

The promising protective effect of Locust beans against hepatotoxicity of Dioxins and dioxin-like compounds

Ftun Khalid Dahy*, Esraa Hagag Ahmed, and Ebtesam Samir Kotb

Chemistry Department, Biochemistry Branch, Faculty of Science, Suez University, Suez, 43518, Egypt

ARTICLE INFO

Article history:

Received 1 May 2023

Received in revised form 13 July 2023

Accepted 7 August 2023

Available online 15 August 2023

Keywords

Dioxins,
Hepatotoxicity,
Antioxidants,
Locust beans.

ABSTRACT

In recent years, waste generation tends to increase in quantity as the population and living circumstances increase. Uncontrolled waste incinerators (solid waste and hospital waste) are frequently the worst offenders when it comes to dioxin leakage into the environment because of incomplete burning. Dioxins are a type of persistent organic pollutants (POPs). Dioxins are primarily by-products of industrial operations such as smelting, chlorine bleaching of paper pulp, and the production of various herbicides and insecticides, although they can also be produced by natural events like volcanic eruptions and forest fires. Dioxins have an impact on several organs and systems. Dioxins removal from the ecosystem is challenging due to their persistence, resistance to biodegradation, and pervasiveness, and now dioxins toxicity is recognized as a problem that needs to be addressed right away. Nowadays, increasing attention has been paid to natural antioxidant compounds with fewer detrimental effects such as locust beans to reduce the toxicity of different chemicals. Locust bean seeds mostly include galactomannans and flavonoids which are antioxidants and are essential in protecting cells from free radicals, which may also be beneficial in liver disease, cancer, and other diseases. Locust beans also may increase the removal of dioxin from the body. Hence, in the current review, we shed light on the promising protective effect of Locust beans against the hepatotoxicity of dioxins and dioxin-like compounds [1].

1. Introduction

Industrial activities frequently release several pollutants (aliphatic & aromatic hydrocarbons, pesticides, herbicides, and chlorinated aromatics) into the environment as products and undesirable by-products, where they accumulate as extremely toxic persistent pollutants. Among this group of chemicals are dioxins. Dioxins and dioxin-like compounds (DLC) are highly persistent organic pollutants (POPs) that are extremely poisonous and highly resistant to chemical, biological, and photolytic destruction [2]. Polychlorinated dibenzofurans (PCDFs), polychlorinated dibenzodioxins (PCDDs), and dioxin-like polychlorinated biphenyl (DL-PCBs) are the three main categories under which POPs are categorized. POPs are produced by the incomplete combustion of plastics, pigments, and paints, particularly polyvinyl chloride (PVC), as well as incineration of hazardous medical municipal, and other waste materials, also from sewage sludge [3].

It can also be generated as a byproduct of industrial processes like paper and pulp manufacture, the chemical industry, and powder boilers, however, it is most frequently found in the metal and chemical sectors. Furthermore, they could be caused by natural disasters like volcanic eruptions and forest fires [3]. Dioxins are a type of pollutant that belongs to the so-called “dirty dozen” of hazardous substances, also called persistent organic pollutants [3]. POPs are an issue that affects both aquatic and terrestrial creatures including humans. They can lead to anomalies in particular species, such as fish, birds, and mammals [4]. Dioxins have high lipophilicity and hydrophobicity, and they become more soluble in organic solvents as the chlorine concentration rises. Since they are not soluble in water, the majority of them adhere tenaciously to anything with a high organic content in aquatic habitats, especially microscopic plants, and animals, which are eaten by larger creatures [5]. Dioxins are a long-lasting contaminant once they enter the body because of their stability and capacity to penetrate fatty tissue, where they are retained. They have a 7 to 11-year half-life in the body. The amount of dioxins in an animal increases with its position in the food chain. The potential for dioxins to be extremely harmful makes them a concern. They have an impact on many organs and systems, according to studies and experiments [6].

Locust bean mostly includes galactomannans and flavonoids which are antioxidants and are essential in

* Corresponding author at Suez University

E-mail addresses: ftunkhaled@gmail.com (Ftun Khalid Dahy)

protecting cells from free radicals, which may also be beneficial in liver disease, cancer, and other diseases [7], [8]. Locust beans also may increase the removal of dioxin from the body. Hence, in the current review, we shed light on the promising protective effect of locust beans against the hepatotoxicity of dioxins and dioxin-like compounds.

Dioxin history:

During the 20th century, many mishaps using dioxin occurred. The American Monsanto chemical company disaster is among the most well-known. The firm produced industrial chemicals, Dioxin, and dioxin-like substance concentrations that were high in PCBs, insecticides, herbicides, and other chemicals. Lysol, a common household cleaner, and Agent Orange, a well-known defoliant, both produced by Monsanto, were among the many goods that were tainted with dioxins [9]. While not being the only producer of Agent Orange, Monsanto Company's products included the highest amounts of dioxins. Between 1961 and 1971, the US Army deployed Agent Orange, a herbicide and defoliant, to eliminate the enemy's food supply and cover in the enemy's forest. It was the herbicide that the US Army program utilized the most. The amount of herbicide sprayed over Cambodia, Thailand, Laos, and Vietnam is estimated to be up to 72 million liters. Vietnam War veterans who took large dosages of Agent Orange experienced severe effects. Veterans from the US filed multiple cases against the businesses that made Agent Orange in American courts [9], [10].

At Times Beach in Missouri, the United States, another accident happened in the 1970s. Dioxins were heavily present in the oil that was used to mist roadways in order to manage dust. Once the contamination was discovered

by the Environmental Protection Agency (EPA), the US government issued an order for the village's evacuation and cleanup of the region. More than 265,000 tons of dioxin-contaminated soil were burned during the operation, and the leftover ash was buried nearby. Now, that location serves as a state park honoring Route 66 [10], [11]. In 1976, a (2,4,5-trichlorophenol) reactor exploded in Seveso, Italy. Significant levels of 2,3,7,8-TCDD were exposed to thousands of people [12].

A significant problem arose in Belgium in 1999 when 500 kg of feed that was contaminated with 50 kg of PCBs and 1 g of dioxin were transported to animal farms, primarily in Belgium but also in the cities of the Netherlands, France, and Germany. The first indications of toxicity started to show up in poultry farms after a few months. Belgium experienced a health catastrophe as a result of toxicological testing. All poultry and its derivatives were immediately pulled off the market, and the majority of them were incinerated. According to health studies, those who ate contaminated food had a threefold increase in body weight. Yet, there were no immediate health impacts noted [11].

The most well-known incident was the effect of dioxin on Ukrainian President Victor Yushchenko in 2004, (Fig. 1). The amount of lipid weight in his blood serum was 108,000 pg g⁻¹, which is 50,000 times more than the level of the ordinary individual. At the Geneva University Hospital in Switzerland, high-resolution mass spectrometry and gas chromatography were used to track Viktor Yushchenko's 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) levels. Mr. Yushchenko experienced serious health issues and the characteristic chloracne facial disfiguration [5].



