# A Review of Deadly Herbicide: Paraquat

***Subita Choudhary**
****Dr. Preeti Gupta**
*****Dr. Priyanka Mathur**

**Abstract**

Agriculture is the practice of cultivating plants and livestock in order to provide facilities to the human beings. It forms the backbone of any civilization. In ancient times, people used organic manures, to increase agricultural productivity, later people have started using pesticides. The production of agricultural products has been enhanced according to the growing population's demand with the use of chemicals but abundant use of chemical fertilizers and pesticides have made our soil sick. Pesticide contamination cause significant risks to the environment and to non-target organisms including beneficial soil microorganisms, insects, plants, fish, and birds. Herbicides also cause potential harm to the environment. Among the available pesticides, paraquat (PQ) is one of the common herbicides used in agriculture Paraquat is a bipyridilium herbicide used widely in our country and is a highly toxic compound. Exposure to this herbicide leads to progressive and fatal pulmonary hemorrhage, collapse, and edema in animals. It induces degenerative lesions in the lung and gastrointestinal, renal, and central nervous system-related clinical signs in animals as well as humans. Therefore, quick, selective, and efficient detection of PQ in soil, water, and ago-products is very much essential to prevent its hazardous effects. Therefore, in this review paper, we focused on Paraquat an herbicide in order to have better understanding on the fate of this pesticide in the environment. Hence, their physical and chemical properties are reviewed based on available references. In this paper, we also discussed the toxicity effects of Paraquat on the environment. This review also described about the treatment technologies for Paraquat exposure.

**Key words**: Mortality, environment, paraquat poisoning, health,lungs,toxic,skin.

**INTRODUCTION**

Application of herbicides is one of the general agricultural practices for maintaining high productivity and plant's growth. Herbicides are commonly used to kill or remove any type of pests. Other chemicals that are categorized as pesticides are fungicides, insecticides, rodenticides, nematicides, termiticides and molluscicides. Herbicide is defined as a group of chemicals known as plant protection products (PPP) that used to kill or repel any type of weedy plant in order to protect the crop [1]. Herbicides help to manage weed problem effectively and economically. Herbicides can

be classified according to its mode and site of action into four major categories, namely insecticides, fungicides, herbicides and rodenticides in addition to miscellaneous substances like nematicides, plant growth regulators, pheromones etc. [2]. They can be further divided based on chemistry, target, mode of action. (3). Herbicides are commonly formulated in two forms including sprayed liquid and dry solids. Paraquat, a toxic bipyridyl herbicide, bright green corrosive liquid with pungent smell. Its herbicidal properties were discovered in 1955 by British ICI crop production and has been legally used in over 130 countries since 1962 (4-7). Paraquat (1,1′-dimethyl-4,4′-bipyridinium) is a fast-acting, on-selective, contact herbicide that finds widespread application in the fields of agriculture and horticulture all over the world. It is helpful in farming by the way of clearing pastures, weed control both in vegetable crops as well as plantation crops. (8-10). It destroys plant cells via preventing the electron transfer during photosynthesis. It is also used as a desiccant during pre-harvesting and for destroying Marijuana plants (9). But despite its advantages it is a toxicological Class 1 substance (11) and is associated with several adverse effects. When exposed to paraquat, both humans and other animals run the danger of experiencing severe poisoning. Ingestion is the most common way for individuals to become poisoned, and this may happen either on purpose or unintentionally. Additionally, incidents of poisoning brought on by other methods, such as contact with the skin or mucous membranes, injection, or inhalation, have also occurred. It is claimed that a dosage of 30 milligrams per kilogram of body weight, which is equivalent to three to six grams of paraquat ion or ten to twenty milliliters of a solution containing twenty percent of paraquat, is sufficient to induce death in an adult. Either deliberate or accidental, uptake of Paraquat severely affects a wide variety of organs and systems in the human body, such as the heart, kidneys, liver, adrenal glands, respiratory and central nervous system, muscles, and spleen (12-14). Further, Paraquat is reported as one of the main causes of Parkinsons disease, Alzheimer's disease and dementia (15-17). Amongst the available herbicides, the highest mortality and morbidity rate is associated with Paraquat (18). The mortality rate is relatively high, ranging from 50% to 90%; which can reach up to 100% in situations involving purposeful self-poisoning using concentrated formulations of the chemical. The high mortality rate is due to inherent toxicity of paraquat and the lack of a viable antidote. The treatment consists of providing supportive care, in combination with immune-modulation therapy, antioxidant therapy, hemoperfusion, and hemodialysis. Because of the high degree of toxicity that it possesses, the usage of paraquat has been severely restricted in a number of places around the world.

