, cyhalothrin, fenpropathrin, deltamethrin, bifenthrin, and cypermethrin | pH-7.0 Temp-27°C              | Maximum 84.7% biodegradation observed with cyfluthrin                           | Chen et al., 2013a |
| 25    | Catellibacterium sp. CC-5               | Cypermethrin, fenvalerate, fenpropathrin, deltamethrin, permethrin, and cyhalothrin | pH-7.0 Temp-30°C              | 90% biodegradation achieved after 7 days with cypermethrin and deltamethrin   | Zhao et al., 2013 |
| 26    | Lysinibacillus sphaericus FLQ-11-1      | Cyfluthrin                                                                      | pH-7.0 Temp-35°C              | Approximately 80% cyfluthrin removal after 5 days                                | Hu et al., 2014 |
| 27    | Ochrobactrum lupini DG-S-01             | Cypermethrin, cyfluthrin, fenpropathrin, cyhalothin, and deltamethrin           | pH-7.0 Temp-30°C              | Maximum 90% biodegradation obtained with cypermethrin within 5 days             | Chen et al., 2011a |
| 28    | Pseudomonas aeruginosa JQ-41            | Fenpropathrin, cypermethrin, deltamethrin, bifenthrin, and cyhalothrin          | pH-7.0 Temp-30°C              | Maximum 91.7% biodegradation obtained with fenpropathrin after 7 days of experiment | Song et al., 2015 |
| 29    | Pseudomonas flouescens                  | Cypermethrin                                                                    | pH-7.0 Temp-25°C              | 37.2% cypermethrin degraded in absence of sucrose after 96 h                   | Grant et al., 2002 |
| 30    | Rhodococcus sp. Jcm5                   | Cypermethrin, bifenthrin, cyhalothin, and deltamethrin                          | pH-7.0 Temp-30°C              | 100% cypermethrin catabolism occurs in 10 days                                    | Akbar et al., 2015b |
| 31    | Stenotrophomonas sp. ZS-S-01            | Fenvalerate, deltamethrin, cypermethrin, cyfluthrin, and cyhalothrin            | pH-7.0 Temp-30°C              | Catabolic degradation in case of fenvalerate complete degradation occurs in 6 days | Chen et al., 2011d |
| 32    | Streptomyces sp. HU-S-01                | Cypermethrin                                                                    | pH-7.5 Temp-26–28°C           | 90% cypermethrin degradation in 24 h                                            | Lin et al., 2011 |
| 33    | Streptomyces aureus HP-S-01             | Cypermethrin, deltamethrin, cyfluthrin, bifenthrin, fenpropathrin, and permethrin | pH-7.5–7.8 Temp-27–28°C       | Cyfluthrin, bifenthrin and fenvalerate degraded completely within 5 days       | Chen et al., 2011c, 2012d |
| 34    | Candida pelliculosa ZS-02               | Bifenthrin, cyfluthrin, deltamethrin, fenvalerate, cypermethin, and fenpropathrin | pH-7.2 Temp-32°C              | Only bifenthrin degraded completely within 5 days                                 | Chen et al., 2012c |
| 35, clc | Cladosporium sp. HU                  | Fenvalerate, fenpropathrin, cypermethin, bifenthrin, and permethrin              | pH-7.2 Temp-26°C              | Fenvalerate, fenpropathrin, cypermethin degraded completely within 5 days       | Chen et al., 2011b |
| 36    | Phaenerochete chrysosporium             | Cyfluthrin                                                                      | pH-6.5 Temp-28°C              | Co-metabolic degradation (60%) after 30 days of experiment                      | Sakia and Gopal, 2004 |
| 37    | Bacillus cereus BCC01                  | Beta-cypermethrin, deltamethrin, cypermethin, permethrin, fenvalerate, and cyhalothrin | pH-7.0 Temp-30°C              | Six metabolites were detected after biodegradation: α-hydroxy-3-phenoxybenzenecarboxylate, 3-phenoxybenzaldehyde, methyl-3-phenoxybenzoate, 3,3-dihydroxybenzoic acid, 3,4-dihydroxybenzoic acid, and 3,5-dimethoxyphenol | Hu et al., 2019 |
in the presence of Tween-80 and 3-phenoxybenzoic acid. It was observed that R-enantiomer of both degradation metabolites (Saikia et al., 2005; Birolli et al., 2019). Study was followed by the extraction and identification of major transformation (Qin et al., 2006).