Figure (1): The effect of dioxin on Ukrainian President Victor Yushchenko [13].

Structure of dioxins:

Dioxins are a class of organic chemicals that have undergone chlorination. This term is frequently used to describe PCDDs and PCDFs. Depending on the quantity and location of chlorine atoms in their structural makeup, some of them exhibit harmful properties. PCDDs and PCDFs arise from two benzene rings connected by an

oxygen atom. Two oxygen bridges connect two rings in PCDDs while a carbon bond and one oxygen bridge do the same in PCDFs. There are eight distinct locations on the molecule where chlorine atoms can be bonded, listed from 1 to 8. Of the 210 dioxin and dibenzofuran congeners, only 17 are toxic [5]. The most well-known and harmful dioxin is 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD), a molecule with four chlorine elements, (Fig. 2). It has the

greatest potential for toxicity (toxic equivalent factor), which is defined in relation to the toxic potentials of the other 16 PCDDs and PCDFs [6].

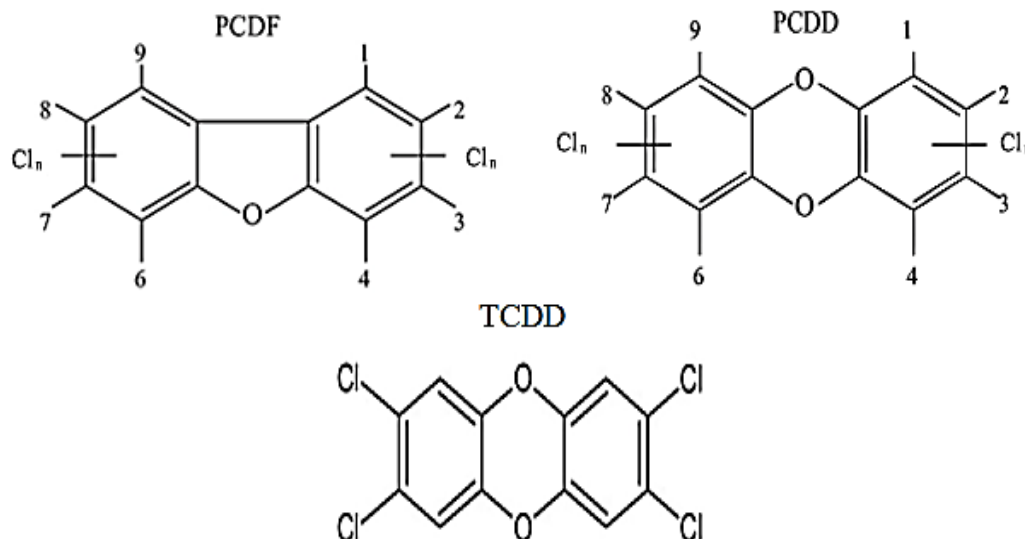


Figure (2): Structures of PCDFs, PCDDs, and TCDD [15].

Dioxins and their related chemicals, such as PBDD, PCDF, PCDF, and PBB, are a class of halogenated aromatic hydrocarbons (HAHs). Additionally, they can be generated commercially for use in lubricating oils, and capacitor fluids as well as electrical transformer fluids [16]. Polychlorinated dibenzofurans (PCDF), polychlorinated dibenzodioxins (PCDD), and dioxin-like polychlorinated biphenyl (DL-PCBs) are the three main categories under which POPs are categorized [17]. Up to 8 chlorine atoms may be connected to the carbon atoms at positions 1:4 and 6:9 in PCDD and PCDF, respectively [14]. Congener is the name for each compound that results from this. The number and placement of chlorine atoms around the aromatic ring help identify and distinguish each congener. 75 PCDD congeners and 135 PCDF congeners are also present. A homologous congener has the same number of chlorine atoms as another congener [18], (Table 1). TCDD is the most prevalent PCDD/ Fs. Congeners with 1, 2, or 3 chlorine atoms are thought to have no significant toxicological side effects, according to certain studies [19].

Exposure to dioxins:

Humans are exposed to PCDFs, PCDDs, and PCBs through environmental, occupational contamination, and accidental exposure [2].

a. Environmental exposure

Dioxins are contaminated in food, particularly animal products. The toxicity levels of dioxins are reported as international toxic equivalents (TEQs) [22], (Fig. 3). Dioxins build up in the food chain, because of their absorption and storage in fatty tissue [23]. This develops when pollutants from various sources (such as the chemicals industry and garbage incineration) are accumulated on cropland and waterbodies. Additional sources include improperly applied pasture flooding, waste effluents, sewage sludge, and particular food industries and processing. Contaminated

feed for chicken, cattle, and farmed fish are also other sources [24].

b. Accidental exposure

Fires in electrical equipment containing PCBs are the most frequent instances of local populations being accidentally exposed to PCDFs, PCDDs, and PCBs. The (2,3,7,8-TCDD or dioxin) serum levels varied up to 56000 pg/g lipid at Seveso (a 1976 chemical factory explosion near Seveso, Italy exposed residents to high amounts of TCDD or dioxin), with median levels of 450 pg/g lipid for Zone A and 126 pg/g lipid for Zone B [26]. Accidental food contamination might also result in high exposure, Where dioxin is an effective endocrine disruptor and a recognized human carcinogen. It has a lengthy half-life in people and is extremely lipophilic. Also, the Yu-Cheng (Taiwan) and Yusho (Japan) food poisonings are two well-known cases of edible oil contamination. The average intake of PCBs, PCDFs, and polychlorinated quarter phenyls (PCQs) through ingestion of contaminated Kanemi rice oil for a group of Yusho patients was calculated to be 154000 pg I-TEQ/kg bw/day, which is five times greater than the reported background ingestion average in numerous nations [27].

C. Occupational exposure

Further human exposure may come from industrial processes that unintentionally produce 2,3,7,8-TCDD and similar compounds, such as those that burn garbage or create certain insecticides or chemicals. The median 2,3,7,8-TCDD levels in the blood of highly exposed workers ranged from 140 to 2000 pg/g lipid historically, according to extrapolation back to the time of last exposures, despite the fact that many industrial sources of 2,3,7,8-TCDD and related compounds have been identified and worker exposure has been reduced or eliminated. The blood levels

found in the general population were measured at levels 1-3 orders of magnitude lower than these estimations. In contrast to background exposure, body burdens brought on by occupational or accidental exposure typically only

contain a small number of congeners and exhibit distinct congener patterns. Due to direct exposure, this has happened [28].

Table 1: Congeners of PCDDs and PCDFs [20], [21].

