

Pesticides responsible for different types of cancer in human: An overview

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Abstract :- Synthetic pesticides are responsible for causing cancer in humans. Some pesticides like organophosphates and organochlorines are responsible for causing cancer and some other toxic effects in the humans. Different pesticides are responsible for different types of pesticides like DDT causing breast cancer, Bifenthrin causing Prostate cancer etc. Governments of India and other countries had given guidelines for the use of pesticides and they also banned some pesticides which are very dangerous and causing some serious effects on human health. Every class of pesticides have different mechanism of action of causing cancer. So, in this review article we will come to know about the types of pesticides and their mechanism of causing cancer in human beings. Guidelines issued by the government for the use of pesticides should be seriously considered by the people for the proper use of pesticides. List of pesticides are banned by the government due to their toxic effects on the human beings. WHO had also banned some pesticides because of their oncogenic effect, and it also provides the amount of pesticides should be use for crop production.

Keywords: Pesticides, Cancer, Guidelines by government, Banned pesticides.

INTRODUCTION

Pesticide: -

Pesticides are widely utilized in agriculture, other workplaces like industries, hospitals, institutions and households. Epidemiologic corroboration on connection between pesticides and cancer is reported in the literatures (references). Because of extensive uses of the pesticides in agriculture and industries and households are contaminated in the environment, food. They are found as a residual in the above said items. Some adulterants in pesticide formulations also may induce a carcinogenic risk. In humans, heavy metal compounds and insecticides used in manufacturing industries and in fields are classified as cancer causing agents by International Agency for Research on Cancer, UK.

The variety of chemicals utilized in pesticides, and possible co-factors resulting in cancer exposed to pesticides, make it impossible to determine direct link between pesticide and cancer. Also, no sufficient evidence found to culminatively show there's no link between pesticide exposure, either through direct chemical or residual contact, and cancer. Hence, additional epidemiologic studies needs to be done with detailed exposure evaluation for individual pesticides, taking into consideration work practices, use of protective equipment, and other measures to scale back risk.

Pesticides are chemical substances which are used to control pests such as fungus, virus, bacteria, nematodes etc. Pesticide is a broad term which includes herbicides, insecticides, rodenticide, bactericide etc. Pesticides are also known to exert some toxic effects to humans like Cancer. Some of the pesticides which are responsible for cancer are DDT, Butylate, Diazinon, and Chlordecone. Types of cancer which are caused by these pesticides are Pancreas cancer, Prostate cancer, Lung cancer, Prostate cancer, respectively.

Pesticides ideally are lethal to its targeted pests and have little to no effect on non-targeted species, however use of some Pesticides are sometimes hazardous to human and animals health that is why to keep use of different pesticides in check, most of the healthcare institutes issues list of Pesticides which could possibly pose unexpected risks to our health. Based on the active ingredients we determine how hazardous a particular pesticide would be to our health.

Cancer: -

Throughout the life of a human the healthy cells divide in a controlled manner and replace themselves with the new cells. When a cell of the body somehow altered and start multiplying itself in uncontrolled manner then this gives rise to cancerous cell. *Most cancers form tumors, but not all tumors are cancerous (Pichardo Gabriel)*. Tumor is the mass composed of such cancerous cells. Cancer is the broad term. It is the uncontrolled growth of the abnormal cell present in the body, these abnormal cells are called as cancerous cells. These cells are having the potential to spread to other parts of the body (Chien et al., 2019). There is one defining of cancer is the rapid creation of abnormal cells that grows unusual beyond their usual boundaries. In 2017, the World Health Organisation had passed the resolution *Cancer Prevention and Control through an Integrated Approach* which impulses the government and WHO to reduce premature mortality form cancer.