TABLE 3 | Continued

| S. No | Bacteria/Fungi/Insect/Other | Pyrethroid used | Standard condition for growth | Specific statement | References |
|-------|-----------------------------|-----------------|-------------------------------|-------------------|------------|
| 38    | Bacillus subtilis BSF01      | Cypermethrin, deltamethrin, cyhalothrin, and β-cyfluthrin | pH 6.7 Temp 34.5°C | Cis/trans β-cypermethrin, 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane carboxylate, α-hydroxy-3-phenoxybenzoic acid, 3-phenoxybenzaldehyde, 3-phenoxybenzoic acid, and 3,5-dimethoxyphenol | Xiao et al., 2015 |
| 39    | Pseudomonas fulva P31       | D-Phenothrin    | pH 7.3 Temp 29.5°C            | 3-Phenoxybenzaldehyde and 1,2- benzene dicarboxylic butyl dicyclic ester identified as major intermediates | Yang et al., 2018 |
| 40    | Saperdonium mahesswarium    | Beta-cyfluthrin | PDA media Temp 25 ± 2°C       | Dissipation study  | Mukherjee and Mittal, 2007 |
| 41    | Penicillium raistrickii CBMAI 93, Aspergillus sydowii CBMAI 835, Cladosporium sp. CBMAI 1237, Microsphaeropsis sp. CBMAI 1675, Acroemnon sp. CBMAI 1676, Westerdykella sp. CBMAI 1679, and Cladosporium sp. CBMAI 1678 | Esfenvlarerate | pH 7 Temp 32°C | All fungal strains degraded esfenvlarerate with different efficiencies | Birolli et al., 2016a; Zhao et al., 2016 |
| 42    | Aspergillus sp. CBMAI 1829, Acroemnon sp. CBMAI 1676, Microsphaeropsis sp. CBMAI 1675, and Westerdykella sp. CBMAI 1679 | Lambda-cyhalothrin | pH 5.6 Temp 28°C | Enantioselctive degradation of cyhalothrin by the fungal strains | Birolli et al., 2016a; Zhao et al., 2018 |
| 43    | Cunninghamella elegans DSM1908 | Cyhalothrin   | pH 8 Temp 30°C | Characterized metabolites in different culture conditions | Wang et al., 2018 |
| 44    | Phthobacterium genghwersense PG6046 | Cyfluthrin | pH 8 Temp 30°C | Strain degraded permethrin as well as wide variety of pyrethroids | Zhan et al., 2018 |
| 45    | Acinetobacter baumani ZH-14 | Permethrin    | pH 7.0 Temp 30°C | Strain degraded permethrin as well as wide variety of pyrethroids | Zhao et al., 2018 |
| 46    | Raoultella ornitholytica ZK4 | Pyrethroids    | pH 6.5 Temp 37°C | Bacteria was isolated from the soil sediment that degraded different pyrethroids | Zhang et al., 2019 |
| 47    | Klebsiella pneumoniae BPBA052 | 3-Phenoxybenzoic acid | pH 7.7 Temp 35.01°C | Bacterium uses 3-phenoxybenzoic acid as carbon and energy source | Tang et al., 2019 |
| 48    | Rhodopseudomonas sp. PSB07-21 | Fenpropothrin | pH 7.0 Temp 35°C | Phototrophic mode of growth was better as compared to photoautotrophic growth mode | Luo et al., 2019 |

**Phanerochaete chrysospernum**, *Aspergillus terricola*, and *A. niger*. Study was followed by the extraction and identification of major degradation metabolites (Saikia et al., 2005; Birolli et al., 2019).

