Article Type: Review Article
J Name: Modern Phytomorphology
Short name: Modern Phytomorphology
ISSN: ISSN 2226-3063/eISSN 2227-9555
Year: 2023
Volume: 17
Page numbers: 01-19
DOI: 10.5281/zenodo.7939615
(10.5281/zenodo.Year-Volume-PDFNo.)
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REVIEW ARTICLE

Environmental toxicants and health adversities: A review on interventions of phytochemicals

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Received: 16.01.2023, Manuscript No.: mp-23-87258| **Editor Assigned:** 19.01.2023, Pre-QC No. mp-23-87258(PQ) | **Reviewed:** 24.01.2023, QC No. mp-23-87258(Q) | **Revised:** 27.01.2023, Manuscript No. mp-23-87258(R) | **Accepted:** 03.02.2023 | **Published:** 15.02.2023

Abstract

Toxicity arising from environmental contaminants has attracted global interest in the last few decades, due to the high morbidity and mortality associated with it. Efforts have been made to combat the consequential outcomes of environmental toxicity in humans through traditional remediation techniques and therapeutic measures that have been hampered by one or more limitations. Consequently, this scenario has triggered interest in the medicinal properties of phytochemicals. Thus, this desk review gives a succinct and in-depth overview of environmental contaminants and their toxicity effects on humans. The classes of phytochemicals and their functions are investigated. This study adopted a desk review of existing literatures from scientific reports and peer-reviewed articles through triangulation of data sources. Environmental contaminants exist as organic, inorganic and radioactive substances; and are generated from natural and anthropogenic activities. Classes of toxicants considered include heavy metals, pesticides, food additives, solvents, cosmetics, combustion products and drugs of abuse. They become inimical to the ecosystem and pose danger to humans' health when exposed to or bioaccumulated beyond the threshold limits. On the other side "Phytochemicals" are group of secondary metabolites obtained from plants with medicinal properties. These compounds include flavonoids, tannins, saponins, alkaloids, cardenoloids, terpenoids, and phytosteroids. This review corroborates the prophylactic and therapeutics efficacy of these phytochemicals as anti-metastatic, anti-inflammatory, anti-ageing, anti-oxidant, anti-microbial and life-saving substances with empirical findings from several laboratories, clinical trials and epidemiologic studies. In this article, we argue that, despite phytochemicals' effectiveness in preventing and treating many diseases in humans caused by environmental toxicity, their over-exploitation, and unsustainably high consumption should be strictly avoided.

Keywords: Environmental toxicants, Phytochemicals, Prophylactics, Therapeutics, Plants, Intervention, Medicinal properties, Public health, Plant biology, Phytosozology, Phytogeography

Introduction

One of the leading causes of diseases, high morbidity and mortality rates in nations across the globe is environmental contamination. According to the World Health Organization (WHO) approximately 7 million deaths per annum is associated with pollution, mostly due to environmental toxicants that are air borne (World Health Organization. 2022}; this casualty is greater than the cumulative death Figures recorded from communicable diseases such as malaria, tuberculosis and HIV/AIDS (World Health Organization. 2014). The greater proportions of these pollution-related deaths take place in developing countries. Exposure to environmental toxicants at an early stage in life is primarily precarious (Olanrewaju J.A et al.,2022; World Health

Organization. 2006). Susceptibility is most pronounced during the first few weeks of the fetal life when the organs primordial are formed. Vulnerability to environmental toxicants during this delicate period can result in perpetual anatomical, behavioural and metabolic alterations. This outcome can be expressed as short or long-term condition at any specific point along the lifespan from the neonatal period to senescence (Grandjean P. et al. 2014). Major acute maladies ascribed to environmental pollution at infancy are diarrheal iseases and pneumonia; while the chronic non-communicable diseases associated with early exposure to environmental toxicants include dysfunctional neurobehavioural development, childhood and adult asthma, hypertension, diabetes, cardiovascular diseases, obesity, and cancer (Sly P.D et al. 2016; Hennig B et al. 2005; Needham L.L et al. 2017). Several reports have linked health challenges and age-associated diseases to environmental contaminants and chemical exposure. People are exposed to harmful chemicals and their combinations through occupational and environmental exposure (Center for Disease Control and Prevention (CDC) 2005; Okareh, O.T et al. 2018). Several contaminants, such as heavy metals and persistent organics pollutants (POPs), bioaccumulate in the human system, and remediation techniques to eliminate these pollutants from the surroundings are often difficult and expensive.

Techniques employed at obliterating environmental toxicity from the biological compartment include chelation and cleansing procedures; and other additional corroborative techniques which are, routinely administered in synergy. The treatment may be very complex and personalized, narrowed to an individual's distinct needs and requiring the skill of an expert (Sokan-Adeaga A.A et al. 2020). Moreover, numerous environmental contaminants induce signalling pathways that lead to oxidative stress which serve as a precursor to the pathogenesis of several long-term maladies. Consequently, techniques that regulate the impact of toxicants on pathophysiologic processes that leads to disease development and escalation will be of immense public health significance (Hennig B et al. 2008). Emerging findings, obtained from fundamental and epidemiologic studies and clinical trials have proven that "phytochemicals" remain the only viable answer to this menace.

This review presents background information on environmental toxicants and some of their selected toxicity in animals and humans. It further delves into the literature survey of some phytochemicals popularly found in medicinal plants and presents evidence-based studies to accentuate the therapeutic properties of these compounds in combating and ameliorating health effects due to environmental toxicity. It is our aspiration that this review will trigger public health interest in the beneficial roles of phytochemicals and aroused further research that will lead to the discovery of many phytochemicals from unexplored medicinal plants across the globe.

Literature Review of Environmental Toxicants

An environmental toxicant can be regarded as any toxic agent or substance produced by humans or introduced into the environment by human activities. Toxicants come in diverse shapes and sizes, and they may emanate from both natural and anthropogenic sources. Thus, toxicants include a wide range of compounds from inorganic substances such as metals to organic compounds such as pharmaceutical medicines. Environmental contamination in any form has been of primary health interest, because it contributes significantly to the pathophysiology of some human diseases (Zar H.J et al. 2002). There are several origins by which chemical toxicants are emitted into the surrounding. These broadly are grouped into seven (7) classes. In this section, we discuss the diverse kinds of contaminants and the classes they belong to.

Types of Contaminants

Three primary groups of contaminants exist: organic, inorganic, and radioactive. There are numerous classes of contaminants under each of these groups. The main categories of contaminants are outlined in (Tab.1). Numerous chemicals are emitted into the surroundings daily. Therefore, during site appraisal surveys, it is necessary to specify the type of contaminants being assessed.

Table 1: Categories of contaminants

S/N	Types	Examples
1	Organic Contaminants	Petroleum hydrocarbons (fuels) – benzene, toluene, xylene, polycyclic aromatics, MTBE.
		Chlorinated solvent-trichloroethene, tetrachloroethene, trichloroethane, carbon tetrachloride
		Pesticides – DDT, toxaphene, atrazine, Polychlorinated biphenyls – PCBs
		Coal tar—polycyclic aromatics
		Pharmaceuticals/food additives/cosmetics – drugs
		Pharmaceuticals/food additives/cosmetics— drugs, surfactants, dyes
2	Inorganic Contaminants	Inorganic "salts"—sodium, calcium, nitrate, sulfate, chloride
		Heavy/trace metals—lead, zinc, cadmium, mercury, arsenic, selenium
3	Radioactive Contaminants	Solid elements—uranium, strontium, cobalt, plutonium
		Gaseous elements—radon

Classes of Toxicants

Heavy Metals: Heavy metals have no standard definition (Sokan-Adeaga A.A et al. 2020). In chemistry, its definition is based on chemical behaviour (Hawkes S.J. 1997), for the physicist, the distinct benchmark for heavy metals definition is atomic number (Gorbachev V.M et al. 1980), in metallurgy, it is defined by density (Morris C.G. 1992). The term "heavy metals" refers to elements with a moderately high density that is lethal even at diminutive concentrations. It is a broad concept that is appropriate to a class of metals and metalloids whose atomic density is more than 4 g/cm3, or at least five times heavier than water (Nriagu J.O. et al.

1988; Hawkes S.J. 1997). Heavy metals are basically classified by chemical characteristics other than by specific gravity; and these include copper (Cu), silver (Ag), iron (Fe), lead (Pb), arsenic (As), mercury (Hg), cadmium (Cd), Zinc (Zn), chromium (Cr), and the platinum group elements (Khanna S et al. 2011). They are intrinsically distributed in disproportionate doses in the environment. They exist either in elemental form or are combined in chemical compounds with other elements. Heavy metals are often conveyed over a wide range either as volatile or fine aerosols. This group of metals becomes deleterious to the health of humans when their concentration surpasses the maximum acceptable limits in the surroundings (Okareh T.O et al. 2020). Their virulence in an ecosystem depends exclusively on their chemical properties and behaviours (Sokan-Adeaga A.A et al. 2020).