Type of cancer caused by pesticides

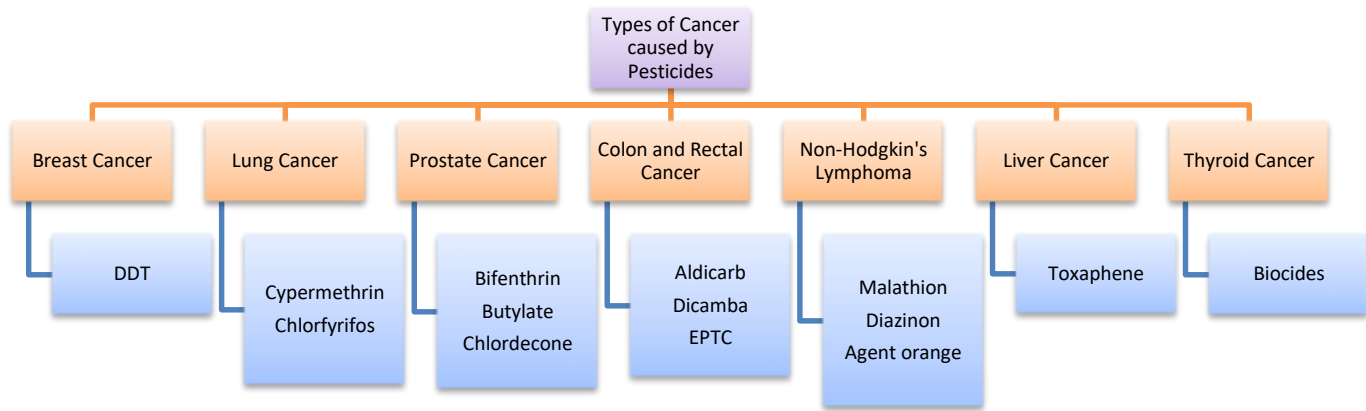