Abbreviation	Homolog name	No. of possible congeners	No. of possible 2,3,7,8-chlorinated congeners
MCDD	Monochlorodibenzo-p-dioxin	2	0
DICDD	Dichlorodibenzo-p-dioxin	10	0
TrCDD	Trichlorodibenzo-p-dioxin	14	0
TCDD	Tetrachlorodibenzo-p-dioxin	22	1
PeCDD	Pentachlorodibenzo-p-dioxin	14	1
HCDD	Hexachlorodibenzo-p-dioxin	10	3
HpCDD	Heptachlorodibenzo-p-dioxin	2	1
OCDD	Octachlorodibenzo-p-dioxin	1	1
MCDF	Monochlorodibenzofuran	4	0
DICDF	Dichlorodibenzofuran	16	0
TrCDF	Trichlorodibenzofuran	28	0
TCDF	Tetrachlorodibenzofuran	38	1
PeCDF	Pentachlorodibenzofuran	28	2
HxCDF	Hexachlorodibenzofuran	16	4
HpCDF	Heptachlorodibenzofuran	4	2
OCDF	Octachlorodibenzofuran	1	1

Risk of exposure to dioxins:

Dioxin exposure can have a variety of hazardous effects on both humans and animals, including:

- Cancer.
- Infertility and reproductive problems.
- Skin blemishes, rashes, and skin discoloration.
- Endometriosis.
- Lung problems.
- Diabetes mellitus.
- Learning disabilities.
- Mild liver damage.

- Defects in the hormonal, nervous, and reproductive systems [29].

In the 1930s, chemical workers exhibited signs that dioxins and dioxin-like compounds made up a major health risk to them as they suffered skin rashes, chloracne, a chronic skin condition that causes skin lesions, and a variety of other symptoms [8]. Moreover, dioxin exposure may have an impact on the skin in different places, In Japan, it resulted in symptoms such as numbness in the limb, pigmentation of the skin, nails, and conjunctivas, as well as acne-like outbreaks on the skin and nails. In 1979, Taiwan saw a similar "oil illness" outbreak that included arthralgia, oral pigmentation, acneiform eruption, and numbness in the hands and legs. In southern Vietnam,

there was direct human exposure to dioxin [30]. According to estimates, the US military sprayed 80 million liters of defoliant herbicides (Agent Orange, a 50:50 mixture of 2,4,5-T and 2,4-D) over a significant region of southern Vietnam's woods and crops from 1962 to 1971, resulting in the contamination of 160 600 kg of dioxin. The defoliant

contained TCDD, a highly toxic type of dioxin known to have harmful effects on human health. Dioxin may have negative effects on the entire body as well as specific impacts on the neurological system, immunological system, hepatotoxicity, metabolism, and enzymatic processes [9].

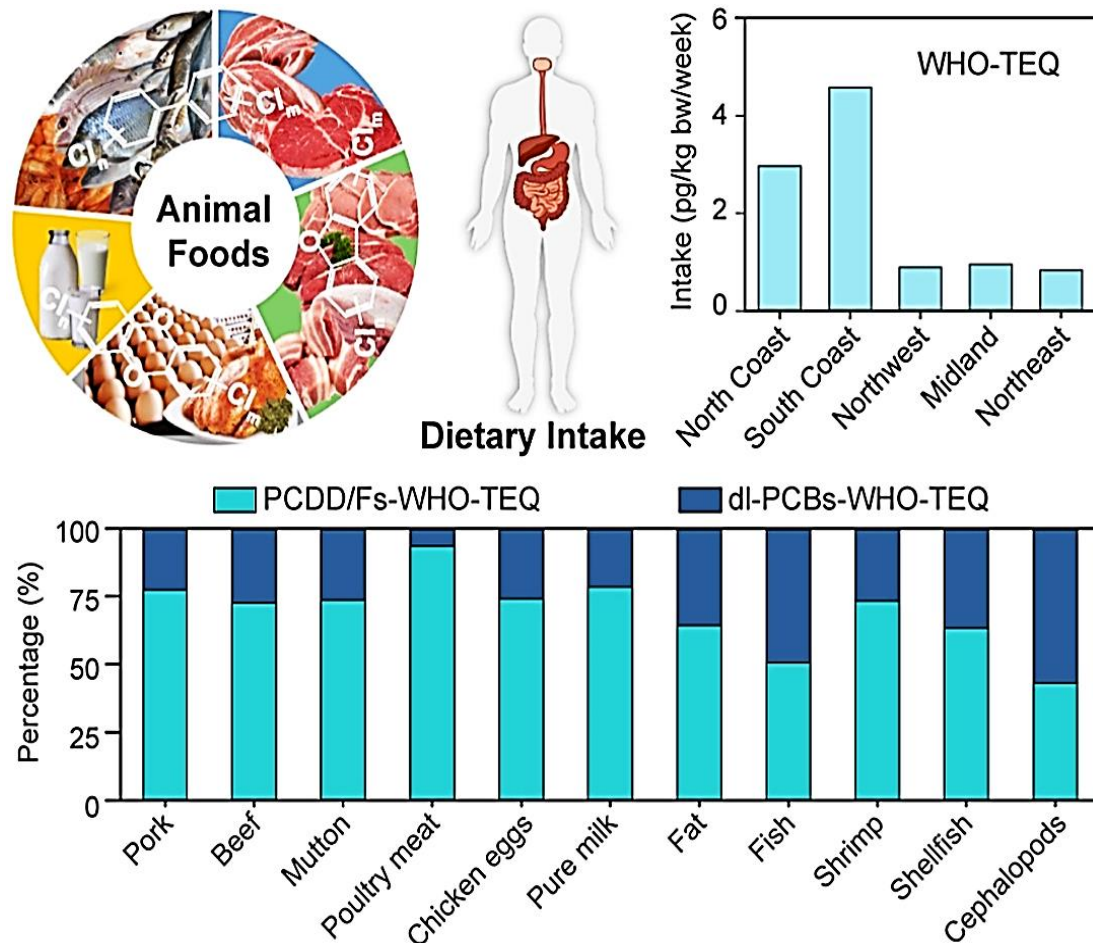


Figure (3): Percentage of dioxins in dietary intake [25].

Mechanism of dioxin action:

People in both industrialized and developing countries are frequently exposed to organic pollutants that are present in the air or food and numerous incidents, like the one at Seveso, have led to excessive exposure to such molecules [11], [31]. These pollutants include POPs, which are known for having a lengthy half-life and are stored in the adipose tissue of exposed species. The most harmful member of the dioxin family and one of the most effective aryl hydrocarbon receptor (AhR) activators is the 2,3,7,8-TCDD [32]. Dioxins are carried by plasma lipids from the external environment to adipose tissue and the liver, where TCDD binds to AhR in hepatocyte cytosol. When the active dioxin-receptor complex moves into the cell nucleus and binds to the DNA's dioxin response sites, a signal is conveyed that the gene for the cytochrome p450, p448 "aryl hydrocarbon hydroxylase-AHH" needs to be transcribed. Hepatocyte endoplasmic reticulum is where

AHH, the enzyme that converts dioxin, is found in the highest concentration. In the initial phase, monooxygenase breaks down dioxin hydrolytically. The products of this reaction are then conjugated with active-form glucuronic acid/glutathione molecules and are then expelled from the body with bile or urea [18]. Dioxin is metabolized more slowly when compared to other high-affinity AhR agonists such as 6-formyl indol [3,2-b] carbazole (FICZ). It should be emphasized that while AhR activation by FICZ "through interleukin-22 (IL-22)" inhibited the experimental colitis and inflammation in the gastrointestinal tract, their activity is considered longer-lasting and not self-limited [33].