Heavy metal pollution in the ambiance occurs via diverse pathways. Owing to their persistence, they permeate the environment for several years after their initial deposition; and contamination of the environment often takes place through weathering fraction (Nordberg G.F et al. 2005). They bioaccumulate in soil and crops via natural and man-made processes, and subsequent impacts posed critical problems in the food chain via biomagnification (Singh J et al. 2011). The principal port of entry in the human community is through ingestion and dermal (Türkdogan M.K et al. 2003). A common way by which adults is exposed is through industrial activities whereas in juveniles is by ingestion (Ngan V. 2006). Inappropriate therapy, radiological techniques and cracked thermometers are less consequential means of exposure (Nriagu J.O. 1990; Smith S.R. et al. 1997). Some of the health outcomes of their bioaccumulation in the body are the substitution of essential ions, cell membrane impairment, interference with phosphate ions & sulfhydryl (SH) groups, and competition with vital metabolites for binding sites (Jaishankar M et al. 2014).

Agricultural Chemicals (Pesticides)

The word "agricultural chemicals" has been widely substituted by the term "pesticides". Pesticides can be described as a group of chemicals or agglomeration of chemicals that are widely utilized in farming or in quarantine programs to control, annihilate, or fight off infections or nuisance from the plant; and protect humans from disease vectors. Typical classes of pesticides include fumigants, herbicides, fungicides, rodenticides, insecticides, and plant growth regulators (Alewu B et al. 2011; NSW EPA.2013; Nicolopoulou-Stamati P. et al. 2016). Pesticides are atypical amidst toxicants because they are applied purposely for the annihilation of certain living things. Ideally, pesticides are expected to be selective, eradicating selected species whilst sparing non-target organism. In reality, most pesticides are unspecific in their action. Taking into consideration the application of pesticides, the gains must be juxtaposed with the threat to environmental safety and mankind well-being. Important factors to be considered are persistence in the surroundings and propensity for bioaccumulation. Susceptibility to these chemicals can be by inhalation, ingestion, or dermal contact. The possible health consequences are governed by the types of pesticides, the time span and means of vulnerability, and the underlying health conditions of the individual. Inside the living system, pesticides may be metabolized, excreted, or bio-accumulated in the body's fat (Pirsaheb M. et al. 2015). Numerous inimical health outcomes attributed to chemical pesticides exposure include but not limited to gastrointestinal, carcinogenic, dermatological, endocrine, and neurological effects (Sanborn M. et al. 2007; Mnif W. et al. 2011; Bassil K.L. et al. 2007). In addition, accidental, purposively, or occupational exposure to pesticides can lead to hospitalization and demise.

Types of Pesticides

Organochlorine Pesticides: The chlorinated hydrocarbon insecticides came to limelight in the middle of the twentieth century, and include common chemicals like dichlorodiphenyltrichloroethane (DDT), chlordane, heptachlor, dieldrin, aldrin, methoxychlor, toxaphene, mirex, endosulfan, dicofol, lindane, endrin, mirex, and toxaphene. The structures of some familiar organochlorine pesticides are shown in (Fig. 1). The most popularly known organochlorine pesticide is DDT, whose indiscriminate utilization raised numerous environmental and public health concerns (Alewu B et al. 2011; Turusov V. et al. 2002; Van den Berg H. 2009). It is ubiquitous and generally conceived to be present in all living beings where it is primarily bio-accumulated in fatty tissue. These groups of pesticides are toxic to the nervous system where they disrupt nerve impulses transmission.

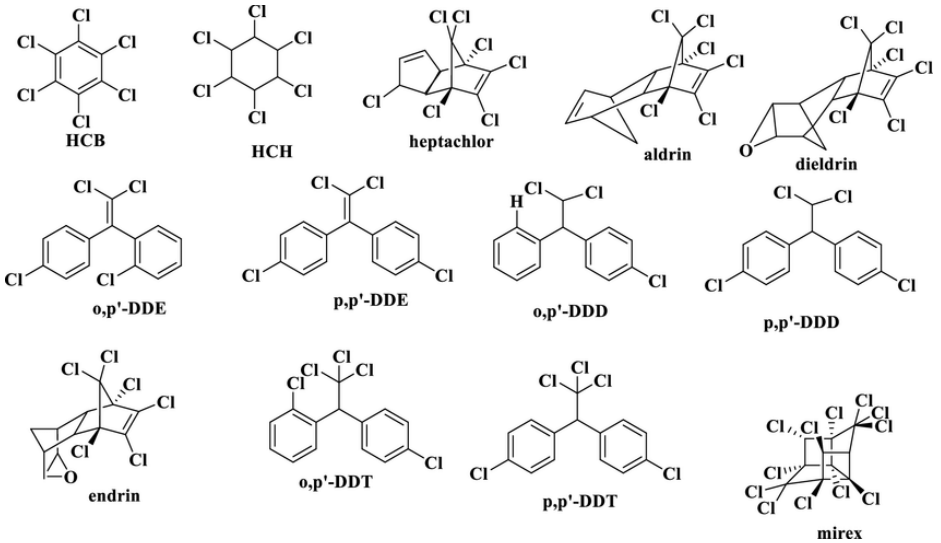

Figure 1: Structures of selected organochloride pesticides

Organophosphorus Pesticides (OPs): are among the popularly used pesticides made up of phosphoric acid esters or thiophosphoric acid esters (Fig. 2). They include common pesticides, like parathion, dimethoate, and malathion; many of which are famous for their hormone interference potential (Mnif W. et al. 2011; McKinlay R. et al. 2008; Gasnier C. et al. 2009). Among the OPs, the most widely utilized are glyphosate because of its environmental friendliness over the organochlorines. These groups of pesticides are linked with disruption of cholinesterase enzymes function (Jaga K. et al. 2003), the decline in insulin production, disturbance of regular cellular metabolism of carbohydrates, lipids and proteins, genotoxic impacts (Li D et al. 2015), and impede the activities of mitochondria, instigating oxidative stress and impairments of the endocrine and nervous system (Karami-Mohajeri S. et al. 2011).

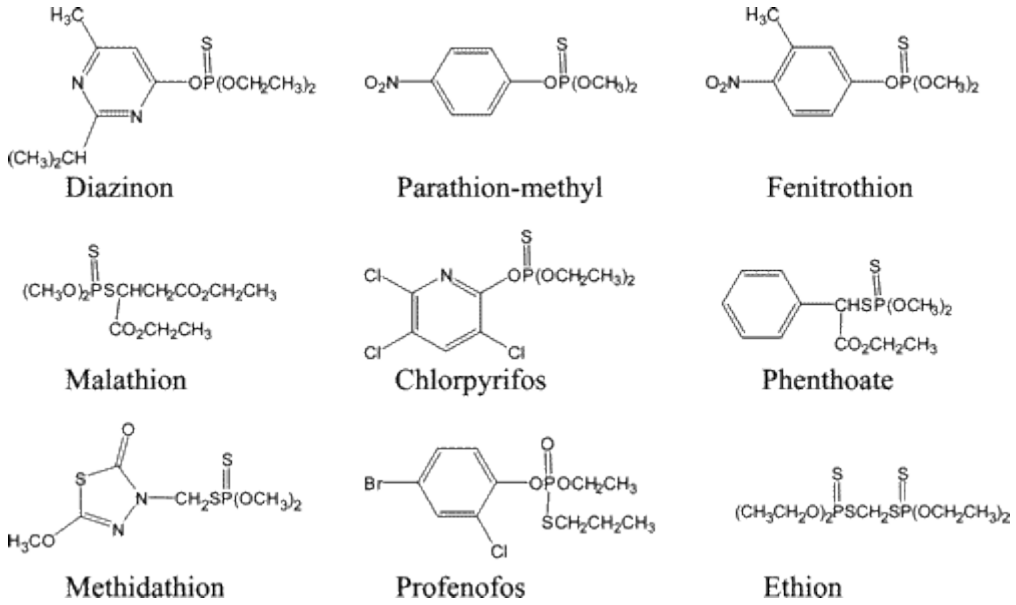

Figure 2: **Chemical structures of main organophosphate pesticides**

Carbamate Pesticides: These are esters of N-methyl (or occasionally N,N-dimethyl) carbamicacid (H2NCOOH). The virulence of this chemical differs based on the alcohol or phenol group. A popularly utilized carbamate insecticide is carbaryl (1-napthylmethylcarbamate), a far-ranging insecticide (Fig. 3). It is generally applied as dust in the agriculture, including home gardens. Carbaryl is not regarded as a persistent compound, due to its rapid hydrolysis. Other carbamate pesticides, such as ziram, aldicarb, and carbofuran have been linked with hormone-disrupting property, probable reproductive defects (Jamal F. et al. 2015, Goad E.R. et al 2004), and interference with mitochondrial roles and cellular metabolic actions.