Property of Paraquat: Paraquat or *N*,*N*′-dimethyl-4,4′-bipyridinium dichloride also known as methyl viologen, is an organic compound with the chemical formula $[(C_6H_7N)_2]Cl_2$. It is classified as a viologen, a family of redox-active heterocycles of similar structure.[19]

This salt is one of the most widely used herbicides. It is quick-acting and non-selective, killing green plant tissue on contact. It is also toxic (lethal) to human beings and animals due to its redox activity, which produces superoxide anions. Paraquat (PQ) is classified in WHO class II (Moderately Hazardous) for acute toxicity (WHO 2005).

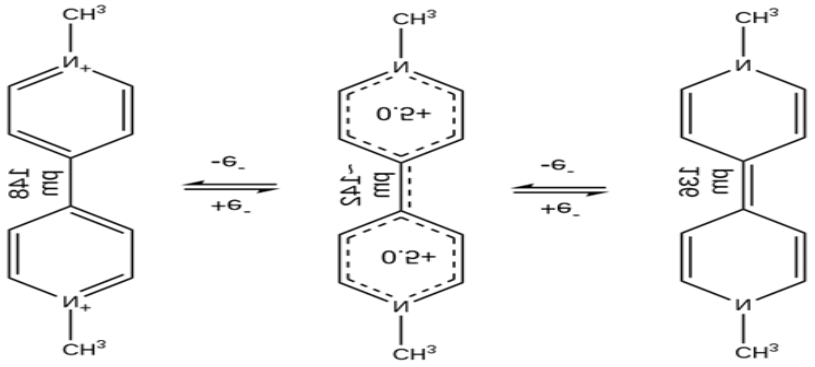

**Fig1: Paraquat, the diction on the left, functions as an electron acceptor, disrupting respiration in plants by forming the mono cation at the center.[20]**

The poisonous nature of PQ is due to the formation of the free radical ($PQ^{+}$.) via the reduction of its bivalent cation ($PQ^{+2}$). The free radical will react with oxygen to produce super oxide radical ($O_2^{-}$), hydrogen peroxide (H2O2) and hydroxyl radical. Since, they are highly reactive and unstable, they will lead to lesions in cell membrane, protein, and Deoxyribonucleic acid (DNA) [21,22]. The major drawback of PQ is that it is highly resistive towards microbial action (non-biodegradable) and sunlight which makes the molecule persistent in soil. This leads to several environmental issues [23]. On the contrary, it is freely soluble in water [24]. Therefore, water is one of the carriers of PQ to human beings.

Paraquat is sold under various trade names, the main product is Gramoxone, marketed by Syngenta. Other bipyridinium products are mixtures of paraquat, diquat or other herbicides. Granular (solid) formulations are used less frequently [25].

Products based on paraquat normally use the dichloride salt of paraquat cation (a quaternary ammonium compound). It is the cation that has the herbicidal and toxic effects [26].

The liquid concentrates of paraquat contain 25% to 44% of the active substance, and also solvent (water) and wetting agents or adjuvants [27].

**Toxicity of Paraquat**

Among 40 herbicides commonly used on field crops in Australia, paraquat has the highest acute toxicity (based on the acute oral LD50 in rats) (28). Risk assessment of pesticides based on the environmental impact quotient (EIQ) ranked paraquat as the seventh most hazardous pesticide (besides six organophosphates) among 85 pesticides and as second most hazardous (out of 38) due to its ecological impacts and effects on farmworkers. More recently, paraquat was among the 15 most hazardous herbicides out of 129 (29,30).

While paraquat is not volatile as a solid, the drift of spray solutions could potentially be a problem for animals due to its toxicity (31,32). In wildlife, the sub-lethal effects from exposure to lower doses of

pesticides can be important, as altered behavior as a consequence of low-level pesticide exposure may be almost as fatal in nature as an acute lethal dose (33).