Radiolabeled (14C) permethrin was used to understand the mechanism of pyrethroid degradation in soil and sediment. It was observed that R-enantiomer of both *trans* and *cis* permethrin mineralized rapidly as compared to S-enantiomer and degradation product of *cis* permethrin was more persistent in the soil environment (Qin and Gan, 2006). Enantioselctive degradation of pyrethroids was also performed at southern California under field condition (soil and sediment) and enantioselctive degradation of *cis*-bifenthrin, cypermethrin and permethrin occurred at half-life of 270–277 days, 52–135 days, and 99–141 days, respectively. Absence of enantioselctivity in biodegradation represents preferential condition for transformation (Qin et al., 2006).

Axenic culture of *Pseudomonas fluorescens*, *B. cereus*, and *Achromobacter* sp. degraded different pyrethroids such as permethrin, fenvalerate, fastac, deltamethrin, and fluvalinate in the presence of Tween-80 and 3-phenoxybenzoic acid was the major metabolite. Permethrin rapidly transformed into 3-phenoxybenzoic acid as compared to other pyrethroids (less than 5 days). In soils, pyrethroids were degraded into a diaryl ether metabolite 3-phenoxybenzoate. Efficiency of *Pseudomonas* strain ET1 in 3-phenoxybenzoate metabolism per cell was calculated as 2.6 ± 0.9 × 10^{-3} gm/cell/hour. Strain *Pseudomonas* ET1 morphologically resembles with *Pseudomonas delafeldii* but differs in 3-phenoxybenzoate degradation (Toppw and Akhtar, 1991). One strain cannot degrade all aromatic compounds due to the structural differences except genetically modified strains, which can be modified to simultaneously degrade different compounds (Gong et al., 2018).

**GENE CLONING AND ENZYMATIC CHARACTERIZATION OF PYRETHROID CARBOXYLESTERASES**

Esterase (carboxyl ester hydrolase) play an important role in initial transformation of parent pyrethroid by attacking ester
bond or cytochrome P-450 dependent monooxygenase on acid or alcohol moieties (Kamita et al., 2016). Many researchers have studied carboxylesterase isolation and purification from B. cereus SM3, Klebsiella sp. ZD112, Sphingobium sp. JJ2, Pseudomonas flourescens SM-3, A. niger ZD11, Ochrobactrum lupini DG-S-01, Streptomyces aureus HP-S-01, Streptomyces sp. HU-S-01, Pseudomonas stutzeri, Microccos sp. CPN 1, Serratia sp. JC1 and Serratia sp. JCN13, Pichia pastoris (Cycoñ and Piotrowska-Seget, 2016; Liu et al., 2017; Tang et al., 2017). Limitations in culture dependent approaches are popularizing the metagenomics tools. Thermostable pyrethroid esterase Sys410 was investigated by metagenomic approach and enzyme contained 280 amino acids having a molecular mass of 30.8 KDa (Fan et al., 2012; Popovic et al., 2017). Cloning was carried out from metagenomic library of soil samples and sequence analysis revealed that 819 bp pye3 gene codes for 273 amino acid protein. Enzyme was further characterized on the basis of enzyme kinetics (K_m and K_cat activity) (Li et al., 2008; Luo et al., 2018).

Reported pyrethroid hydrolases have different pH and molecular weight. Carboxyl esterase enzymes can catabolize wide array of similar ester containing compounds. Because of enantioselectivity, a few esterases exhibit specific or moderate kinetic abilities, which differ from pyrethroid degrading enzymes. Enzyme expression and metabolites production during pyrethroid degradation is differential and can be sequentially up-regulated or down regulated (Bhatt et al., 2019b). Metagenomic based library was useful for the identification and mining of pyrethroid degrading genes, such as pytY and pytZ (O. anthrophi strain YZ1), estP (Klebsiella sp. JD112), pytH (Sphingobium sp. JZ-1), and pye (soil). These genes can be used for isolation and comparison of novel pyrethroid degrading microbial strains.

Bacterial cells produce CO_2 from 3-phenoxybenzoate at K_m (Michaels constant) value of 1.4 ± 0.8 μM that reveals high affinity of bacterial cells to 3-phenoxybenzoate. Metabolism of this pyrethroid intermediate is constitutive rather than catabolite repression. Maloney et al. (1993) were the first to report enzymatic catalysis of pyrethroids in B. cereus strain SM3. Enzyme initially named as permethrinase (61 ± 3 KDa) was finally termed as carboxylesterase after successive studies. Pure culture and cell free extract of B. cereus SM3 successfully hydrolyzed 2nd and 3rd generation pyrethroids. Permethrin was hydrolyzed more rapidly as compared to flumethrin.