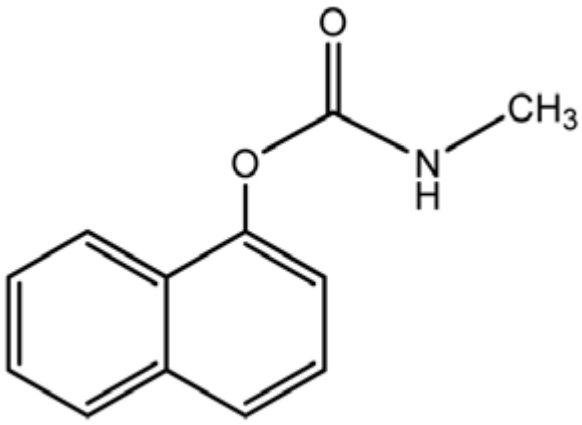

Figure 3: **Structure of Carbaryl (insecticide carbamate)**

Other Classes of Chemical Pesticides: Botanical insecticides have been in application since ancient times to control insects and are extracts obtained from plants. An example is Nicotine ((S)-3-(1-methyl-2-pyrrolidyl) pyridine), an alkaloid found in several plants, whose insecticidal property was first utilised in 1763. Nicotine is partly toxic dermally and orally. Another botanical insecticide is Pyrethrin (Fig. 4), which is an extract obtained from numerous kinds of chrysanthemum, and is among the foremost pesticides utilized by man. It is used at low concentrations and is regarded as non-persistent. Synthetic pyrethroids like permethrin, sumithrin, and fenvalerate, are viewed to be among the innocuous insecticides presently use for agricultural and public health purposes (Kolaczinski J.H. et al. 2004; Ray D.E. et al 2006). Nevertheless, there is proof of their potential to exhibit hormone-interference activity (Mnif W. et al. 2011; Jaensson A. et al. 2007; Pandey S.P et al. 2014), and to influence reproductive

variables in experimental animals (Jaensson A. et al. 2007; Moore A. et al. 2001}. Triazines, viz simazine, ametryn, and atrazine, are another group of chemical pesticides. Atrazine is popular among the triazines, and it has been basically linked with oxidative stress that leads to endocrine-disrupting consequences and reproductive toxicity (Jin Y. et al. 2014), cell toxicity (Huang P. et al. 2014), and dopaminergic effects (Ma K. et al. 2015). Neonicotinoid pesticides, like thiacloprid, guadipyr, and imidacloprid, are quite new and widely utilized insecticides (Goulson D. 2013), that were popular because of the minimal danger they posed to non-target organism (Jeschke P. et al 2005). However, research conducted in 2016 denoted that neonicotinoids are capable of accelerating the activity of aromatase, an enzyme involved in breast cancer, and also plays a vital part in its carcinogenesis timeline (Caron-Beaudoin E. et al. 2016).

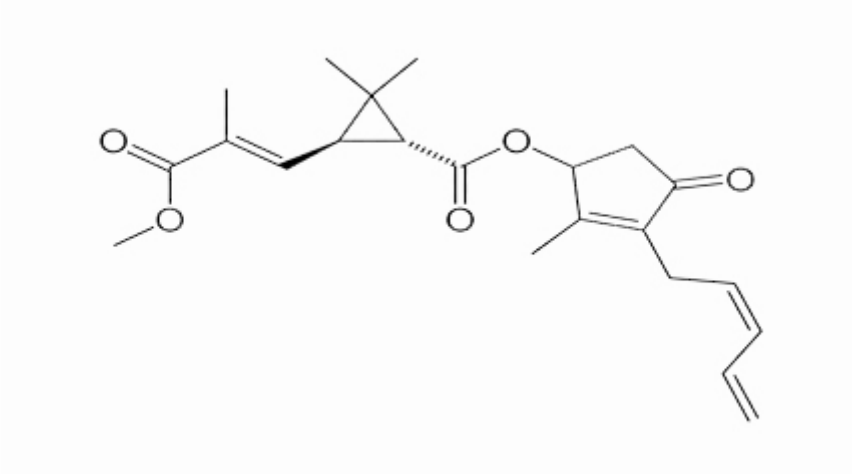

Figure 4: **Structure of Pyrethrin**

Food Additives and Contaminants

Chemicals are introduced into food for several reasons: as preservatives with antioxidants, antibacterial, or antifungal features; to modify physical properties, especially for processing; to adjust color; and to modify odor. In totality, food additives have been established to be innocuous and lack long term toxicity. Several of them were introduced at a period when toxicity testing was at its rudimentary; albeit, some of these have been afterward proven to be toxic, such as the type of the inorganic, the most important of which are nitrite and nitrate. Definitely, several of the food additives currently in use globally, lack proper testing. The issue of synergism among these compounds is poorly explored. Moreover, not all toxicants in food are artificial; there are some that are natural (Kotsonis F. N. et al. 2001).

Solvents

These are commonly found in the workplace although they can still be present in residences. In addition to cutaneous consequences, such as local irritation and defatting; several have systemic toxic impacts, such as impacts on the nerves or, as with benzene, on hematopoietic elements. The well-known solvents fall into the below classes (Bruckner J. V. et al. 2001).

Glycols and Glycol Ether: Ethylene and propylene glycols, for instance, in antifreeze give rise to significant exposure in the general population.

Aliphatic Hydrocarbons: like hexane. These may be straight or branched-chain compounds and often occur in mixtures.

Aromatic Hydrocarbon: Benzene is probably of greatest interest in this group; however, others, like toluene are also of public health interest.

Halogenated Aliphatic Hydrocarbons: The most popular examples are chloroform, carbon tetrachloride, and methylene dichloride; nevertheless, chlorinated ethylenes are also given wider attention.

Aliphatic Alcohols: Popular examples are methanol and ethanol.

Drugs of Abuse

Drugs of abuse (Fig. 5) can be defined as drugs that either have no medicinal importance or are used at dose concentrations that exceed the dosage needed for treatment. Albeit many of these substances alter only the higher nervous function like reaction time, coordination, and mood; some cause physical addiction and have consequential physical impacts, with fatal overdoses being a periodic phenomenon. This class of drug includes central nervous system (CNS) depressants, viz secobarbital, ethanol, methaqualone (Quaalude); CNS stimulants, like caffeine, nicotine, cocaine, and methamphetamine (speed); opioids, viz mependine (demerol) and heroin; and hallucinogens like phencyclidine (PCP), lysergic acid diethylamide (LSD), and tetrahydrocannabinol the most active component of marijuana (Brent J.A. 2006)

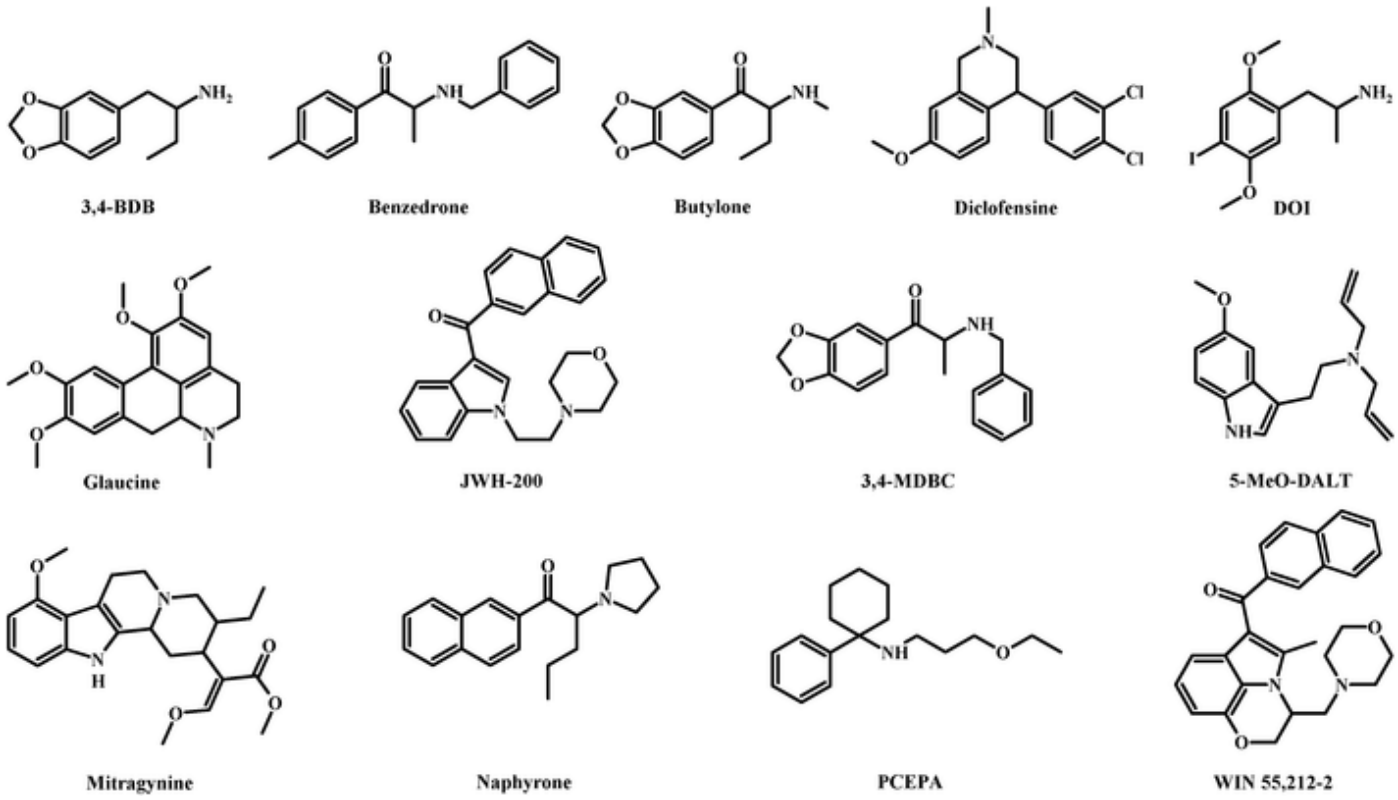

Figure 5: **Chemical structures of the investigated drugs of abuse**

Cosmetics

The well-known harmful upshots of modern cosmetics are sporadic allergic reactions and contact dermatitis. Although, the organometallics and aromatic amine dyes or azo employed in ancient times are now obsolete. Bromates and Thioglycerol applied in some cold-wave neutralizers and lotion may be markedly injurious if ingested; ditto ethanol applied as a solvent in perfumes and hair dyes. Applied as instructed, cosmetics seen to pose a limited risk of systemic poisoning, owing partly to the elimination of hazardous constituents in them and partly to the minute amount absorbed (Hodgson E. et al. 1994).