Dioxins and liver damage:

It is believed that the liver is the main site of toxicity for dioxin and is the key organ for TCDD poisoning, (Fig. 4). Environmental toxins may speed up the development of fibrosis in persons with non-alcoholic fatty liver disease (NAFLD), who are more susceptible to have chronic liver

diseases, according to emerging epidemiological research [11], [31]. TCDD interacts with AhR in hepatocyte cytosol after dioxins are transported by plasma lipids from the external environment to adipose tissue and the liver. Following ligand binding, the AhR transcriptionally activates the transport and enzymatic machinery necessary for the detoxification pathways that lead to the removal of xenobiotics. Yet, these activities also have the potential to be harmful because of unfavorable chemical interactions like oxidative stress. Environmental factors may begin the

progression of NAFLD to nonalcoholic steatohepatitis (NASH) by increased formation of reactive oxygen and/or nitrogen species, according to certain theories [32]. Along with its role in detoxification, the AhR has been found to affect lipid metabolism and contribute to the development of hepatic steatosis. By raising free fatty acid (FA) absorption and reducing FA-oxidation, de novo lipogenesis, and the generation of very low-density lipoprotein (VLDL), TCDD induces fatty liver in rodents through an AhR-dependent process [32], [33].

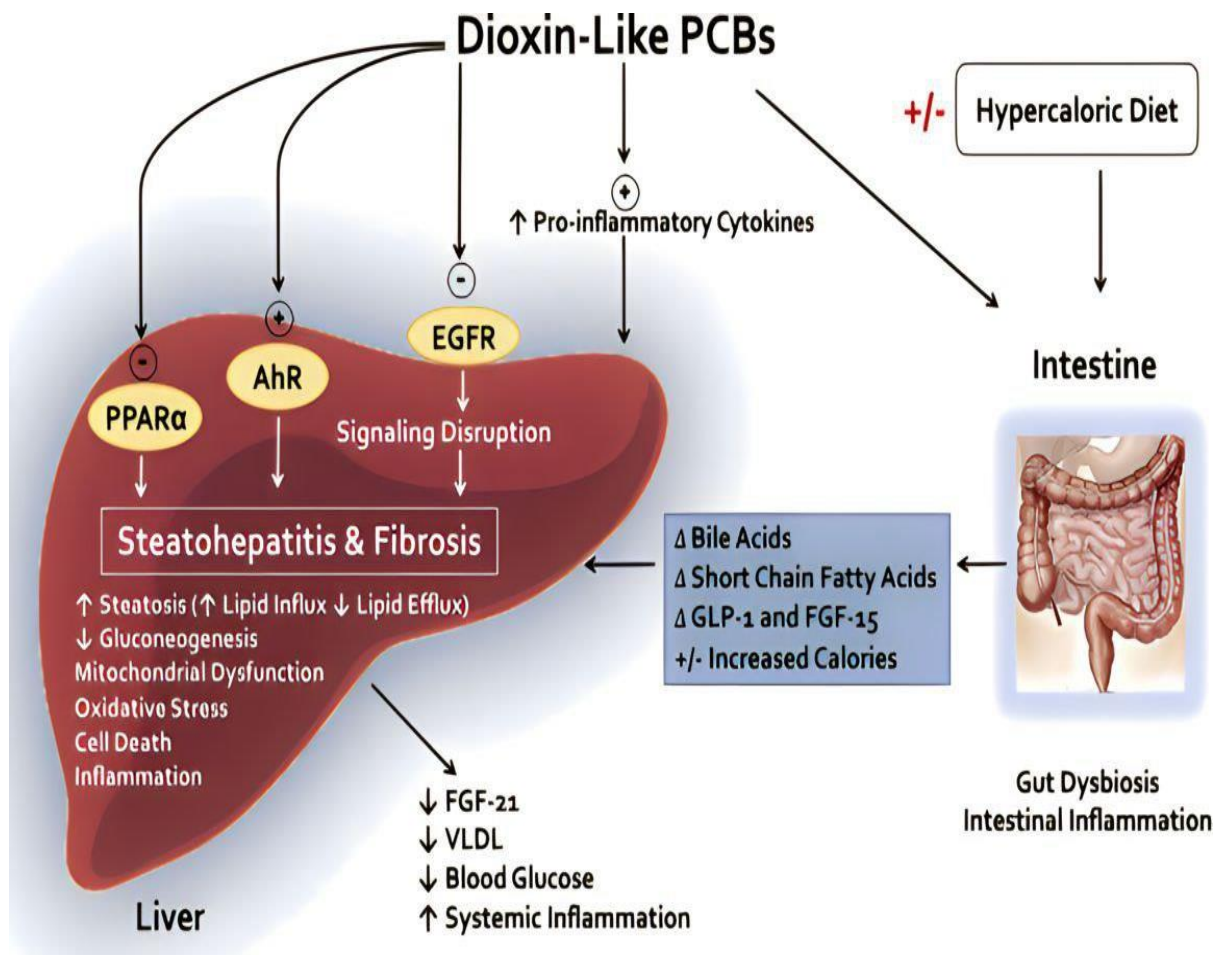


Figure (4): Pathophysiology of liver damage caused by dioxin and dioxin-like compounds [34].

Dioxin-like PCBs' role in NAFLD is illustrated schematically. Dioxin-like (DL) PCBs cause signaling disruption and transcriptional reprogramming that promote fatty liver accumulation, inflammation, and cell death. They do this by causing proinflammatory cytokines, directly activating the AhR, and reducing (estimated glomerular filtration rate) EGFR. With or without a high-calorie diet, dioxin-like polychlorinated biphenyls (DL PCBs) change the intestinal microbiota, resulting in gut dysbiosis, which promotes host inflammation, alteration of bile acid and

short-chain fatty acid metabolism, and enterokine synthesis. Additionally aggravating the symptoms of NAFLD is how this influences liver behavior and function. Polychlorinated biphenyl (PCB), nonalcoholic fatty liver disease (NAFLD), aryl hydrocarbon receptor (AhR), epidermal growth factor receptor (EGFR), fibroblast growth factor (FGF), peroxisome proliferator-activated receptor (PPAR), and very low-density lipoprotein (VLDL) are all abbreviations for this illustration figure [34].