Esterase is ranked under subcategory of hydrolases and Esterase is ranked under subcategory of hydrolases and microbial strains. These genes can be used for isolation and comparison of novel pyrethroid degrading microbial strains. Bacterial cells produce CO_2 from 3-phenoxybenzoate at K_m (Michaels constant) value of 1.4 ± 0.8 μM that reveals high affinity of bacterial cells to 3-phenoxybenzoate. Metabolism of this pyrethroid intermediate is constitutive rather than catabolite repression. Maloney et al. (1993) were the first to report enzymatic catalysis of pyrethroids in B. cereus strain SM3. Enzyme initially named as permethrinase (61 ± 3 KDa) was finally termed as carboxylesterase after successive studies. Pure culture and cell free extract of B. cereus SM3 successfully hydrolyzed 2nd and 3rd generation pyrethroids. Permethrin was hydrolyzed more rapidly as compared to flumethrin. Esterase is ranked under subcategory of hydrolases and Esterase is ranked under subcategory of hydrolases and International Union of Biochemistry classified carboxylesterase as subgroup 3.1.1. Active site of this enzyme contains serine residue that plays role in acylation during pyrethroid biodegradation through nucleophilic attack by hydroxyl group (OH). Transformed pyrethroid metabolites are easily excreted in urine because of their better water solubility than original pyrethroids. It justifies high concentrations of carboxylesterase enzyme in mammalian serum and liver (Sogorb and Vilanova, 2002). There are two major categories of carboxylesterases in human body (carboxylesterase-1 and carboxylesterase-2), which can degrade pyrethroids (Wang et al., 2018). Pyrethroid trans forms are more easily degraded by carboxylesterases as compared to cis-isomer. Due to high affinity for Na^+ channels, trans isomers are more toxic to mammalian tissues. Rabbit serum contains higher cypermethrin degradation activity (WHO Task Group on Environmental Health Criteria for Permethrin et al., 1990).

Novel pyrethroid hydrolyzing esterase was reported from Klebsiella sp. strain ZD112. Gene estP contains an open reading frame of 1914 bp, encoding a protein of 637 amino acids and molecular mass of 73 KDa. Purified enzyme can effectively degrade wide variety of ester bond containing pesticides. K_m value for trans and cis permethrin indicated that EstP has higher catalytic power than carboxylesterase enzyme (Wu et al., 2006). A novel pytH esterase gene, coding pyrethroid hydrolyzing carboxylesterase was also reported in Sphingobium sp. strain JZ1 having an open reading frame of 840 bp. Further cloning and purification of this enzyme revealed its molecular weight of about 31 KDa, isoelectric point (pl) of 4.85, and it does not require any cofactor for degrading different pyrethroids (Wang et al., 2009). Degradation of fenpropathrin and fenvalerate in alkaline and acidic soil was observed as enantioselective under aerobic conditions (Li et al., 2009).

Co-expression of two target genes [organophosphate hydrolase (opd) and carboxylesterase B1 (b1)] from Fallovobacterium sp. and Calex pipens is used for degradation of organophosphorous, carbamate, and pyrethroid pesticides. Carboxylesterase 001D that was isolated from Helicoverpa armigera and heterologously expressed in bacteria (E. coli) potentially hydrolysed cypermethrin and fenvalerate (Li et al., 2016). Advanced genetic engineering techniques can enable a single microorganism to degrade multiple pesticides (Lan et al., 2006).

Fungal enzymes have also been reported for pesticide biodegradation. Some fungal enzymes catalyze esterification, hydroxylation, dehydrogenation, and deoxygenation during the degradation process. A. niger YAT carries out etherification reaction during cypermethrin biodegradation. Similar to metabolites of pyrethroid bacterial biodegradation, degrading enzymes of fungal strains have been confirmed as well (Maqbool et al., 2016).