Combustion Products

Most air pollutants are from natural and man-made combustion. In terms of human health impacts, the most prominent are the Polycyclic Aromatic Hydrocarbons (PAHs). Albeit they are present in natural products like crude oil and coal, and commonly linked to incomplete oxidation of organic substances. Smoke from coal, wood, tobacco, and oil, for instance, in broiled foods also emits these contaminants. Due to the carcinogenicity of some of these substances, they have been studied diligently from the position of interactions with DNA, metabolic activation, and other facets of chemical carcinogenesis (Hodgson E. et al. 1994).

Toxicity of Some Selected Environmental Toxicants

Toxic Effects of Mercury

Mercury is a popular poisonous metal and its lethal is a frequent cause of acute heavy metal poisoning as reported by the American Association of Poison Control Centers with cases of 3,596 in 1997 (Jaishankar M. et al. 2014). Methylmercury is a neurotoxic compound that is liable for microtubule ruination, lipid peroxidation, mitochondrial impairment, and accretion of neurotoxic like glutamate, serotonin, and aspartate (Patrick L. 2002). It is postulated that 8 to 10% of American females possessed inherent mercury levels that may likely trigger neurological abnormalities in the infants they birthed, as enunciated by both the National Academy of Science and Environmental Protection Agency (Haley BE. 2005). Animal studies have affirmed that exposure to toxic mercury caused inimical neurological and behavioral modifications in animals. The primary target organ for mercury is the brain; although it can impair other organs and result in a defect in the muscles, nerves, and kidneys. It leads to derangement of the membrane potential and disrupts intracellular calcium homeostasis. Mercury attaches to free unconjugated thiols as the affinity constants are high (Patrick L. 2002). Mercury vapors can result in asthma, bronchitis, and short-term respiratory difficulties. Mercury contributes significantly to the damaging of tertiary and quaternary protein structure and modifies the cellular properties by binding to the selenohydryl and sulfhydryl groups that react with methyl mercury and disrupt the cellular structure. It also interferes with the transcription and translation process leading to the obliteration of ribosomes and destruction of endoplasmic reticulum and natural killer cells properties. In addition, compromise the cell integrity that results in free radical production (Jaishankar M. et al. 2014).

Toxic Effects of Lead

Lead metal brings about injury to the cellular component sequel by ionic mechanism and that of oxidative stress. Numerous studies have demonstrated that oxidative stress in biological systems is instigated by the disequilibrium between the free radical's generation and antioxidants production to neutralize the transitional or mend the outcome impairment (Sokan-Adeaga A.A et al. 2020; Jaishankar M. et al. 2014). The potential of lead metal ions to substitute other bivalent cations like Mg^{2+}, Ca^{2+}, Fe^{2+} and monovalent cations such as Na^{+} is primarily responsible for its ionic toxicity effects and resultant impairment of the metabolic activities in a biological system. Lead toxicity arising from ionic mechanisms is responsible for adverse alterations in diverse biological activities including protein folding, cell binding, apoptosis, intra- and inter-cellular signaling, maturation, protein folding, enzyme regulation, active transport, and neurotransmitter production. Lead has the capacity to replace calcium even at picomolar concentration altering protein kinase C, which modulates memory storage and neural excitation (Flora S.J.S. et al. 2008).

Toxic Effects of Arsenic

The toxic impacts of Arsenic can either be short or long-term. Chronic Arsenic Toxicity (CAT) is termed arsenicosis. Numerous reports of CAT in humans center on dermal externalizations due to its particularity in diagnosis. Keratosis and pigmentation are the unique skin aberrations that point to CAT (Martin S. et al. 2009). Lower exposure levels to arsenic can trigger gastrointestinal disorders, decreased blood cell production, irregular heartbeat, vascular vessel impairment, and prickling sensation at the extremities. Chronic exposure can result in the development of internal cancer, skin lesions, respiratory disease, neurological malignancies, hypertension, vascular disease, diabetes mellitus, and cardiovascular disease (Smith A.H. et al. 2000). Long-term arsenicosis leads to permanent modifications of the essential organs with an attendant high death rate. Despite the enormity of this imaginably deleterious toxicity, there is the absence of an effective remedy for this malady (Mazumder G. 2008).

Toxicity of Persistent Organic Pollutants (POPs)

The outcomes of acute and chronic exposure to POPs are still ambiguous. However, laboratory probing as well as environmental impact studies in the natural surrounding have stipulated that POPs can lead to immune and reproductive disorders, hormonal disruption, central nervous system (CNS) dysfunction, cancer and developmental anomalies. A few organochlorine chemicals are possibly carcinogenic by aiding tumor development. Polychlorinated Biphenyls (PCBs) (are a group of over 200 anthropogenic and artificial chlorinated and organic chemicals with the same basic chemical structure) are categorised as probably carcinogenic to man, while an additional eight of the 12 other POPs pinpoint in the Stockholm Convention are ranked as possibly carcinogenic to mankind. The leftover three – endrin, aldrin and dieldrin are grouped by the World Health Organisation as very deleterious (class 1b) owing to their short-term toxicity to laboratory animals. Fetuses and newborns are especially susceptible to POPs exposure because of the transmission of POPs from the mother during the crucial period of gestation. Susceptibility in the course of development has been associated with decreased immunity, CNS damage, developmental anomalies, and cancer/tumor induction or promotion in neonates and juveniles. The likelihood of causing human breast cancer has also been reported (Stober, J. 1998).

Tab. 2 depicted the list of 12 POPs that are humans' carcinogenic agents as highlighted by the International Agency for Research on Cancer during the Stockholm Convention.

Table 2: Classification of POPs according to International Agency for Research on Cancer

IARC Classification	POPs
Group 1: The agent (mixture) is carcinogenic to humans.	2,3,7,8-Tetrachlorodibenzo-para-dioxin (TCDD)
Group 2A: The agent (mixture) is probably carcinogenic to humans.	Mixtures of polychlorinated biphenyls (PCB)
Group 2B: The agent (mixture) is possibly carcinogenic to humans.	Chlordane
	DDT
	Heptachlor
	Hexachlorobenzene
	Mirex
	Toxaphene (mixtures of Polychlorinated camphenes)
Group 3: The agent (mixture or exposure circumstance) is unclassifiable as to carcinogenicity in humans.	Aldrin
	Dieldrin
	Endrin
	Polychlorinated dibenzo-para-dioxins (other than TCDD)
	Polychlorinated dibenzofuran

Toxicity of Polycyclic Aromatic Hydrocarbons (PAHs)

Each of the PAH compounds exhibits unique health outcomes (Rengarajan T. et al. 2015; Abdel-Shafy H. I. et al. 2016). Several PAHs are teratogenic, carcinogenic, mutagenic, and immunotoxin to innate beings, such as microbes, animals, and humans

(Burchiel S. W. 2014; Rengarajan T. et al. 2015; Rajpara R.K. et al. 2017). The manner of exposure, period, and dosage are crucial variables for determining the virulence of PAHs' toxic outcomes (Rajpara R.K. et al. 2017). Fatal outcomes of PAHs may differ based on variables such as age and underlying health state. Short-term health impacts include regurgitation, eye soreness, disarray, skin irritation, diarrhea, and inflammation (Abdel-Shafy H. I.et al. 2016). Anthracene, benzo(a)pyrene, and Naphthalene are explicit skin irritants and skin sensitizers for animals and humans (Rengarajan T. et al. 2015). Long-term impacts are renal and hepatic derangement, eye cataracts, respiratory distress, pulmonary dysfunction, asthma-like symptoms and compromised immunity (Abdel-Shafy H. I.et al. 2016). Naphthalene can bring about the degradation of erythrocytes if inhaled or ingested in large quantities (Rengarajan T. et al. 2015).

Overview of Phytochemicals

What are Phytochemicals?

The term 'phytochemicals' refers to a perplexing number of small molecules from plants, which can be categorized into diverse marked classes based on their biosynthetic origin and structure. On a wider definition, it means plant (Phyto) chemical denoting a large diversity of compounds that are found in plants naturally. A great many bioactive phytochemicals occur in popularly consumed plant foods and products. Broadly, these compounds can be classified into six main categories based on chemical structures and properties. These groups are carbohydrate, lipids, terpenoids, phenolics, alkaloids, and other nitrogen-containing compounds (Campos-Vega R. et al. 2013). Each group can be subdivided based on biosynthetic origin or biogenesis into different subgroups. Contemporarily, the word 'phytochemical' has been employed to differentiate plant chemicals that do not satisfy the traditional meaning of 'essential nutrients. Many of these phytochemicals trigger reactions in living organisms, including humans, by expressing both therapeutic and prophylactic features that have been associated with the provision of nutrient for normal cell growth and repair, impede carcinogens and acts as antioxidants, and declines the risk of major non-communicable chronic diseases (Ogunwenmo K.O. et al. 2007; Ngoci S.N. 2011).