Dioxins quantification and detection techniques:

The toxicity levels of PCDDs/Fs have been figured out and reported as international toxic equivalents using gas chromatography/high-resolution mass spectrometry (HRGC/HRMS) analyses for congener concentrations [22]. Dioxins are typically found in mixes of different types of dioxins and dioxin-like compounds, each of which has a different level of toxicity. The idea of international TEQ has been established to provide a single number that represents the total toxicity of such a mixture. The TEQ system compares the toxicity of various substances to that of the most hazardous substance, TCDD. A unique "Toxic Equivalency Factor" (TEF) is assigned to each chemical, this factor displays how harmful the chemical is when compared to 2,3,7,8-TCDD, which has a reference value of 1 [17]. Interactions with cellular AhR receptors can have adverse effects (like cancer), but nothing else. The total TCDD TEQ of a mixture of dioxins is calculated by multiplying the concentrations of each poisonous component by their TEFs, which are then arranged according to the TEQ method. By using this method, it is not possible to measure other hazardous effects of dioxins and dioxin-like compounds. For various animal species, different TEF have varied values [16], [35].

The most common method for analysis and detection

Solvent extraction was advised for dust and soil samples that have big particles, such as pebbles and twigs [36].

- **Extraction of dioxin from water samples.**

To capture dissolved dioxins, Gao et al. (2014) [37] suggested filtering the water samples and running them through a column made of the hydrophobic resin XAD-2. Following drying, the dioxins are eluted using a 1:1 mixture of dichloromethane and hexadecane. The resulting solution is then collected and chilled before analysis [38].

- **Extraction of dioxin from air samples.**

The sample should be run through a 1:1 combination of hexadecane and dichloromethane. The resultant solution was then put through an activated carbon column and a multilayer silica gel column to remove any remaining undissolved particle debris. Following that, the adsorbed dioxins can be extracted using a dichloromethane-hexadecane mixture, and all samples must be kept cool before being analyzed [38].

- **Extraction of dioxin from soil samples.**

In the case of soil samples, the samples are placed in a sieve and stirred to remove larger particulate matter. The samples are then mixed with a 1:1 solution of hexadecane and acetone, the combination is filtered, and the mixture is maintained in cold storage until the analysis is completed [39].

- **Extraction of dioxin from sludge samples.**

Sludge extracts are treated with high concentrations of sulfuric acid and then placed in hexane. Following evaporation, extracts are scrubbed using a multi-layered

silica gel column, a basic alumina column, and a PX-21 active carbon column [40], [41].

- **Extraction of dioxin from milk samples.**

In other studies, the Soxhlet extraction method was used to analyze milk, which was then cleaned automatically using a Power-Prep system, and subjected to gel permeation chromatography, alumina cleanup, and porous graphitized carbon chromatography [42].

- **Extraction of dioxin from blood plasma and animal tissue.**

The extraction and clean-up are performed in a series of steps, with the first step involving the use of a C18 bonded silica cartridge, the second step involving the use of a dual-cartridge made of bonded benzenesulfonic acid in series with a silica cartridge, and the third and final step involving the use of a florisil cartridge [22], [35].

Treatment of dioxins toxicity:

Dioxin and dioxin-like chemicals are now known problems that must be quickly resolved since as the population increases, so does the threat of dioxins also increases too. Several researchers have proposed utilizing several types of tea to treat the dioxin-related condition known as NAFL or NASH, which can proceed to hepatocellular cancer (HCC). Although the understanding of how NAFLD develops, there are still no pharmacological therapies that can successfully stop the condition from progressing [43]. Many types of tea contain a variety of bioactive ingredients, including free amino acids, alkaloids, pigments, polysaccharides, and polyphenols. The majority of tea research over the years has primarily centered on green tea, and different animal studies have demonstrated that green tea has multiple protective qualities, including antioxidant, anti-inflammatory, anti-diabetic, anti-hypertension, anti-obesity, and hepatoprotective roles. White tea has been demonstrated to have a stronger anti-hypertensive effect than catechins. In fact, oblique both in vitro and in vivo studies have confirmed white tea's antioxidant and anti-obesity properties. White tea's impact on liver conditions like NAFLD hasn't been thoroughly studied, and the underlying mechanisms are still unknown [44]. One of the beneficial and eco-friendly substances that has a significant effect on the treatment of liver fibrosis and plays an effective role in the removal of dioxin from the body is locust beans. Locust bean is a non-digestible lipophilic dietary fat substitute that increased the patient's intestinal excretion of TCDD by eight to ten folds, hence it may aids in understanding the consequences of pollutants (dioxins and dioxin-like compounds), This is enough to minimize the half-life of TCCD from 7 years to 1-2 years [35].

Locust beans components and their promising protective role:

Locust bean seeds contain antioxidants, Galactomannans, and a large number of amino acids (Glutamic acid, Aspartic acid, Arginine, etc..). Flavonols, Flavonoids (Catechin, Quercetin, Epicatechin) Minerals: Calcium, Potassium, Magnesium, Sodium, Phenolic acids,

and Tannins. Antioxidants and galactomannans play a vital part in defending cells against free radicals, which may also contribute to heart disease, cancer, and other disorders, according to the facts that surround locust beans and their structure [7]. Second, there are flavonoids, which have several medical advantages, including anticancer, antioxidant, anti-inflammatory, and antiviral characteristics [45]. Moreover, They have both cardioprotective and neuroprotective characteristics. These biological processes are influenced by the type of flavonoid, its possible mechanism of action, and its bioavailability [46]. Moreover, locust bean flour contains Flavone glycosides, Flavanones, Flavanols, Gallate derivatives, minerals, vitamins E, D, C, B, Niacin, Folic acid, B₂, A, B₁₂ Phenolic acids (Gallic acids, Ellagic acid, etc.), Sugars (D-pinitol), Isoflavones, Tannins, and Ellagitannins. Mainly, D-Pinitol functions as a natural antidiabetic and insulin regulator, as well as an active anti-Alzheimer's, anti-cancer, anti-inflammatory, antioxidant, hepato-, and immune-protective agent [8]. The flavor of locust beans contains gallic acid and its ester derivatives. Many scientific studies on the biological and pharmacological effects of these phytochemicals have been published, with an emphasis on their anti-inflammatory, anti-cancer, anti-microbial, anti-inflammatory, cardioprotective, gastroprotective, and neuroprotective properties [47].

The pulp contained phenolic compounds, which are known to have antioxidant properties because of the hydroxyl substituent on aromatic rings, which is reactive and can release hydrogen atoms to radicals to create stable phenoxyl radicals [48]. The phenolic compounds that are naturally present in pulp may have an impact on its antioxidant capacity; therefore, determining the amount of phenolic compounds is important when assessing the pulp's antioxidant capacity. Moreover, phenolic compounds can also prevent the production of oxidized low-density lipoprotein (LDL), which is regarded to be the main cause of cardiovascular disease, by suppressing unsaturated lipids from auto-oxidizing [49]. According to the result described by Lobo et al. (2010) [50], the ferric-reducing antioxidant power (FRAP) results, the pulp has a significant amount of ferric-reducing ability (14.08 mg/g). This shows that the sample might serve as a reducing agent by neutralizing free radicals and giving them an electron, which would reduce their ability to cause adverse effects [7], [8]. In addition to locust bean germ which contains gallic acid a naturally occurring phenolic substance with known antioxidant properties [50].