Carboxylesterases of Lucila cuprina and Drosophila melanogaster with mutagenesis in active site were used to study pyrethroid degradation. Carboxylesterase was cloned and expressed by genetic engineering to observe their pyrethroid degradation efficiency (Heidari et al., 2005). Human liver carboxylesterase heE1 and heE2 degraded both type I and type II pyrethroids with stereoselectivity. Trans-isomers were degraded more rapidly by these enzymes as compared to cis-isomer (Table 4). K_m values of enzyme catalysis were lower as compared to pyrethroid compounds (Nishi et al., 2006). Human, rat and rabbit hepatocarboxylesterase also depicted capability to degrade pyrethroids (Ross et al., 2006). Esterases in Heliothis virescens larvae were found to be associated with their resistance to pyrethroids (Huang and Ottea, 2004). Development of next generation sequencing (NGS) methods has enabled us to use genetically engineered microorganism for large-scale pyrethroid hydrolases. Heterologous expression of human and insect pyrethroid hydrolases can be more beneficial for pyrethroid removal from contaminated sites.
| S. No. | Pyrethroid isomer used for study | Microbes/other source | Enzymes | Metabolites | References |
|--------|---------------------------------|-----------------------|----------|-------------|------------|
| 1      | Trans-permethrin, cis-permethrin, and racemic permethrin | Bacillus cereus | Permethrinase with molecular weight 61KDa | B-naphthylacetate was used as substrate, no specific data of pathway reported | Maloney et al., 1993 |
| 2      | Trans-permethrin and cis-permethrin | Lucila cuprina and Drosophila melanogaster Helicoverpa armigera | Carboxylesterase enzyme plays role in pyrethroid hydrolysis | No data | Heidari et al., 2005; Li et al., 2019 |
| 3      | Trans-permethrin, cis-permethrin, cypermethrin, fenvalerate, and deltamethrin | Aspergillus niger ZD11 | Novel pyrethroid hydrolase degrades permethrin and similar compounds | No data | Liang et al., 2005 |
| 4      | Deltamethrin, bifenthrin, cyfluthrin, and l-cyhalothrin | Human liver | hCE-1 and hCE-2 carboxylesterases hydrolyze the pyrethroids and pyrethroid like fluorescent surrogates | No data | Nishi et al., 2006; Wang et al., 2018 |
| 5      | Pyrethroids and organophosphate | Falobacterium sp., Culex pipiens | Co-expression of organophosphate hydrolase and carboxylesterase B1 gene that can degrade many pesticides together | No data | Lan et al., 2006 |
| 6      | Trans and cis-permethrin | Klebsiella sp. ZD112 | Esterase enzyme with molecular weight 73KDa has high efficiency than insect and mammals | p-Nitrophenyl ester was used for enzyme catalysis | Wu et al., 2006 |
| 7      | Permethrin, deltamethrin, cypermethrin, and esterfivaleter | Intestinal, liver and serum carboxylesterase | Hydrolysis of pyrethroids by humans and rat tissues | No data of metabolite | Crow et al., 2007 |
| 8      | Biocresmethrin a-cypermethrin deltamethrin | Hepatic cells | Hepatic carboxylesterase | Hepatic carboxylesterase metabololoe ester containing xenobiotics | Ross et al., 2006 |
| 9      | Cypermethrin | Soil samples | Soil dehydrogenase | Increased dehydrogenase activity when nitrogen was added into cypermethrin | Xie et al., 2008 |
| 10     | Prethroids in soil | Soil samples | Pyrethroid hydrolyzing esterase | The genes coding esterase cloned and expressed from metagenomic library | Li et al., 2008 |
| 11     | Cypermethrin | Bacillus spp. | Esterase and aldehyde dehydrogenase | Upregulation of the enzymes in response to pesticide stress | Bhatt et al., 2019a |
| 12     | Cypermethrin | Bacillus sp. | Esterase, dehydrogenase, and many other proteins and enzymes | Differential expression was observed with cypermethrin in Bacillus sp. | Bhatt et al., 2016a |
| 13     | Permethrin, fenpropathrin, cypermethrin, deltamethrin, cyhalothrin, fenvalerate, and bifenthrin | Sphingobium sp. JZ-1 | Pyrethroid hydrolyzing carboxylesterase | 840bp of gene coding for the enzyme carboxylesterase (molecular mass-31 KDa and PI-4.85) | Wang et al., 2009 |
| 14     | Fenpropathrin, cypermethrin, permethrin, cyhalothrin, deltamethrin, fenvalerate, and bifenthrin | Sphingobium sp. JZ-2 | Pyrethroid hydrolyase | This enzyme was a monomer of a 31KDa with pl-4.85. | Guo et al., 2009 |
| 15     | Cyhalothrin, cypermethrin, and deltamethrin | Soil samples | Thermostable pyrethroid esterase | Isolated and identified from metagenomic approach. Molecular mass of the enzyme was 30.8 KDa | Fan et al., 2012 |
| 16     | Lambda-cyhalothrin, beta-cypermethrin, beta cyfluthrin, deltamethrin, and permethrin | Ochrobactrum anthropi YZ-1 | Novel pyrethroid hydrolyzing carboxylesterase | High enzyme specificity, broad substrate activity makes this enzyme a potential candidate for pyrethroid degradation | Zhai et al., 2012 |
| 17     | Beta-cypermethrin, deltamethrin, cypermethrin, permethrin, fenvalerate, and Cyhalothrin | Bacillus cereus BCC01 | Carboxylesterase EstA | Enzyme showed excellent adaptability under various circumstances | Hu et al., 2019 |
| 18     | Fenpropathrin | Rhodopseudomonas palustris PSB-S | Esterase (Est3385) | The optimal temperature (35°C) and pH (6.0) for esterase | Luo et al., 2018, 2019 |
| 19     | Cypermethrin | Bacillus subtilis | Esterase and laccase | pH-7.0 Temp-32°C | Gangola et al., 2018 |
METABOLIC PATHWAYS OF PYRETHROID BIODEGRADATION