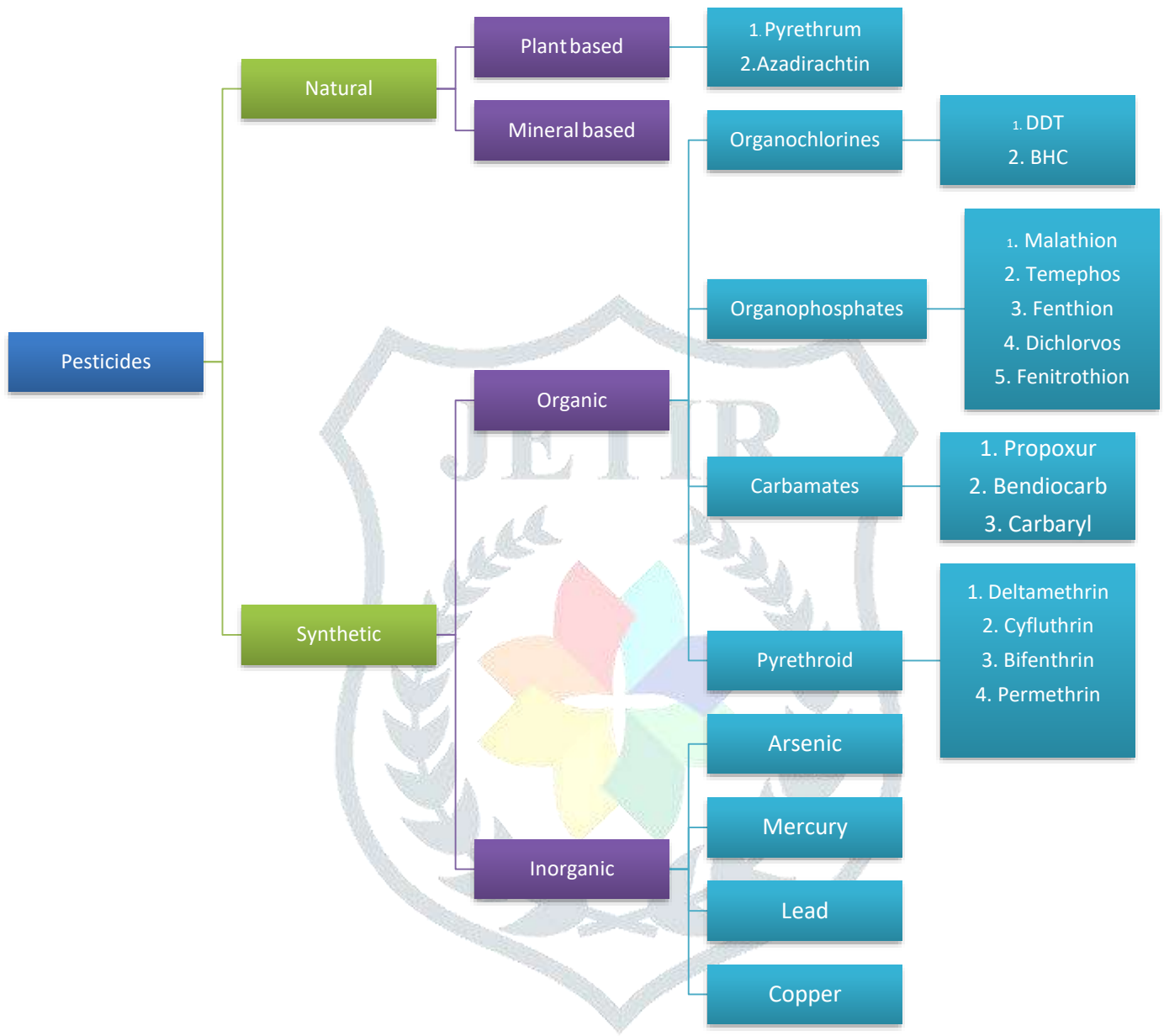
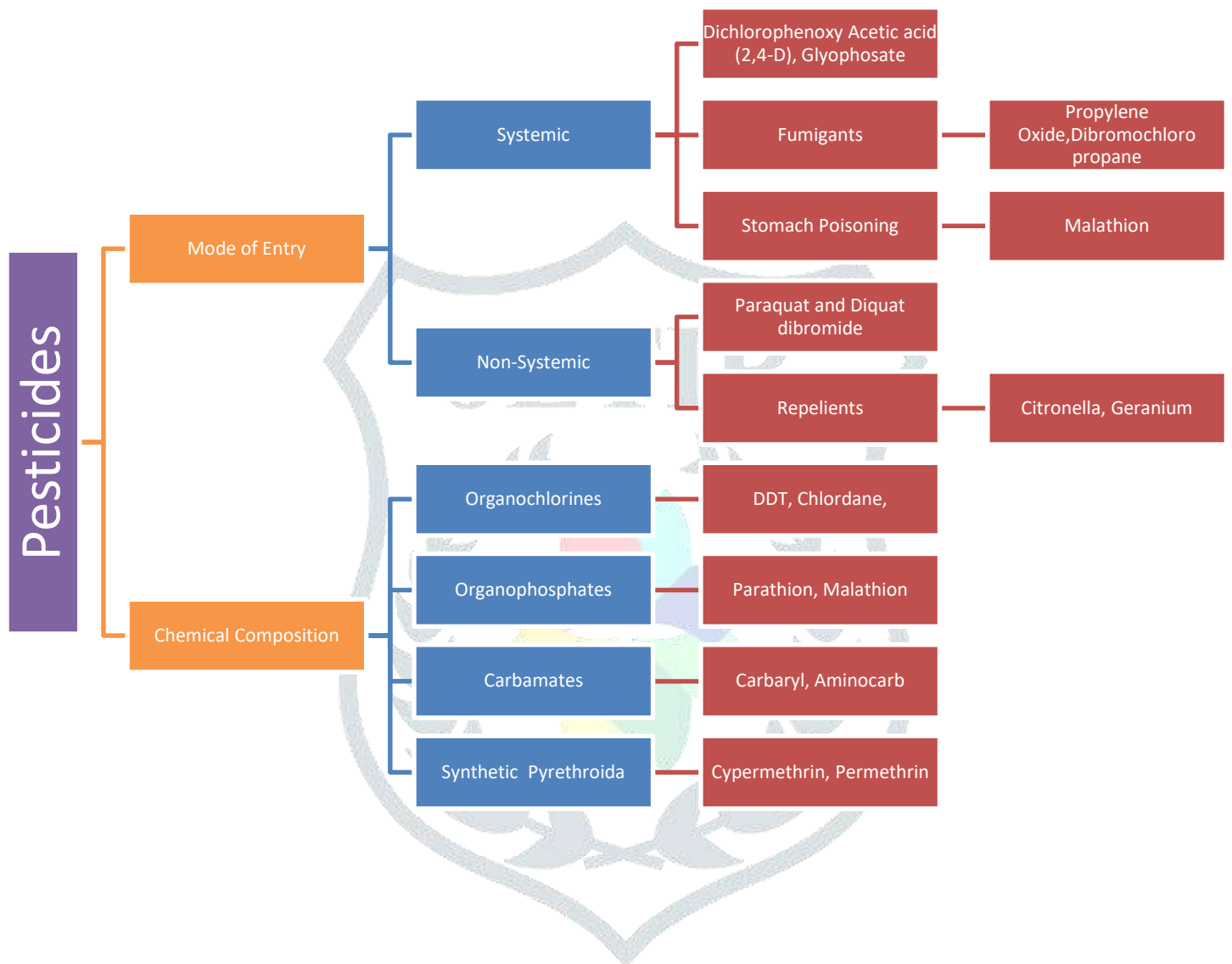