From these facts, we, therefore, propose that consuming locust beans may aid in the elimination of dioxin and polychlorinated diphenyls (PCDS) from the body. Dioxin-like substances are kept deposited in the body's adipose tissue as we suppose locust bean can get rid of these toxins considerably more quickly since it travels through the gut, they will diffuse from the body fats carried by fats in the blood and from there into the intestine, and after that, it will be held in the colon together with water trapping, leading to osmotic diarrhea, which aids in raising the pace of dioxin removal where they are excreted as

feces [51], [52]. So, we are recommended performing more studies to confirm the promising protective role of locust beans against hepatotoxicity.

Conclusion

In the past century, there were numerous accidents linked to excessive dioxin exposure. They have confirmed to us how harmful and toxic dioxins are. However, many nations have not made routine dioxin monitoring a reality, primarily due to the high cost of technology. This research certainly helped in our comprehension of the significance of effective management of hazardous compounds and the requirement to constantly reduce their release into the environment in order to protect human health. Today, research has focused on natural antioxidant compounds with fewer detrimental effects such as locust beans, which provide a strategy for cutting down on the toxicity of dioxin and other toxins. However, more studies are required to confirm the promising protective role of locust beans against dioxin hepatotoxicity.

Acknowledgments: We wish to express our deepest thanks, gratitude, and appreciation to the chemistry department- Faculty of Science-Suez University, and all the staff for their outstanding support, and generous help, and for allowing us to share in the Fifth Suez Scientific Students Conference.

References

- [1] K.C. Patrick- Iwuanyanwu, M.O. Wegwu and J.K. Okiyi.(2010). Hepatoprotective Effects of African Locust Bean (*Parkia clappertoniana*) and Negro Pepper (*Xylopiya aethiopica*) in CCl₄-Induced Liver Damage in Wistar Albino Rats. *International Journal of Pharmacology*, vol. 6, no. 5, pp. 744-749, DOI: 10.3923/ijp.2010.744.749
- [2] M. Ishii and K. Yamamoto.(2013). "An Environmental Risk Evaluation Method Employing Atmospheric Dispersion Models and GIS," *J Environ Prot*, vol. 04, no. 12, pp. 1392–1408, doi: 10.4236/jep.2013.412160.
- [3] R. N. Prabhu and J. Lakshmi Praba. (2022). "Persistent Organic Pollutants (Part I): The 'Dirty Dozen' – Sources and Adverse Effects," in *Organic Pollutants: Toxicity and Solutions*, Springer International Publishing, pp. 1–27, doi: 10.1007/978-3-030-72441-2-1.
- [4] J. Tuomisto. (2019). "Dioxins and dioxin-like compounds: toxicity in humans and animals, sources, and behaviour in the environment," *WikiJournal of Medicine*, vol. 6, no. 1, pp. 1–26.
- [5] J. Fukush, H. Tsushima, Y. Matsumoto, Ch. Mitoma, M. Furue, H. Miyahara and Y. Nakashima. (2019). "Influence of dioxin-related compounds on physical function in Yusho incident victims," *Heliyon*, vol. 5, no. 10, p. e02702, doi: <https://doi.org/10.1016/j.heliyon.2020.101616>.
- [6] R. Hoogenboom. (2019). "Incidents with dioxins and dioxin-like PCBs in the food chain," *Chemical hazards in foods of animal origin*, pp.503-528, doi.org/10.3920/978-90-8686-877-3_20.
- [7] S. Arinola, A. Olanrewaju, O. James, and A. Omowaye-Taiwo. (2018). Evaluation of physicochemical properties and phytochemical composition of African locust bean (*Parkia biglobosa*) pulp. In the *Proceedings of the 4th Regional Food Science and Technology Summit (ReFoSTS)*, pp. 134.