Phytochemicals wield their medicinal prowess by acting synergistically or additively and this nullifies the precarious outcomes linked to the high usage of a mono xenobiotic compound, thus giving the herbal drug(s) a broad spectrum of activity, in addition to diminishing the probability of the pathogens developing resistance or adaptive responses (Briskin D.P. 2000, Olila D. et al. 2001). Some phytochemicals are enunciated in the subsequent sub-section.

Classes of Phytochemicals

Flavonoids: are structural derivatives of flavones (Fig. 6). Consisting of conjugated aromatic systems, often bind to sugar(s) as glycosides, and they are phenolic and hydrophilic in nature (Harborne J.B. 1973). Flavonoids are a vital class of natural products; they are in the group of plant secondary metabolites possessing a polyphenolic structure, and are generally found in vegetables, fruits, and some beverages (Ovando C. et al. 2009). Flavonoids are linked with a wide range of health-enhancing properties and are invaluable constituents in diverse pharmaceutical, nutraceutical, cosmetic and medicinal applications. This is due to their anti-inflammatory, antioxidative, anti-carcinogenic and anti-mutagenic characteristics coupled with their ability to regulate vital cellular enzyme functions. Likewise, they are regarded as powerful inhibitors for numerous enzymes, viz cyclo-oxygenase (COX), xanthine oxidase (XO), phosphoinositide 3-kinase, and lipoxygenase (Metodiewa D. et al. 1997). Flavonoids have numerous subgroups, such as flavones, isoflavones, flavanones, chalcones, flavanonols, flavonols or catechins, chalcones, and anthocyanins. These subgroups have distinct major sources (Panche A.N. et al. 2016). Flavonoids lacking hydroxyl (-OH) on their structure are more potent against microbes vis-à-vis those with –OH, and this corroborates the fact that their target in microbes is the membrane (Ngoci S.N. 2011).

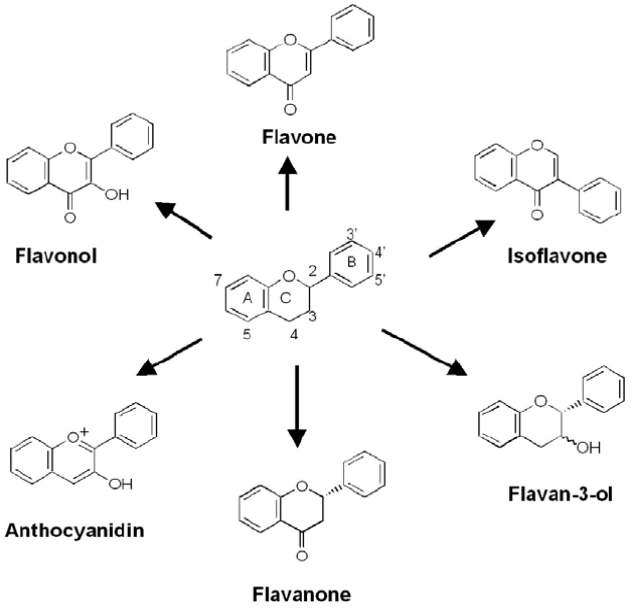

Figure 6: General Structure of Flavonoids

Tannins: these are caustic, pungent phenolic compounds that either coarse or precipitate or contract proteins. They consist of numerous groups of oligomers and polymers. They can adhere to cellulose, minerals, proteins and starch to form complexes. Tannins are hydrophilic compounds with the exclusion of some higher molecular weight structures. Tannins are generally categorized into two groups namely: hydrolyzable tannins such as elligatannin, complex tannins, proanthocyanidins, and gallotannins; and condensed tannins (Fig. 7). These compounds are usually found in both gymnosperm and angiosperm. They have been discovered in 180 families of dicotyledons and 44 families of monocotyledons. Tannins are commonly found in the following families of plant species: Actinidiaceae, Burserarceae, Bixaceae, Anacardiceae, Dipterocarpaceae, Combertaceae, Grossulariaceae, Ericaceae, Myriacacea for dicotyledons; whereas Typhaceae and Najadaceae for monocotyledons. They exhibit their physiological function by behaving as antioxidants via free radical scavenging action (Navarro M.C. et al. 2003; Ngoci S.N. 2011) thus regulating oxidative stress and averting deteriorating illness. They also hinder tumor growth by activating cell death (Scalbert A et al. 2005) and impeding the mutagenicity of carcinogens (Okuda T. 2005.; Ngoci S.N. 2011).

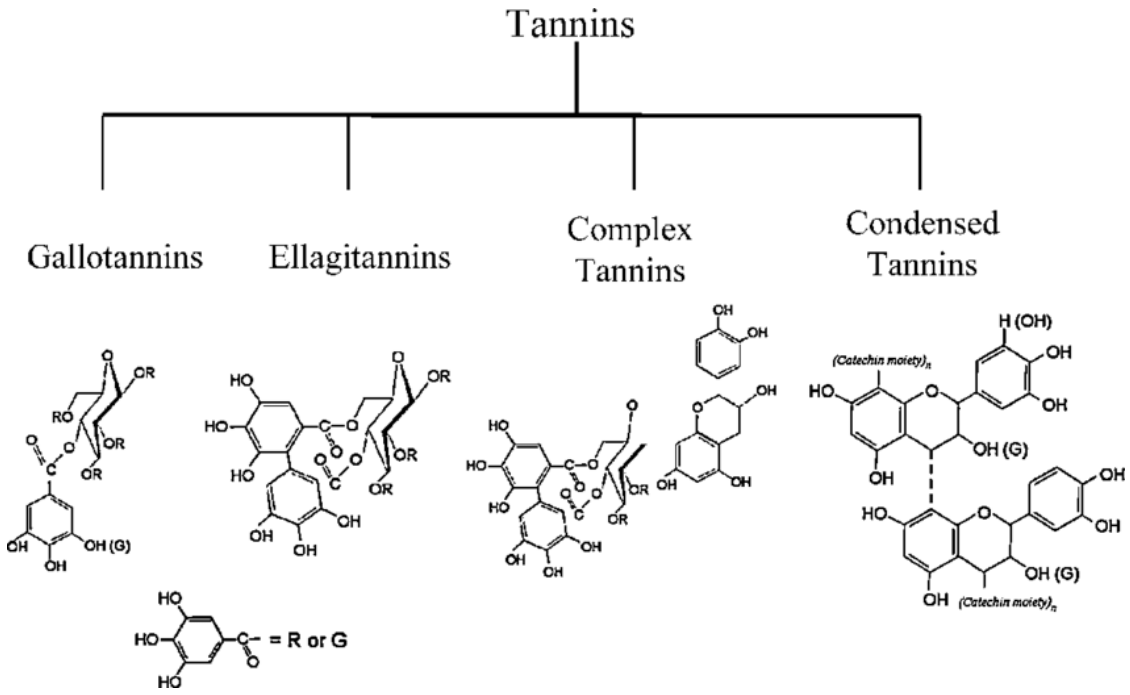

Figure 7: **Main chemical structures of the tannins**

Saponins: refer to a group of bioorganic compounds that are found largely amidst plant biodiversity. More precisely, they are naturally occurring glycosides with soapy properties, and as a result, they generate bubbles when agitated in aqueous solutions (El Aziz M.M.A. et al. 2019). Structurally saponins possess one or more hydrophilic glycoside sugar moieties (Fig. 8), aggregated with a lipophilic triterpene molecule (Vasudeva R.N. et al. 2015). Studies depict that saponins exercise biological function and therapeutic effects like hemolytic factor, anti-inflammatory, antifungal, antibacterial, antiviral, anticancer, cytotoxic, molluscicidal and insecticidal action (Hassan S.M. et al. 2010; Sparg S.G. et al. 2004; Cheng T.C. et al. 2011). The saponin molecule undergoes hydrolysis to give rise to two fragments, an aglycone and a sugar moiety. Isolated amorphous solid saponins have large molecular weight, and contain 27 to 30 carbon atoms in the non-saccharide fraction (the hydrocarbon skeleton part lacking a sugar chain). This non-saccharide segment referred to as sapogenin, aglycone, or genin. Based on the kind of sapogenin available, the saponins can be segregated into three distinct groups: triterpenoid glycosides, steroid glycosides, and alkaloid glycosides (Hostettmann K. et al. 2005). The second partition i.e. the saccharide moiety – consists of heterogeneity of pentoses or hexoses (El Aziz M.M.A. et al. 2019).