Figure : 1 :- Types of cancer caused by different types of pesticides



Classification of Pesticides on the basis of Origin (Rajveer kaur 2019)



Classification of Pesticides on the basis of mode of Entry in the body and Chemical Composition of the**Pesticides: -**

WHO and FAO collaboratively developed “The International Code of Conduct on Pesticide Management” for managing use of pesticides throughout their lifecycle. The Code of Conduct issues guidelines on registration, distribution and sale of pesticides and application of pesticides through ground and aerial.

WHO Guidelines

1. Pesticides which requires proper handling and application for the use of personal protective equipment that is uncomfortable, expensive or not easily available should be avoided, especially in the case of small scale users and farm workers in hot climates.

2. Governments should use all possible means for collecting of important data and maintaining statistics on human health effects by pesticides and pesticide poisoning incidents, using harmonized tools where available, and submit the reports when required, the Rotterdam Convention Human Health Incident Report Forms on Severely Hazardous Pesticide Formulations (SHPF), to the relevant designated national authority. Trained personnel and minimum resources should be made available to ensure the accuracy of information collected.

3. Governments should introduce the necessary policy and legislation for the regulation of pesticides, their marketing and use throughout their life-cycle, and make provisions for its effective coordination and enforcement, including the formation of appropriate educational, advisory, extension and health-care services, using as a basis FAO and WHO guidelines, the provisions of relevant legally binding instruments. Governments should take full information of factors such as local needs, social and economic conditions, levels of literacy, climatic conditions, availability and affordability of appropriate pesticide application and personal protective equipment.

4. Prohibition of the importation, distribution, sale and purchase of highly hazardous pesticides may be considered if, based on risk assessment, risk mitigation measures or good marketing practices are (LIST OF PESTICIDES WHICH ARE BANNED, 2019)insufficient to ensure that the product can be handled without unacceptable risk to humans and the environment.

5. All entities addressed by this Code should support the process of information exchange and facilitate access to information on matters including pesticide hazards and risks, residues in food, pure drinking water and the environment, the use of pesticides in non-food products, IPM/IVM, pesticide efficacy, alternatives to highly hazardous pesticides and related regulatory and policy actions.

(Yadav 2016).