Every living cell that can survive in different environmental conditions must have metabolic pathways, which help to fetch required food (nutrition) from the surroundings (soil, water). Oxygenases (monoxygenases and dioxygenases) play important role in biodegradation of pesticides by common pathways (Fuchs et al., 2011; Birolli et al., 2016b; Bhatt et al., 2019b). Pyrethroid degrading cells (bacteria, fungi and some animal cells) produce metabolites and make them accessory for downstream pathways (Figure 2). Casida identified the pyrethroid breakdown pathway in 1960. Pyrethroids are metabolized in human body via catabolic pathway. Distribution of carboxylesterases in different tissues has been reported and major esterase of intestine is called carboxylesterase 2 (hCE2) that has higher catalytic activity as compared to liver and other tissue cells (Crow et al., 2007).

Hydroxyster metabolites are produced during oxidative pathways whereas oxidative ester cleavage is the minor pathway of some pyrethroids. Isomers of various pyrethroids are affected differently by initial hydrolytic attack. Pyrethroid degradation by hydroxyl group (OH⁻) nucleophilic attack under alkaline conditions is similar to simple aliphatic ester. Chemically, ester or nitrile hydrolysis occurs under alkaline conditions. Ester (bond) hydrolysis produces acid (RCOO⁻) and 3-phenoxybenzaldehyde, via fast decomposition of intermediary compound cyanohydrins. Another parallel hydrolysis pathway produces primary amide that again hydrolyze into RCOO⁻ acid and 3-phenoxybenzaldehyde (Wang et al., 2018). Microbial degradation follows the same pattern and most of the metabolites are common in
all microbial pathways with only a few exceptions. Strains belonging to genera Bacillus, Micrococcus, Staphylococcus aureus, R. ornithinolytica, and Catellibacterium are used for pyrethroid detection (Tallur et al., 2008; Chen et al., 2013b; Zhao et al., 2013; Zhang et al., 2019). Consortium biodegradation pathways of B. cereus ZH3 and S. aureus, and Bacillus licheniformis B1 and Sphingomonas sp. SC-1 have also been reported (Chen et al., 2012b; Liu et al., 2013; Wang et al., 2019). 3-Phenoxybenzaldehyde and 2,2,3,3-tetramethylcyclopropanecarboxylic acid were detected during cypermethrin degradation by Bacillus sp. SG2 and Bacillus subtilis BSF01 (Tallur et al., 2008; Bhatt et al., 2016b). Cyclopropanecarboxylic acid, 2,2-dimethyl-3 (2-methyl-1-propenyl), 2-ethyl, 1,3 dimethyl cyclopent 2-ene carboxylic acid, chrysanthemic acid and allethrolone (2-cyclopenten-1-one-4 hydroxy-3 methyl 2 (2 propenyl) were found as major metabolites of allethrin during degradation by Acidomonas sp. Hydrolysis, oxidation and dehydrogenation reactions mediated allethrin biodegradation (Paingankar et al., 2005; Bhatt et al., 2016b; Birolli et al., 2016b).