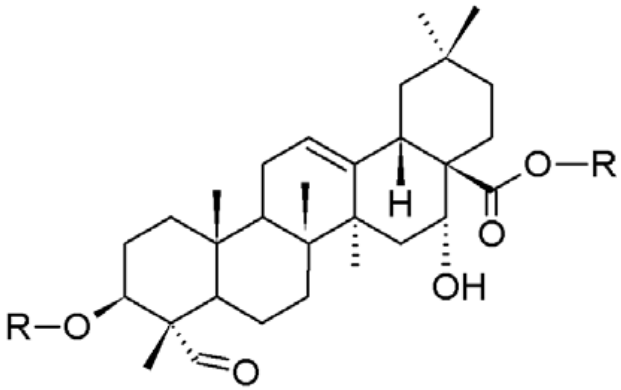

Figure 8: **Generic structures of saponins. R= sugar moiety**

Alkaloids: These are a large class of naturally existing organic compounds with nitrogen atom or atoms (amino or amido in certain instances) in their structures often located in some cyclic or ring configuration (Fig. 9). The presence of nitrogen in these compounds is responsible for their alkalinity. Broadly, based on structure, alkaloids can be classified into groups like quinolones, pyrrolidines, isoquinolines, indoles, tropanes, steroids, pyridines, pyrrolizidines, and trepenoids. Another categorization modality is based on the family of plant species in which these substances are found. A typical example is the opium alkaloids that are found in the opium poppy (Papaver somniferum) (Kurek J. 2019, Chisholm H. 2015). These two dissimilar classification systems create a disparity between their biological distribution and the chemical varieties of alkaloids because there is no distinctive connection. In its pure form, alkaloids are often odorless, crystalline solids, colorless, although often yellowish and have an astringent taste at times. Presently, over 3000 alkaloids are identified in more than 4000 diverse plant species. Alkaloids are a fascinating class of compounds with a divergent range of functionalities in man and animals. Alkaloids have various physiological outcomes: antimitotic, local anesthetic, antibacterial, psychotropic, analgesic, hypnotic, antitumor, anti-inflammatory and several others. Popularly known alkaloids are caffeine, nicotine, ephedrine, strychnine, quinine, atropine, and morphine (Kurek J. 2019, Chisholm H. et al. 2015).

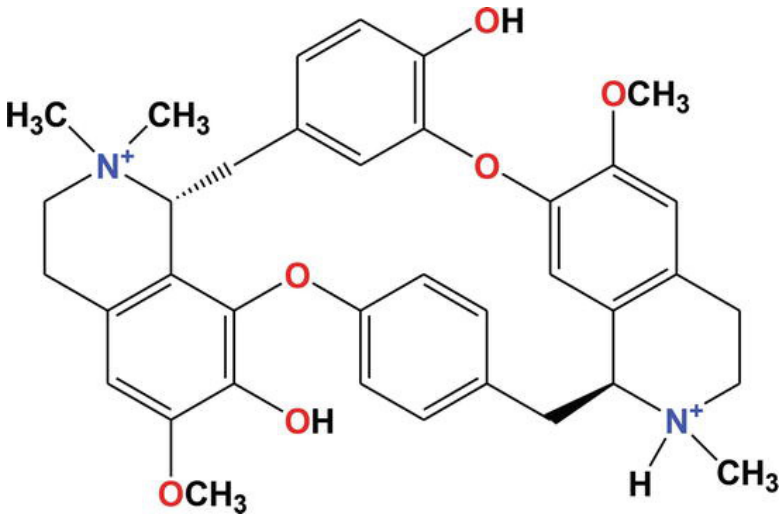

Figure 9: General structure of Alkaloids

Cardenoloids: These are also known as cardiac glycosides and they consist of the most drug-like molecules subjugated to numerous examinations and were affirmed to be effective in manufacturing efficacious drugs (Prassas I. et al. 2005; Nagy Morsy. 2017). These groups are liable for being virulent to livestock and serve as therapy for congestive heart failure. Cardenoloids are steroids capable of exerting a precise forceful effect on the myocardia. A minute quantity can affect a salubrious simulation on an ailing heart. These compounds are beneficial in the treatment of congestive heart failure, flatter, atrial fibrillation, and they behave as emetics and as diuretics (Ngoci S.N. 2011). They speed the force of contraction in the heart, which is incapable of meeting the rise in oxygen expenditure. As a result, the myocardium acts a potent pump and is capable of satisfying the need of the vascular system (Nagy Morsy. 2017; Kelly RA. 1990). Cardiac glycosides consist of two distinct categories of compounds that vary in their aglycone structure (Fig. 10). They may be C23 or C24 steroids with a primary nucleus of cyclopentanoperhydro phenanthrene substituted at C17. Cardenolides possessed a five-membered lactone group in the C17 with α,α- unsaturated αlactone ring (butenolide), while the other class, the bufadienolides, was first identified in toad as skin lethal. The C17 substituent has a doubly unsaturated six-membered lactone ring (αpyrone). Plants are capable of producing both cardenolides and bufadienolides. A different group is isocardenolides, which possessed a double bond of butenolide ring at position 21 or 22 rather than at position 20. Most clinical interests were pointed to the cardenoloides due to their medicinal importance. The two commonly utilized digitalis inotropes are Digoxin and digitoxin. Generally, most isocardenolides lack any cardiac activity (Nagy Morsy. 2017).

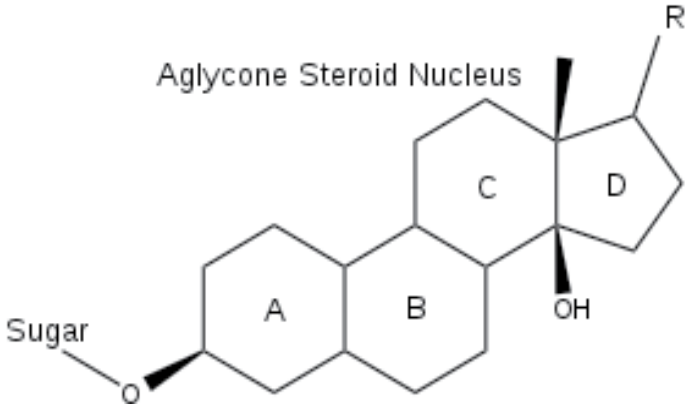

Figure 10: Structure of Cardiac glycosides

Terpenoids: Otherwise called isoprenoids, are a wide and divergent class of naturally existing compounds whose precursors are five carbon isoprene units (Fig. 11). Terpenoids distinguished from one another by their basic skeleton and functional groups. Terpenoids are ubiquitous; hence, they occur virtually in all living beings. They add to the scents, color, and flavor of plant's flowers, leaves and fruits. Terpenoids are also crucial for plant growth and development. The terpenoids generated by plants not only safeguard them from insects and predators but also offer defense from fungal diseases and infections, while in animals, terpenoids serve as precursors of steroids and sterols. Terpenes are simple hydrocarbons, whereas terpenoids are an adjusted class of terpenes with varying functional groups and oxidized methyl groups oscillating at different positions. Terpenoids are categorized into monoterpenes, sesquiterpenes, diterpenes, sesterpenes and triterpenes based on their carbon units. Terpenoids differ in structures and are biologically viable and utilized globally for the therapy of numerous maladies. Several terpenoids impeded diverse human cancer cells and are employed as anticancer medicines such as Taxol and its derivatives. Terpenes and its derivatives are utilized as antimalarial drugs such as artemisinin and associated compounds. They performed various functions viz anti-fungal, anti-protozoan, anti-bacterial, anti-allergens, anti-viral, immune boosters and antineoplastic (Perveen S. 2018; Nagy Morsy. 2017; Roberts S.C. 2007).

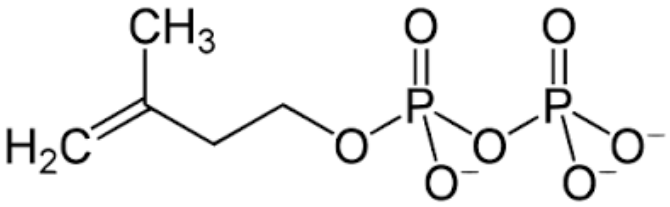

Figure 11: Structure of Terpenoids

Phytosteroids: these are groups of specialised metabolites obtained from plants that are attached to steroid receptor in animals and can activate or suppress downstream receptor-mediated signaling events. Phytosteroids (Fig. 12) have varying structures, occasionally very dissimilar from the endogenous steroids; however, they behave as antagonists, agonists, or habitually exhibit mixed agonist/antagonist properties for steroid receptors (Lesovaya E. et al. 2015; Toh M.F. et al. 2014). Furthermore, some phytosteroids interrelate with several steroid receptors (Pihlajamaa P. et al. 2011) or hamper steroid metabolizing enzymes (Blachley J.D. et a. 1980), hence exhibiting complicated impacts on the reproductive and hormonal systems. They possess a similar basic cyclic configuration to animal steroids however they differ due to different chemical groups attached to the central ring in various positions (Nagy Morsy. 2017). They are basically used in the treatment of reproductive ailments viz treatment of sexually transmitted diseases, enhance fertility in women and sex drive in males, and ensure safe parturition. They also behave as sex hormones derivatives and thus they are a possible sources of contraceptives (Nagy Morsy. 2017; Edeoga H.O. et al. 2005; Hostettmann K. et al. 2005). They are also analgesic, anti-microbial, anti-inflammatory, and of use in curing of stomach complications and in reducing serum cholesterol levels (Nagy Morsy. 2017, Hostettmann K. et al. 2005). Phytosteroids are marked as powerful inhibitors of macrophage activation, impeding the generation of pro-inflammatory cytokines and LPS-induced fatality and consequently they can act as immunosuppressive agents particularly the physalins.