- [8] V. D. Prajapati, P. M. Maheriya, S. D. Roy, T. K. Giri and B. Ghosh and Eds. (2021). "Chapter 7 - Locust bean gum-derived hydrogels," in *Plant and Algal Hydrogels for Drug Delivery and Regenerative Medicine* Woodhead Publishing, pp. 217–260, doi: <https://doi.org/10.1016/B978-0-12-821649-1.00016-7>.
- [9] K. R. Olson and L. W. Morton. (2019). "Long-term fate of Agent Orange and dioxin TCDD contaminated soils and sediments in Vietnam hotspots," *Open Journal of Soil Science*, vol. 9, no. 01, p. 1.
- [10] P. Ssebugere, M. Sillanpää, H. Matovu, and E. Mubiru. (2019). "Human and environmental exposure to PCDD/Fs and dioxin-like PCBs in Africa: A review," *Chemosphere*, vol. 223, pp. 483–493.
- [11] J. Ames, W. Marcella, S. Claudia, S. Stefano, B. Paolo, M. Paolo, and E. Brenda. (2019). "Prenatal dioxin exposure and neuropsychological functioning in the Seveso Second Generation Health Study," *Int J Hyg Environ Health*, vol. 222, no. 3, pp. 425–433.
- [12] S. Kakia, G. Pozoukidou, and D. G. Vagiona. (2023). "Providing an Integrated Vulnerability Assessment Indicator System (VAIS) to Measure the Spatial Vulnerability of Areas near Seveso Establishments in Thessaloniki (Greece)," *Sustainability*, vol. 15, no. 3, p. 2303, Doi: [10.3390/su15032303](https://doi.org/10.3390/su15032303).
- [13] A. Schecter, L. Birnbaum, J. Rayan and J. Constable. (2006). Dioxins: An overview. *Environmental research*. Vol. 101, no. 10, pp. 419-28, DOI:10.1016/j.envres.2005.12.003 .
- [14] R. D. Kimbrough . (2014). "Chlorodibenzofurans (CDFs)" in *Encyclopedia of Toxicology (Third Edition)*, P. Wexler, Ed., Oxford: Academic Press, pp. 876–879, Doi: <https://doi.org/10.1016/B978-0-12-386454-3.01113-1>.
- [15] B. Loganathan. (2016). "Persistent organic chemicals in the Pacific Basin countries: An overview," in *ACS Symposium Series, American Chemical Society*, pp. 1–15, Doi: [10.1021/bk-2016-1243.ch001](https://doi.org/10.1021/bk-2016-1243.ch001).
- [16] N. Larebeke, L. Hens, P. Schepens, A. Covaci, J. Baeyens, K. Everaert, J. Bernheim, R. Vlietinck, and G. Poorter. (2001). "The Belgian PCB and Dioxin Incident of January-June 1999: Exposure Data and Potential Impact on Health," *109*, 273-265, Doi: <https://doi.org/10.1289/ehp.01109265>.
- [17] S. Song, X. Zhou, Ch. Guo, H. Zhang, T. Zeng, Y. Xie, J. Liu, Ch. Zhu and X. Sun. (2019). "Emission characteristics of polychlorinated, polybrominated and mixed polybrominated/chlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs, PBDD/Fs, and PBCDD/Fs) from waste incineration and metallurgical processes in China," *Ecotoxicol Environ Saf*, vol. 184, p. 109608.
- [18] D. Palmer, J. O. Pou, L. Gonzalez-Sabaté, and J. Díaz-Ferrero. (2018). "Multiple linear regression-based congener profile correlation to estimate the toxicity (TEQ) and dioxin concentration in atmospheric emissions," *Science of The Total Environment*, vol. 622–623, pp. 510–516, Doi: <https://doi.org/10.1016/j.scitotenv.2017.11.344>.
- [19] W. Yoshioka and C. Tohyama. (2019). "Mechanisms of Developmental Toxicity of Dioxins and Related Compounds," *Int J Mol Sci*, vol. 20, no. 3, p. 617, Jan. Doi: [10.3390/ijms20030617](https://doi.org/10.3390/ijms20030617).
- [20] A. N. Gilbreath and L. J. McKee. (2015). "Concentrations and loads of PCBs, dioxins, PAHs, PBDEs, OC pesticides and pyrethroids during storm and low flow conditions in a small urban semi-arid watershed," *Science of the Total Environment*, vol. 526, pp. 251–261, Sep. Doi: [10.1016/j.scitotenv.2015.04.052](https://doi.org/10.1016/j.scitotenv.2015.04.052).
- [21] M. Van Den Berg, L. Birnbaum, A. Bosveld, B. Brunström, Ph. Cook, M. Feelay, J. Giesy, A. Hanberg, R. Hasegawa, S. Kennedy, T. Kubiak, J. Larsen, R. Leeuwen, D. Liem, C. Nolt, E. Peterson, L. Poellinger, S. Safe, D. Schrenk, D. Tillitt, M. Tysklind and M. Younes. (1998). "Reviewv' Toxic Equivalency Factors (TEFs) for PCBs, PCDDs, PCDFs for Humans and Wildlife, *Environmental health perspective* ", Vol. 106, No. 12. <https://doi.org/10.1289/ehp.98106775>
- [22] A. Esser, P. Ziegler, A. Kaifie, T. Kraus, and T. Schettgen. (2021). "Estimating plasma half-lives of dioxin-like and non-dioxin-like polychlorinated biphenyls after occupational exposure in the German HELPCb cohort," *Int J Hyg Environ Health*, vol. 232, p. 113667, Doi: <https://doi.org/10.1016/j.ijheh.2020.113667>.
- [23] N. González and J. L. Domingo.(2021). Polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs) in food and human dietary intake: An update of the scientific literature. *Food and Chemical Toxicology*, vol. 157, 112585, <https://doi.org/10.1016/j.fct.2021.112585>.
- [24] R. Weber, C. Herold, H. Hollert, J. Kamphues, M. Blepp, and K. Ballschmiter. (2018). "Reviewing the relevance of dioxin and PCB sources for food from animal origin and the need for their inventory, control, and management," *Environ Sci Eur*, vol. 30, no. 1, p. 42, Doi: [10.1186/s12302-018-0166-9](https://doi.org/10.1186/s12302-018-0166-9).
- [25] S. Sun, R. Cao, X. Lu, Y. Zhang, Y. Gao, J. Chen, H. Zhang. (2021). "Levels and patterns of polychlorinated dibenzo-p-dioxins and dibenzofurans and polychlorinated biphenyls in foodstuffs of animal origin from Chinese markets and implications of dietary exposure," *Environmental Pollution*, vol. 273, p. 116344, Doi: <https://doi.org/10.1016/j.envpol.2020.116344>.
- [26] B. Eskenazi, p. Mocarelli, M. Warner, L. Needham, D. G. Patterson, S. Samuels, Jr, W. Turner, P. M. Gerthoux and P. Brambilla. (2004). Relationship of serum TCDD concentrations and age at exposure of female residents of Seveso, Italy. *Environ Health Perspect*. 112(1):22-7. Doi: [10.1289/ehp.6573](https://doi.org/10.1289/ehp.6573).
- [27] H. Kondo, K.Tanio, Y. Nagaura, M. Nagayoshi, Ch. Mitoma, M. Furue and T. Maeda.(2018). "Sleep disorders among Yusho patients highly intoxicated with dioxin-related compounds: A 140-case series," *Environ Res*, vol. 166, pp. 261–268, Doi: <https://doi.org/10.1016/j.envres.2018.05.033>.
- [28] T. VoPham, K. A. Bertrand, J. A. Fisher, M. H. Ward, F. Laden, and R. R. Jones. (2022). "Emissions of dioxins and dioxin-like compounds and incidence of hepatocellular carcinoma in the United States," *Environ Res*, vol. 204, p. 112386, Doi: <https://doi.org/10.1016/j.envres.2021.112386>.
- [29] M. Viluksela and R. Pohjanvirta. (2019). "Multigenerational and Transgenerational Effects of Dioxins," *Int J Mol Sci*, vol. 20, no. 12, p. 2947, Doi: [10.3390/ijms20122947](https://doi.org/10.3390/ijms20122947).
- [30] C. Y. Huang, Ch. Wu, Ch. Long, Y. Yang, Ch. Chang, J. K. Wei, Y. C. Chang, Y. Yun, J. Shang, Ch. Chang, H. Ran.(2015). "Association between dioxin and diabetes mellitus in an endemic area of exposure in Taiwan a population-based study," *Medicine (United States)*, vol. 94, no. 42, p. e1730, Doi: [10.1097/MD.0000000000001730](https://doi.org/10.1097/MD.0000000000001730).
- [31] M. Seger.(2017). Narrating Dioxin: Laura Conti's A Hare With The Face of a Child. *Interdisciplinary Studies in Literature and Environment*. Volume 24, Issue 1, Pages 47–65, <https://doi.org/10.1093/isle/isw086>.