Bacillus sp. DG-02 primarily degraded fenpropimorph through carboxylester linkage cleavage to yield 2,2,3,3-tetramethylcyclopropanecarboxylic acid phenyl ester and α-hyrox-3-phenoxybenzeneacetonitrile which transformed into 3- phenoxybenzyaldehyde spontaneously, followed by the oxidation of 3-phenoxybenzaldehyde via diaryl cleavage (Chen et al., 2014). B. thuringiensis ZS-19 transformed cyhalothrin by cleavage of both the ester linkage and diaryl bond to yield six intermediate products including α-hydroxy-3-phenoxy-benzeneacetonitrile, 3-phenoxyphenyl acetonitrile, N-(2-isoproxy-phenyl)-4-phenoxy-benzamide, 3-phenoxybenzaldehyde, 3-phenoxybenzoate, and phenol, respectively (Chen et al., 2015; Wang et al., 2018). Esterase is essential for ester bond cleavage during pyrethroid degradation. Initially carboxylesterase activity forms two metabolites (RS)-α-cyano-3-phenoxybenzyl alcohol and 2,2,3,3-tetramethylcyclopropanecarboxylic acid. Finally 2,2,3,3-tetramethylcyclopropanecarboxylic acid is converted into CO₂ after few steps but (RS)-α-cyano-3-phenoxybenzyl alcohol is transformed into stable 3-phenoxybenzaldehyde (3-PBA). This step is catalyzed by 3-phenoxybenzaldehyde alcohol dehydrogenase that transoms 3-phenoxybenzaldehyde to 3-phenoxybenzoate. Another enzyme phenoxybenzoate 1,2-dioxygenase transforms 3-phenoxybenzoate into 3,4-dihydroxybenzoate (protocatechu) and phenol. Protocatechu and phenols are further converted into primary and secondary metabolites by microorganisms (Wang et al., 2019). Tricarboxylic acid and glycolysis pathways are mainly used by microbes to produce energy from the pyrethroids (Wang et al., 2014; Gajendiran and Abraham, 2018).

**CONCLUSION AND FURTHER ASPECTS**

To feed the world’s rapidly growing population, large-scale use of pesticides in agricultural systems cannot be stopped. Pyrethroid insecticides are used in most of the countries and exhibit comparatively less toxicity than organophosphate and organochlorine pesticides. Recently, toxicity of pyrethroids on marine life (fish), humans and phytotoxicity has been reported. Esterase can degrade ester bond of pyrethroids to produce metabolite 3-penoxbybenzaldehyde. Pyrethroid degrading esterase and 3-phenoxybenzaldehyde can be used as signature molecule for pyrethroid biodegradation. Based on this potential marker, pyrethroids degrading microorganism can be selected in a shorter period. Molecular chronometer based coverage of esterase enzyme is possible with existing data. Consortium based pesticide biodegradation approach is more suitable but it has not been significantly studied for pyrethroid degradation. Previous data favors the development of pyrethroid degradation mechanism through microbial system. In future, omics technologies could potentially be used for pyrethroid degradation and to understand molecular biology, enzyme kinetics, and metabolic pathways. System biology of pyrethroid degradation can be further useful for the investigation of multiple information at one platform.

**AUTHOR CONTRIBUTIONS**

SC conceived the idea. PB wrote the manuscript and prepared the figures and tables. YH, HZ, and SC revised the manuscript. All authors approved the final manuscript for publication.
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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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