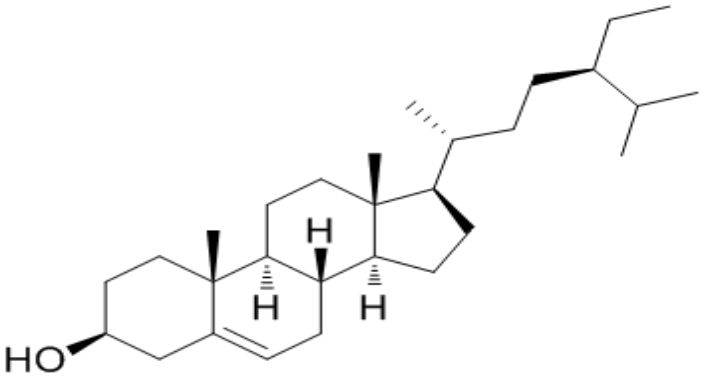

Figure 12: Structure of Phytosterol

Interventional Roles of Phytochemicals on Various Toxicity Outcomes

Intervention in Oxidative Stress, Metabolic Syndrome and Aging

It has been known since antiquity that natural products prolonged the life-span of an organism (Dias D.A et al. 2012). Epidemiological and laboratory studies suggested these compounds to be potent antioxidants that ameliorate stress-related ailments. Various studies have postulated the efficacy of these compounds in metabolic symptoms and ageing (Patti A.M et al. 2018; Tabatabaei-Malazy O et al. 2015). Consequently, comprehensive preclinical assessment on the fundamental pharmacology of these natural compounds may serve as strong scientific basis for clinical implementations. Polyphenols and most especially flavonoids have been proven to offer protection from several age-associated morbidities (Truong V.-L et al. 2018). Numerous studies

have shown that augmentation with dietary polyphenols like (-)-epigallocatechin-3-gallate (EGCG) and curcumin can enhance age-related cellular impairment by decreasing production of reactive oxygen species (ROS) (Queen B. L et al. 2010). Conversely, resveratrol and pterostilbene are regarded as outstanding anti-aging chemicals that can regulate oxidative destruction, cell aging, and inflammation; constituents linked with aging (Li Y.R et al. 2018), including flavonoids which is proven to aid anti-aging primarily by regulating metabolic syndrome (Prasain J. K et al. 2010).

A few of the proven flavonoids that can handle factors linked to senescence or metabolic syndrome are naringin, hesperidin, and naringenin (Alam M. A et al. 2014). Importantly, there is an increase in the data bank of preclinical application of phytochemicals in the therapy of diverse conditions attributed to senescence. Nevertheless, certain limitations exist to their applications such as option of experimental models that is clinical pertinent, nebulous elucidated mechanism of action, and appropriate dosage and duration for data interpretation.

As Anti-Cancer Agent

Despite significant progress having been made, some tumour pose poor prognosis and study is still ongoing toward the utilisation of innocuous doses of plant-extracted substances. The innovation to treatment strategy due to natural molecules and drugs was instigated by the recognition and application of natural chemotherapeutic substances vis taxanes, anthracyclines, and vinca alkaloids (Nobili S et al. 2009). Thus, it is reasonable to postulate that compounds in food presumably have some protective impacts.

Intriguingly, contemporary research findings suggest an increasing function of polyamines metabolism as an innovative approach against inflammatory ailments. Polyamines are naturally occurring aliphatic compounds, ever-present in all living thing, which interface with nucleotides and proteins and are needed for the growth, viability and specialisation of eukaryotic cell (Hussain T et al. 2017; Forni C et al. 2019). Based on the aforementioned roles, polyamines metabolism constitutes an intriguing target for anticancer treatment (Lentini A et al. 2010). Hence, the application of various natural substances, especially polyphenols, emanating from plants constituents may produce auspicious outcomes in antitumour treatment due to their anti-oxidant properties (Mao X. Y et al. 2018). Interestingly, it has been shown that high flavones intake, particularly quercetin and kaempferol, is capable of inducing a significant decrease in serum IL-6 concentration, a popular inflammation-associated cytokine (Bobe G et al. 2010). Likewise, curcumin depicts anti-inflammatory and antioxidant characteristics, and prospective anti-cancer property (Anand P et al. 2007). Genistein a soybean isoflavone, has exhibited antitumour property in diverse types of cancer including chronic lymphatic leukemia and neuroblastoma and in diverse organs like ovary, prostate, breast, colon, urinary bladder, stomach, and stomach (Mukund V et al. 2017). Genistein is regarded as a phytoestrogen because of its structural similarity with mammalian estradiol. Numerous studies have shown the consequential function of isoflavone in the prevention of cancer development in animal models. Indeed, it is proven that dietary soy supplementation mitigate inflammation associated with prostate carcinogenesis (Lesinski G. B et al. 2015). Another popular anticancer agents possessing both anti-inflammatory and antioxidant feature is lycopene that exhibits treatment actions on numerous tumours (Carini F et al. 2017). Specifically, it has been established that lycopene ingestion hinders the development of cancer (Rowles J. L et al. 2017). The recognition of the importance of these natural compounds to the advancement of cancer treatments are well documented nonetheless it is crucial to conduct more meticulous researches and preclinical studies to shed more light on their prospective chemopreventive and antitumour activities.

As Therapy for Vascular Diseases

In this review, we shall discuss only the therapeutic impacts of omega 3 Polyunsaturated Fatty Acids (PUFA) and the flavonoid resveratrol due to their prevailing effects on Senescence-Associated Secretory Phenotype (SASP), vascular dysfunction, and Cardiovascular Disease (CVD).

The effects of omega 3 PUFAs are ascribed to their lower lipid effects which help to decline atherosclerosis development (Wahle K. W. J et al. 2004). Omega 3 PUFAs have been demonstrated to mitigate vascular inflammation by down-regulating adhesion molecules and restricting leukocytes binding to the wall of blood vessel (Baker E. J et al. 2018). This latter explicitly sways endothelial-derived nitric oxide production owning to stabilization of lipid rafts like the endothelial cells caveolae, as shown in retinal endothelial cells (Colussi. G et al. 2017). Nevertheless, the laboratory studies seem to corroborate PUFA's beneficial roles vis-à-vis the clinical proof. Actually, the omega 3 PUFA outcomes on aggrandised endothelial regenerative ability and preservation of vascular endothelial cells homeostasis by virtue of membrane stabilizing potential were marked to have consequential effects on CVD prevention (Colussi. G et al. 2017). A well-detailed appraisal of the literature recently displayed on Cochrane Database Systematic Review (Abdelhamid A. S et al. 2012), encapsulated the findings of numerous randomized clinical trials investigating the impacts of varying doses of PUFA on CVD manifestations. Findings from this survey depicted that higher PUFA intake only moderately lessen risk of coronary heart disease and CVD acute events (i.e., stroke), but in generality has no important influences on its outcomes. A large number of the positive outcomes were linked to modulation of lipid metabolism (Scalbert A et al. 2005). Anyway, even a little but notable decline in 10% of morbidity and death for CVD linked to PUFA supplementation remains a momentous clinical outcome (Kones R et al. 2018). Conclusively, other phytochemicals with antioxidant properties have been highlighted to contribute a protective action to CVD development and consequently were recommended as significant substances in diet, for example like, αcarotene,curcuma, and others (Gammone M. A et al. 2018; Zhang H et al. 2018). Specifically, numerous studies underscore the anti-atherogenic role of lycopene in relation with the interdiction of proinflammatory cytokines release (Gammone M. A et al. 2017).

Role as Anti-Inflammatory

It has been demonstrated that natural compounds influence numerous pro-inflammatory mediators. Herbal medicines, nutraceuticals, or beneficiary foods with anti-inflammatory properties, can be utilised as an adjunct to anti-inflammatory drugs resulting in the decline of their consumption, leading to the mitigation of their side effects. A comprehensive review on the anti-inflammatory properties of phytochemicals has been done by several researchers (Howes M. J. R et al. 2017). Various anti-inflammatory mechanisms have been linked to numerous flavonoids with diverse chemical configurations (Gomes A et al. 2008). Glycosides of apigenin and luteolin are widely distributed flavones (King H. G. C et al. 1962). Apigenin subdue nitric oxide (NO) and prostaglandin production through hampering of inducible nitric oxide synthase (INOS) and COX-2, appropriately (Raso G. M et al. 2001). Luteolin was also demonstrated to impede chronic inflammation by in vitro co-culture of adipocytes and macrophages and the phosphorylation of Jun N-terminal kinases (JNK) in macrophage (Hirai S et al. 2010). The most efficacious tumor necrosis factor - α(TNF-α) inhibitors among the flavonoids are luteolin and quercetin (Xagorari A et al. 2001). The anti-inflammatory potency of quercetin was clinically assessed in female with rheumatoid arthritis showing an important impact in modulating inflammation and clinical manifestations (Javadi F et al. 2017). In spite of their function in the production of TNF-α green tea extract has also been shown in contemporary clinical trials to have anti-inflammatory and immunomodulatory properties in autoimmune disease (Shamekhi Z et al. 2017). Consequently, although these compounds cannot replace anti-inflammatory drugs, such as the Disease Modifying Anti-Rheumatic Drugs (DMARDs), but they significantly aid to the decline in their dosage, leading to less costly and innocuous treatment strategy of autoimmune diseases and other inflammation-associated morbidities.