- WHO and other Regulatory authorities also issues list of pesticides based on how hazardous they are to human and animals health? There are several registered pesticides which are considered harmful to health and environment that is why government has banned some carcinogenic pesticides which are:

Table 1: Pesticides banned for manufacture, import and use in India by Government

S.No.	Manufacture, import and use of different Pesticides banned in India by Government			Manufacture, import and use of different Pesticides banned in India by Government	
		Types of Cancer			Types of Cancer
1	Aldicarb	Colon cancer	15	Toxaphene	Hepatic carcinoma
2	Aldrin	Uterine Cervical Cancer	16	Tridemorph	
3	Benomyl	Breast Cancer	17	Trichloro Acetic Acid	
4	Calcium Cyanide		18	Linuron	
5	Chlordane	Hepatic Carcinoma	19	Metoxuran	
6	Chlorofenvinphos		20	Menazon	
7	Diazinon	Non-hodgkin lymphoma, Lung Cancer	21	Nitrofen	
8	Diealdrin	Uterine cervical cancer	22	Pentachloro Nitrobenzene	
9	Endosulfron	Uterine cancer	23	Phenyl Mercury Acetate	
10	Endrin		24	Sodium Cyanide	
11	Ethyl Parathion		25	Sodim Methane Arsonate	
12	Fenarimol		26	Tetradifon	
13	Fenthion		27	Thiometon	
14	Lindane				

Table no. 2 - There are some pesticides which are restricted for the use in the country because of their harmful effects for the environment as well as for the humans.

S. No.	Pesticides	Details of restriction
1	Captafol	Captafol as foliar spray is banned and can only be used as seed dresser. The manufacturing of Captafol (80 %) powder for dry seed treatment (DS) has been banned for use in the country except manufacture for export.
2	Dazomet	The use of Dazomet is not permitted for Tea.
3	Dichloro Diphenyl Trichloroethane (DDT)	DDT use is restricted for the domestic Public Health Programme up to 10,000 Metric Tonnes per annum, except for any major outbreak of epidemic. DDT is not used for the production of crops, vegetables. State and Central government can purchase the DDT for plant protection work only under very special circumstances.
4	Fenitrothion	It is banned for the production of crops or it is banned for Farming. It can only be used for Locust control.
5	Monocrotophos	It is banned for use of Vegetables.

Classes of Pesticides

Organophosphates: -

These are the chemical substances which is formed by the reaction between phosphorus and alcohol known as esterification process. These are the pesticides which contains organophosphorus esters. This group is responsible for the toxicity of organophosphates in the humans, it inhibits the acetylCholine esterase by phosphorylation, which ultimately leads to the accumulation of inactive enzymes in cholinergic synapses.[Leibson T, Lifshitz M, 2008] Symptoms of organophosphates toxicity includes fatigue, Fasciculation, Paralysis. Due to accumulation of acetylcholine in the neuron junction results in convulsions, ataxia, potentially coma. [Eskenazi B et. al., 1999][Kamanyire, R and L. Karalliede, 2004].

a) Diazinon: -

Diazinon is an insecticide used for controlling cockroaches, silverfish, ants, and fleas in residential, non-food-preparation buildings.[Lerro et al.,2015] It is used to lure and control scavenger yellow jackets in the United States. It is also used in gardens and on farms to manage sort of sucking and leaf-eating insects. It is available in dust,

granules, seed dressings, wettable powder, and emulsifiable solution formulations.[Bhupendra P and Saxena A 2005]

b) Malathion

Malathion is a wide-spectrum insecticide that was developed in 1950. It is used for controlling sucking and chewing insects on fruits and vegetables and also to manage mosquitoes, flies, household insects, and animal parasites.[Tchounwou et al., 2015]

Carbamates

It is extracted from the Calabar bean, which is usually found in Western Africa .The extract contains physostigmine, methylcarbamate ester, (Baron, 1991). Carbamates are the derivatives of carbamic acid.

It is widely used as insecticides in 1950s, and there are 25 types of carbamates which are used as pesticides.