Paraquat is moderately hazardous to bird species based on ratings by the WHO Ranking of Acute Hazard (34). An acute LD50 of 35 mg/kg b. w. for birds signifies that paraquat can be highly hazardous to some bird species (35,36). On embryotoxicity to birds' eggs it was observed that the exposure of eggs from chicken and Japanese quail to a spray solution of 0.4% caused mortality and defects of the lung in young birds. Immersion in a 0.05% solution led to a decrease in hatching success. Paraquat appeared to be the most highly embryotoxic and teratogenic (causing malformations of an embryo or foetus) herbicide. The lethal concentration (LC50) for immersion of mallard eggs in a solution was 0.18% (37).

To mammals, paraquat is highly to moderately hazardous, based on WHO ranking and LD50 values ranging from 22 to 157 mg/kg b. w. (38). In the EU review for authorizing paraquat, it was found that hares died and small mammals were affected, but the extent could not be estimated (39). The principal target organs for paraquat poisoning are the lungs and kidneys. Paraquat concentrates in alveolar type I and type II cells as it is similar to polyamines which are taken up by the alveolar cells. Paraquat is also actively secreted by the kidney and is accumulated in higher concentrations in the proximal tubular epithelial cells. Paraquat causes redox cycling and production of toxic reactive oxygen species after accumulation in the alveoli and nephrons. This oxidative stress leads to pulmonary damage (alveolitis and fibrosis).[40] At moderate doses, the initial lung injury develops into pulmonary fibrosis. This is due to loss of pulmonary architecture caused by excessive proliferation and differentiation of fibroblasts. [40]. Direct injury to the lung is caused by the exposure to respirable size droplets of Paraquat. [41]. Also, irritant effects on the upper airway are common [42].

A WHO study identified paraquat as a pesticide, which needs further examination with priority due to its wide use and numerous severe and fatal poisonings [43]. While many cases were accidental, acute poisoning with paraquat is characterized by delayed pulmonary fibrosis, and it could not be excluded that chronic exposure to low (non-fatal) doses could have an influence on the lung function [43].

A study was conducted with 338 workers from plantations in Costa Rica. It was reported that paraquat exposure was associated with small but statistically significant changes in gas exchange in the lung. An increased relative risk for chronic cough of 1.8 and an increased relative risk for shortness of breath accompanied by wheeze of 2.3 was associated with the cumulative exposure to paraquat [44]. It was associated with an increase in the ventilatory equivalent for $CO_2$ and with oxygen desaturation (5% or more) with a relative risk of 1.7 [44]. These findings suggest that exposure to paraquat may be associated with sub-clinical abnormalities in gas exchange of the lung [44 & 45].

It was reported that non-asthmatic Farmers in the US who used paraquat, had over a threefold relative risk for wheeze (whistling in the chest). And if asthmatics were included, the risk significantly increased by 27%, [46]. When the trousers of nine workers in South African vineyards were soaked with paraquat spray, they developed redness and burning of legs. Out of these nine

workers, in six workers, diffusion of carbon monoxide in the lung was reduced, while two of the workers developed chronic coughing and expectoration, and one had difficulty in breathing [47].

In human lymphocytes and lung cells of hamsters, positive test results for mutagenicity were found [48]. The evidences show that the genotoxicity of paraquat is because of the reactive oxygen species produced by it. In animal studies, however, genotoxic effects of paraquat have been observed even following the absorption through skin [49].

A slight but significant increases in the frequency of sister-chromatid exchange, caused by paraquat, was observed in human lymphocytes (White blood cells)[50]. This indicates damage to chromosomes (structure carrying genetic information) leading to an increased susceptibility to malignant tumors [51].

Paraquat has been rated as "Unlikely to be carcinogenic" (category E) by the US Environmental Protection Agency [52a&b]. It had previously been rated as "possible carcinogen" (category C) based on the induction of squamous cell carcinoma (one of the three main types of skin cancer) in rats [53] The incidence of skin lesions was increased among factory workers who had manufactured 4,4'-bipyridyl (a precursor used in paraquat production and these progressed to Bowen's disease (precancerosis of the skin) and, in fewer cases, to squamous cell carcinoma. It appears that exposure to sunlight was a cofactor and production has been modified in the meantime [42].