Neurodegenerative Diseases Prevention

Presently, there is no panacea treatment for neurodegenerative diseases (NDD), and, in a bid to discover new treatment or adjuvant approach for NDDs, numerous natural medicinal plants have attracted interest as prospective neuroprotective agents, and several researches have alluded to the fact that a diet enrich with vegetable products can avert or prolong the initiation of NDD (Joseph J et al. 2009). These attributes may be associated to the presence of polyphenols, a crucial group of phytochemicals that are readily found in vegetables, beverages, fruits, and cereals. In this section we shall discussed the auspicious role of certain phytochemicals in the prevention and treatment of NDD, as illustrated by selected evidence-based studies.

Numerous studies have established that resveratrol possessed important neuroprotective feature both in vitro and in vivo (Granzotto A et al. 2011; Yan W et al. 2018). In vivo, in a mouse model with cerebral amyloid accumulation, orally administered resveratrol lessen microglial activation related to cortical amyloid plaque development (Capiralla H et al. 2012). Moreover, chronic dietary resveratrol decrease cognitive damage and perform a neuroprotective role, reducing the amyloid load and decreasing tau hyperphosphorylation in SAMP8 mice, a model of age-associated Alzheimer's disease (AD) (Porquet D et al. 2013). Rising evidence has also submitted that resveratrol confers increased advantages to cell and animal models with Parkinson's disease (PD) (Zhang F et al. 2010). Curcuminoids comprise three components: curcumin (75%-805), demethoxycurcumin (15%-20%), and bisdemethoxycurcumin (3%-5%). Curcumin also trigger neuroprotective outcomes via the regulation of pathogenetic oxidative and inflammatory actions both in vitro and in vivo models of AD and PD. In Neuro2a mouse neuroblastoma cells infected with Japanese encephalitis virus, curcumin promotes cell activity by reducing reactive oxygen species (ROS) and hindering proapoptotic signals (Dutta K et al. 2009). Pretreatment of primary hippocampal cultures with quercetin substantially diminished Aα(1-42)-induced cellular toxicity, lipid peroxidation, protein oxidation, and cell death by regulating oxidative stress (Ansari M. A et al. 2009). More captivatingly, quercetin diminishes extracellular αamyloidosis, astrogliosis, microgliosis, and tauopathy in the hippocampus and the amygdala and enhances execution of learning and spatial memory burden in old triple AD model mice (Sabogal-Guaqueta A. M et al. 2015). Aggregating, the above findings, point to polyphenols as neuroprotective agents. The addicted consumption of dietary polyphenols is validated to impede diverse secondary sources of ROS and proinflammatory cytokines, hence mitigating of NDDs (Gardener H et al. 2018). An advantageous clinical utilisation of polyphenols to lessen oxidative impairment in senescence and age-associated ailments may be a potent and auspicious strategy for NDDs therapy.

As Powerful Antioxidant Agents

The first antioxidant molecule identified is ascorbic acid, also known as vitamin C, which is generated in the course of aerobic metabolism, and react rapidly with O_2^*, singlet oxygen and ozone (chemically), and H_2O_2 (enzymatically) via ascorbate peroxidase to detoxify their deleterious effects. Aside this, in plants, such acids likewise take part in the regeneration of carotenoids and vitamin E (tocopherol). The latter can also behave as antioxidant and vital liposoluble redox system, serving as protection against lipid peroxidation (Foyer C.H et al. 2005). Carotenoids, which are potent antioxidants, are responsible for several colouring in fruits, flowers and leaves; and they are involved in the scavenging of peroxyl radicals through quenching (Jomova K et al. 2013; Stahl W et al. 2003).

Phenolic compounds are one of the most auspicious molecules for advancing salubrity studies. These phytochemicals comprise of a wide diversity of molecules (circa 8000 numerous structures), playing essential functions in the metabolism of the plant (Hassan S et al. 2012), where they are largely distributed. The far-ranging of organic activities of phenolics, one of which is antioxidant and antitumour characteristics, is widely established in different studies (Foyer C.H et al. 2005; Moran J.F et al. 1997). The existence of at least a single phenol ring is vital for such role, with methyl, hydroxyl, or acetyl groups substituting the hydrogen. An elevated antioxidant function has been linked to the increased number of free hydroxyls and conjugation of side chains to aromatic rings (Moran J.F et al. 1997). Terpenoids constitute additional huge family of plant secondary metabolites (Jomova K et al. 2013). *In vitro*

assays depicted that sesquiterpenes, monoterpenes, and diterpenes derived from aromatic plants have significant antioxidant activity (Stahl W et al. 2003). The hypoglycemic and antioxidant property of alkaloid - vindoline, vindolicine, vindolinine, and vindolidine, gotten from Catharanthus roseus leaves, have also been highlighted (Hassan S et al. 2012).

Therapeutic Effects on Skin Pathologies

According to the European Medicines Agency, 12 herbal substances, preparations, and mixtures are used as traditional herbal medicinal products. These herbal substances include - *Foeniculum vulgare, Sideritis scardica, Valeriana ofcinalis, Echinacea purpurea, Hamamelis virginiana, Tymus vulgaris, Vitis vinifera, Eleutherococcus senticosus, Melaleuca spp., Calendula ofcinalis, Mentha spp., and Pimpinella anisum.* Their inclusion inside such official list is maintained by scientific evidence denoting their treatment efficacy in several diseases conditions vis basal cell carcinoma, carbuncle, allergy, cellulitis, acne, eczema, impetigo, chickenpox, hives, dermatitis, melanoma, rosacea, vitiligo, wart, psoriasis, impetigo, lupus, measles, blister and squamous cell carcinoma (Forni C et al. 2019; Aharoni A et al. 2005; Baratta M.T et al. 1998; Tiong S.H etal. 2013).

A meta-analysis published show *Vitis vinifera* as an efficacious constituent of medical accessory beneficial in the therapy of local atopic dermatitis (Micali G et al. 2018). Intriguing outcomes have also been reported in oncological circumstances; *Vitis vinifera* has demonstrate some effectiveness in decreasing radiotherapy-induced dermatitis (Franco R.D et al. 2013) and in impeding cell multiplication in melanoma and skin non-melanoma cancer (Turk S et al. 2017), denoting grape seed proanthocyanidin as an apoptosis and autophagy inducer. Limited allergic reactions are enunciated for *Vitis vinifera* (Brito F.F et al. 2008). In comprehensive elucidation, local utilisation of *Melaleuca alternifolia* derieved oils has been persistently aired to attain a notable amelioration of acne lesions, as reported by numerous autonomous studies (Hammer K.A et al 2015). The clinical efficiency of Melaleuca oil is possibly associated to its familiar antibacterial mechanism (Kwon H.H et al. 2014) in addition to anti-inflammatory action (Ramage G et al. 2014). The essential oil from *Melaleuca alternifolia* also depicts antioxidant properties probably efficacious in dermatitis and skin cancers (Pazyar N et al. 2013). Therapeutic benefits to skin diseases are suggested for *Agrimoniae herba* (*Agrimonia eupatoria*; in secondary inflammation and superficial lacerations), *Echinacea purpurea* (in modest perfunctory wounds and mild acne), *Soiae oleum* (*Glycine max*; in benign periodic eczema), *Juglandis folium* (*Juglans regia*; in minor skin irritation), *Matricariae aetheroleum* (in anus and genitals inflammation), *Matricariae fos* (*Matricaria recrutita*; in mild skin allergies and sunburns and superfcial wounds), *Melaleuca spp.* (in insects bites, mild acne, prickling, lesser skin irritation), *Meliloti herba* (*Melitotus ofcinalis*; in minor skin inflammation), *Origani dictamni herba* and *Origani majoranae herba* (*Origanum spp.*; in petty skin irritation and inflammation). Several others phytochemicals are reported in literature with prospective effects on skin, such as anti-senescence property (Sundaram I.K et al. 2018), photoprotection (Prasad R et al. 2017), wound recuperation (Sarandy M.M et al. 2017), and anti-infection (Houston D.M.J et al. 2017).

Conclusions

The review critically highlights the environmental pollutants and their toxicity on living organisms. It also delves into several classes of phytochemicals and their prophylactic and therapeutic interventions in various maladies challenging humanity. This review enunciates that environmental contaminants are generated from both natural and anthropogenic activities, and they become deleterious to the environment and pose a risk to living things when they bioaccumulate above their threshold limits. They are of significant public health interest across the globe, due to their indispensable role in the pathophysiology of several human diseases. Several remediation techniques and treatment measures employed towards mitigating the outcomes effects of environmental toxicity to humans are characterised by one or many limitations; which make the exploitation of phytochemicals a global interest. Phytochemicals are secondary metabolites found in plants and are popular for their numerous pharmacological and medicinal properties. Hence, they exhibit anti-inflammatory, anti-metastatic, anti-oxidant, immune-modulative, nutritive, prophylactic, anti-microbial and life-saving properties. We believe that in order to avert the unsustainable use and over exploitation of these medicinal plants, it is necessary to enforce sustainable utilisation and legal production of medicinal concoction from these plants for the benefit of humanity. Moreover, there is a need for extensive studies about the optimisation and large-scale production of medicinal formulation from these phytochemicals.

Author Contributions

AASA conceived the concept. AASA, MASA, and EDSA were involved data sourcing and collation. AASA, MASA, and EDSA wrote the initial draft and revised the manuscript. ANO, HE, EOT, FAB and MA critically revised the manuscript. All authors read and approved the final version of the manuscript.

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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