MOA

They have the same mechanism of action like organophosphates, they are also acetylcholine esterase inhibitors, and they inhibit AchE reversibly

There are 2 major classes of carbamates which are used as pesticides (Miller, 1982). First class is choline esterase inhibiting carbamates which includes monomethylcarbamates, dimethylcarbamates, they are primarily used as insecticides and also used as miticides, rodenticides, nematocides. They are also used to treat glaucoma and myasthenia gravis.[Cocco P, 2002]

Methylcarbamates and dimethylcarbamates inhibits cholinesterase by carbamylation of the estiratic site of the enzyme, they also prevent the AChE from de-estererifying acetylcholine.

Seceond class of carbamates are dithiocarbamates, these are the sulfur containing carbamates they have very less or no affinity to inhibit cholinesterase enzyme, they are used are fungicides and herbicides.

1. **Bendicarb:** - It is broad spectrum insecticide which is used in households and fields to control mosquitoes, flies and as agricultural pests.

Environmental characterstics of Bendicarb: - It has low soil persistence with half life of 1 to 4 weeks depending upon the soil type (Worthing, 1987; Kidd and James, 1991). Bendicarb is degraded in solution by hydrolysis and it will not accumulate in the water (Kamrin, 1997).

2. **Methomyl:** - It is classified by EPA as highly toxic insecticide for humans and is a restricted use pesticide due to its high toxicity to humans. It is a broad spectrum insecticide and first registered in 1968. Methomyl can kill insects directly by acting on their surface and also by after absorbtion in the body that means it is effective both as contact and systemic insecticide.[Petreas M et al., 2004]

3. **Organochlorine:** - These are the group of organic compounds that contains chlorines and polychlorinated biphenyls, dibenzo-p-dioxins and organochlorine pesticides. Examples of organochlorine pesticides are Dichlorodiphenyl trichloroethane (DDT), lindane, dieldrin etc.[Kanja L et al., 1992][Charlier C et al., 2003].

Most of the human exposure to organochlorine occurs during prenatal and neonatal period. Organochlorine can crosses the placenta easily and can reach to the developing fetus and cause harm.[Raaschou-Nielsen O et al., 2005].

Organochlorines are lipophilic so they can easily secrete from the milk and during lacion period it reaches to the

new born baby. A surge in incidence of cancer has been observed over the last few years, especially for hormonally related cancers, such as breast, prostate and testis cancer.[Vineis P and D Amore, 1992]

Mechanism of Action

Organochlorine compounds escalates the risk of breast cancer because carcinogenic and the weak hormonal (estrogenic and anti-estrogenic) effect of many organochlorines. Organochlorine may mimic the endogenous hormone and causes hindrance with the normal mechanism. DDT, PCBs and dioxins could also reduce cell-mediated immune function, which could increase susceptibility to developing breast cancer [Krieger RI. Hayes, 2010]. Endogenous metabolism of estrogens by the process of hydroxylation which leads to the formation of two compounds. Estrogens are converted to the 2-hydroxyestrone, which stops the cell proliferation or to a 16-hydroxyestrone, which increases the breast growth or may responsible for the development of breast cancer. Bradlow and co-workers [Nasuti C et al., 2003] have stated that the 2-hydroxy and 16-hydroxy metabolites of 17 β estradiol and estrone plays important role in development of breast cancer. Hence, it can be inferred that organochlorines are responsible for the development of breast cancer by influencing estrogen metabolism.

4. Pyrethroid

Pyrethroids are the synthetic pesticides which are derived from the natural pyrethrins. It is obtained from the flower of plant chrysanthemum flower (*Chrysanthemum cinerariaefolium*)[Palmquist K et al., 2012].

The pyrethroid which is first obtained known as first generation pyrethroids such as permethrin and allethrin. They are devoid of cyano group so they are less persistent in the environment, so these are used to control the indoor pests[Palmquist K et al., 2012][Peto J, 2001].