The male agricultural workers exposed to paraquat developed increased risk for malignant melanoma (Skin cancer). In eight out of ten cases melanoma were situated on the lower limbs, where exposure to sunlight is less plausible than skin contact with pesticides - DBCP and paraquat in particular [54]. Total pesticide use (indexed per agricultural labourer) on coffee and banana was associated with increases in the relative risk for skin melanoma, lung and penile cancer in male workers. Paraquat is used extensively on banana and coffee. The increase could not be explained by smoking [55].

Evidences suggest that paraquat has chronic effects on the brain. In a study in Taiwan, it was reported that farmers using paraquat had greater risk of Parkinsons diseaseas compared to those who were using other herbicides/pesticides. [56]. Another study falso supported the above reports that paraquat exposure was associated with Parkinson's [57].

A study on factors influencing Parkinson's disease reported relative risks of 1.41 and 1.67 again, not statistically significant - for herbicide and paraquat exposure, respectively [58].

Parkinsonism is caused due to insufficient levels of dopamine in the brain. Paraquat was found to be toxic to dopamine-producing nerve cells in animal studies [59, 60, 61, 62, 63 &64]. It appears that paraquat produces synergistic effects when used together with maneb, a fungicide [65]. Acute and persistent parkinsonism has followed exposure to diquat [66].

Renal tubular necrosis is caused by Paraquat because of vacuolation in the cells of the proximal convoluted tubules.[67]

Corrosion of the gastrointestinal tract is caused by Paraquat, as it is a caustic herbicide. Mucosal

lesions of the mouth and the tongue are called “paraquat tongue”. These lesions appear within the first few days and later become ulcerated with bleeding. Pain and dysphagia are caused in Esophageal ulceration which later on progresses to perforation, mediastinitis, and pneumomediastinum. [68]. The stomach absorbs only 20% of the ingested Paraquat and then it is distributed in the organs like lungs, kidney, liver, and muscle. Paraquat is not metabolized by the body and is excreted unchanged by the kidney.

Other modes of exposure to paraquat include contact through skin/eyes and inhalation. Local effects include skin irritation, blistering, and full-thickness burns. Inhalational exposure can occur due to spraying of paraquat as fine mist (spray droplets as per recommendation are too large to be inhaled). Spraying of paraquat leads to inhalation exposure and it causes local irritation but rarely results in important systemic absorption.[67]

The clinical features of paraquat poisoning are dose-dependent and are classified into the mild, moderate, and fulminant poisoning. Table 1 shows the classification of paraquat poisoning based on the severity.[67]

**Table 1: Classification of severity of paraquat poisoning**

| **Mild/subacute poisoning** | **Moderate/severe acute poisoning** | **Fulminant/hyperacute poisoning** |
|---|---|---|
| <20 mg/kg body weight | 20–40 mg/kg body weight | >40 mg/kg body weight |
| Asymptomatic | Immediate—vomiting | Immediate—vomiting |
| Mild gastrointestinal symptoms | Hours—diarrhea, abdominal pain, oral ulcers | Hour to days—diarrhea, abdominal pain, renal failure, hepatic impairment, GI ulceration, pancreatitis, myocarditis, refractory hypotension/coma |
| Minimal pulmonary/renal involvement | Days—renal failure, hepatic impairment, hypotension/tachycardia<br>Weeks—alveolitis, pulmonary fibrosis | Survival difficult |
| Complete recovery | Death within 2–3 weeks (deteriorating lung function) | Death within 1–4 days (multiorgan failure) |

**Conclusion**

Paraquat, known for its effectiveness in weed control, poses substantial dangers to human health, including acute poisoning and potential links to chronic conditions like Parkinson's disease. In conclusion, the review of Paraquat underscores its profound toxicity and harmful effects on both human health and the environment Despite regulatory measures in various countries, its accessibility and misuse continue to result in fatalities and serious health complications. The review emphasizes the urgent need for stricter regulations, increased public awareness, and sustainable alternatives to mitigate the adverse effects of Paraquat on both human health and the environment. Moving forward, it is imperative to prioritize stricter regulations, enhanced safety protocols, and the development of safer alternatives to Paraquat to safeguard human health and environmental integrity. Additionally, increasing public awareness about the dangers associated with Paraquat and promoting sustainable agricultural practices are crucial steps towards reducing its widespread use and minimizing its adverse impacts.

***Department of Botany**
**University of Rajasthan**
**Jaipur (Raj.)**

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