- [32] W. Zhang, H. Q. Xie, Y. Lie, M. Zhou, Z. Zhou, R. Wang, M. E. Haha and B. Zhao. (2021). The aryl hydrocarbon receptor: A predominant mediator for the toxicity of emerging dioxin-like compounds. *Journal of Hazardous Materials*, vol. 426, 128084, <https://doi.org/10.1016/j.jhazmat.2021.128084>.
- [33] H. Fu, L. Wang, J. Wang, B. D. Bennett, J. Li, B. Zhao, G. Hu. (2019). "Dioxin and AHR impairs mesoderm gene expression and cardiac differentiation in human embryonic stem cells," *Science of the Total Environment*, vol. 651, pp. 1038–1046.
- [34] B. Wahlang, J. E. Hardesty, J. Jin, K. C. Falkner, and M. C. Cave. (2019). "Polychlorinated biphenyls and nonalcoholic fatty liver disease," *Curr Opin Toxicol*, vol. 14, pp. 21–28, Doi: <https://doi.org/10.1016/j.cotox.2019.06.001>.
- [35] B. D. Kerger, H. W. Leung, P. Scott, D. J. Paustenbach, L. L. Needham, D. J. Patterson, P. M. Gerthoux and P. Mocarelli. (2006). Age- and concentration-dependent elimination half-life of 2,3,7,8-tetrachlorodibenzo-p-dioxin in Seveso children. *Environ Health Perspect*. 114(10):1596-602. Doi: 10.1289/ehp.8884.
- [36] B. Subedi, L. Aguilar, E. S. Williams, B. W. Brooks, and S. Usenko. (2014). "Selective pressurized liquid extraction technique capable of analyzing dioxins, furans, and PCBs in clams and crab tissue," *Bull Environ Contam Toxicol*, vol. 92, no. 4, pp. 460–465, Doi: 10.1007/s00128-013-1162-9.
- [37] L. Gao, Q. Zhang, B. Zhang, W. Liu, and K. Xiao.(2014). "Polychlorinated dibenzo-p-dioxins and dibenzofurans in water and six fish species from Dongting Lake, China," *Chemosphere*, vol. 114, pp. 150–157, Doi: <https://doi.org/10.1016/j.chemosphere.2014.04.015>.
- [38] S. Li, G. Liu, M. Zheng, W. Liu, M. Wang, K. Xiao, Ch. Li, Y. Wang. (2015). "Comparison of the contributions of polychlorinated dibenzo-p-dioxins and dibenzofurans and other unintentionally produced persistent organic pollutants to the total toxic equivalents in air of steel plant areas," *Chemosphere*, vol. 126, pp. 73–77, Doi: <https://doi.org/10.1016/j.chemosphere.2015.02.014>.
- [39] A. Shelepchikov, E. Brodskiy, D. Feshin, V. Zhil'nikov, E. Mir-Kadyrova, and S. Balashova.(2011). "Polychlorinated dibenzo-p-dioxins, dibenzofurans, and biphenyls in soils of Moscow," *Eurasian Soil Science*, vol. 44, pp. 286–296, Doi: 10.1134/S1064229311030124.
- [40] A. L. Tasca, S. Vitolo, R. Gori, G. Mannarino, A. M. Galletti and M. Puccini. (2022). Hydrothermal carbonization of digested sewage sludge: The fate of heavy metals, PAHs, PCBs, dioxins and pesticides. *Chemosphere*, vol. 307. <https://doi.org/10.1016/j.chemosphere>.
- [41] R. P. Schwarzenbach, T. Egli, T. B. Hofstetter, U. Von Gunten, and B. Wehrli.(2010). "Global water pollution and human health," *Annu Rev Environ Resour*, vol. 35, pp. 109–136, Doi: 10.1146/annurev-environ-100809-125342.
- [42] L. Zhang, Z. Pei, B. Lyu, J. Li, Y. Zhao, and Y. Wu. (2023). "Polychlorinated dibenzo-p-dioxins and dibenzofurans and dioxin-like polychlorinated biphenyls in human milk from national human breast milk monitoring in 2016–2019 in China," *Science of The Total Environment*, vol. 872, p. 162243.
- [43] Y. S. Zhen. (2002). *Tea: Bioactivity and Therapeutic Potential* (1st ed.). CRC Press. <https://doi.org/10.1201/b12659>.
- [44] X. Deng, H. Shang, J. Chen, J. Wu, T. Wang, Y. Wang, C. Zhu, and W. Sun. (2022). "Metabolomics Combined with Proteomics Provide a Novel Interpretation of the Changes in Flavonoid Glycosides during White Tea Processing," *Foods*, vol. 11, no. 9, Doi: 10.3390/foods11091226.
- [45] P. I. Akubor, J. O. Onuh and C. O. Orishagbemi. (2017). Evaluation of the Phytochemical Composition and Pasting Characteristics of African Locust Bean Pulp Flour, Wheat Flour and Blends. *Asian Journal of Biotechnology and Bioresource Technology*, 1 (4). Pp. 1-8. DOI: 10.9734/AJB2T/2017/36478.
- [46] D. Zhang, R. Zhang, L. Yin, J. Chen, and X. Zhang. (2011). "Comparative study on antioxidant capacity of flavonoids and their inhibitory effects on oleic acid-induced hepatic steatosis in vitro," *Eur J Med Chem*, vol. 46, no. 9, pp. 4548–4558, Doi: 10.1016/j.ejmech.2011.07.031.
- [47] N. A. AL Zahrani, R. M. El-Shishtawy, and A. M. Asiri. (2020). "Recent developments of gallic acid derivatives and their hybrids in medicinal chemistry: A review," *Eur J Med Chem*, vol. 204, p. 112609, Doi: <https://doi.org/10.1016/j.ejmech.2020.112609>.
- [48] A. O'Connell, F. M. Goycoolea, A. Gulotta, P. Holmqvist, P. Schuetz, and J. Mattsson. (2023). "The structure and dynamics of locust bean gum in aqueous solution," *Food Hydrocoll*, vol. 138, p. 108446, Doi: <https://doi.org/10.1016/j.foodhyd.2022.108446>.
- [49] M. M. Rahman, S. Rahaman, R. Islam, F. Rahman, F. Mithi, T. Alqahtani, M. Almikhlaifi, S. Alghamdi, A. Alruwaili, S. Hossain, M. Ahmed, R. Das, T. Emran and S. Uddin. (2022). "Role of phenolic compounds in human disease: Current knowledge and future prospects," *Molecules*, vol. 27, no. 1, Doi: 10.3390/molecules27010233.
- [50] V. Lobo, A. Patil, A. Phatak, and N. Chandra. (2010). "Free radicals, antioxidants, and functional foods: Impact on human health," *Pharmacognosy Reviews*, vol. 4, no. 8. Pp. 118–126, Doi: 10.4103/0973-7847.70902.
- [51] A. Sokic-Milutinovic, A. Pavlovic-Markovic, R. S. Tomasevic, and S. Lukic. (2022). "Diarrhea as a Clinical Challenge: General Practitioner Approach," *Digestive Diseases*, vol. 40, no. 3. pp. 282–289, Doi: 10.1159/000517111.
- [52] O. Aozasa, S. Ohta, T. Nakao, H. Miyata and T. Nomura. (2001) Enhancement in fecal excretion of dioxin isomer in mice by several dietary fibers, *Chemosphere*, Volume 45, Issue 2, Pages 195-200 ,[https://doi.org/10.1016/S0045-6535\(00\)00557-9](https://doi.org/10.1016/S0045-6535(00)00557-9).