Type 2 pyrethroid are called as second generation pyrethroid as it found later, they have cyano group in their structure at alpha position and have more efficacy and persistence. For example Cypermethrin, deltamethrin, fenvalerate.[IARC Volume 53, 1990].

Pyrethroid insecticides and Hematological Cancer

WHO through the IARC identified some carcinogenic pesticides [Rusiecki JA et al., 2009]. However, there is large number of pesticides which are carcinogenic in nature and has not been classified as carcinogens due to lack of evidences. Some pyrethroids like permethrin are not classified as carcinogens due to lack of evidences [Mates, et al., 2010]. However, the EPA classifies permethrin as a human carcinogen [Mates, et al., 2010][Martinez VD et al., 2011].

Mechanism

Exposure to permethrin leads to childhood and adult leukemia and lymphoma such as MLL and IGH genes. An assay was performed using centromeric FISH (Flourescence insitu Hybridsation) which showed that permethrin has the potential to cause aneuploidy of chromosomes 12, 18, 14/22. (Navarrete-meneses 2018).

Permethrin interacts through intercalation and by direct binding to major and minor grooves of DNA. (Ahmadi F n.d.). Pyrethroid can cause DNA methylation and due to this it affects the reproductive function. Pyrethroid can also act as endocrine disruptor because it is an agonist as well as antagonist for estrogen receptors, androgen receptors and thyroid hormone. By the activation of estrogen receptor it increases the proliferation of breast

carcinoma. (Chen H et al., 2009.). Pyrethroids affect chromatid remodeling by activating the estrogen receptor. Pyrethroid also cause hindrance in the mechanism of catechol estrogen by peroxidases, which ultimately leads to the production of quinones and semoquinones, which is capable of forming reactive oxygen species (ROS) (Schnyder S n.d.). Quinones which are formed they potentially affects DNA topoisomerase II which leads to the breakdown of certain sites in genome

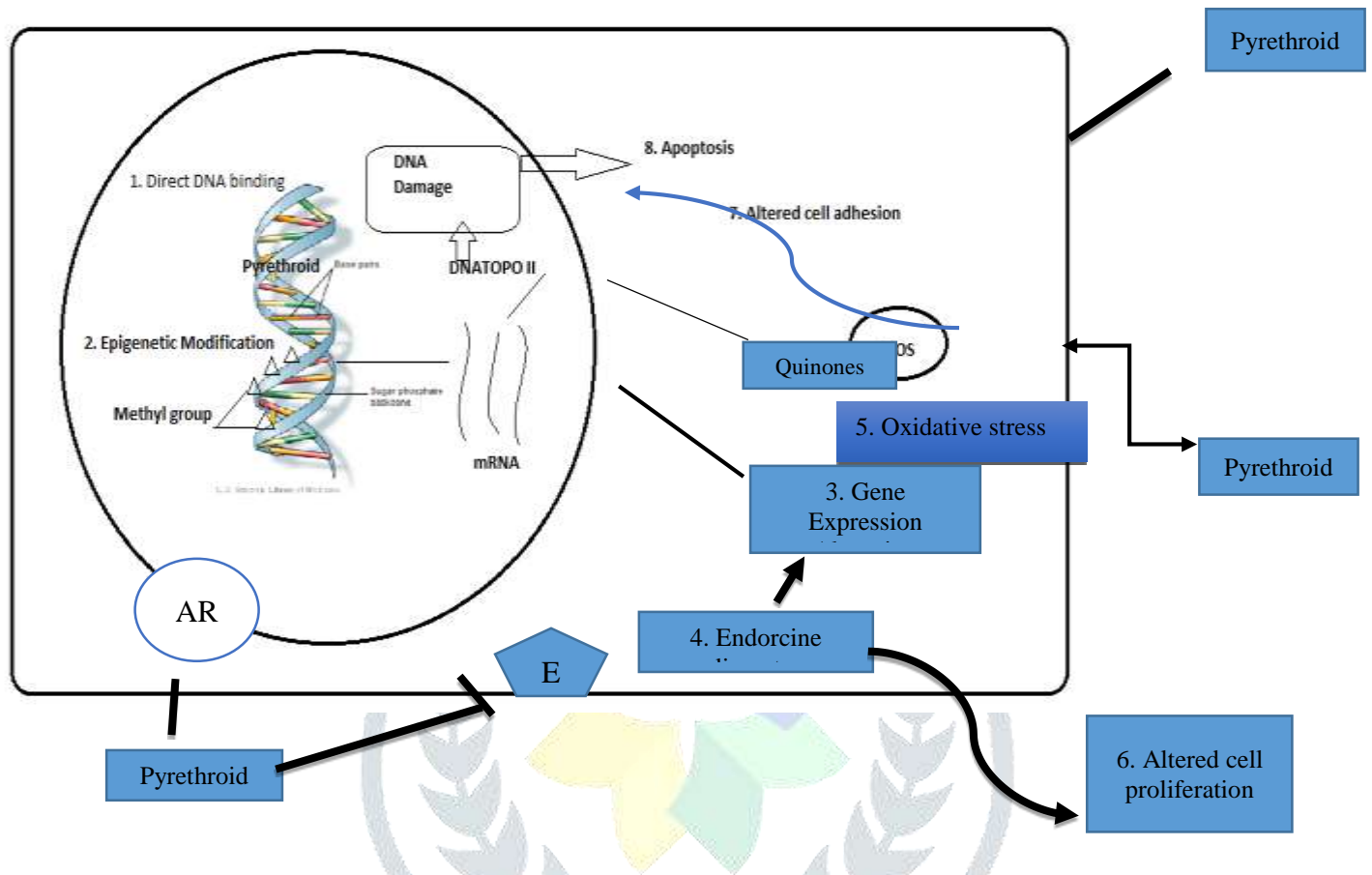


Figure 1: - ROS – Reactive Oxygen Species, AR – Androgen Receptor, ER – Estrogen Receptor
Mechanism of action of Pyrethroids causing cancer in human beings

Naturally obtained pesticides (Plant originated)

Naturally occurring pesticides do not have harmful effects as synthetic pesticides have. They are not responsible for causing any type of cancer in humans, as well as their residues are also not having cancer-causing or cancer-inducing properties in humans. For example, Pyrethrum, Azadirachtin

Pyrethrum extract is responsible for the toxic effects in humans but it is not causing cancer in humans. (Mossa n.d.)

Heavy Metals Used as Pesticides

Exposure to the heavy metals present in the environment as a residue after using pesticides represents a significant health concern to human beings. They have many toxic effects on humans but the most serious effect is their carcinogenicity, which is of serious concern. [Mates, et al., 2010]. For example, Arsenic, Mercury, Lead

Exposure to the Arsenic is due to ingestion of contaminated food and water, environmental pollution[Martinez VD et al., 2011] [Chakraborti D etv al., 2017]. Environmental exposure to arsenic is due to contaminated soil which enters in the food chain. [Chen K et al., 2014]. It has carcinogenic activity, it is responsible for the lung, bladder and skin cancer[Mates et al., 2010] [Nachman KE et al., 2017]. Low level exposure to the arsenic is responsible for pancreatic cancer, and non-Hodgkins Lymphoma[Satguru S et al., 2017] [Amaral AF et al., 2011].

Conclusions

Now after all the research I had done I concluded that there are so many pesticides available in the market which have some serious harms on the health of human beings.

As explained above some synthetic pesticides are responsible for causing cancer in humans, some are aldicarb, Cypermethrin, Toxaphene, Diazinon, Malathion, DDT, they are very toxic to humans as they causes some other diseases also. Pesticides spreads in the environment when they sprayed in the fields, from there they entered into the human body by different routes and causes some serious types of cancer like Hepatic, Lung, Uterus.

Some very harmful pesticides are banned by the government because they causes some fatal diseases to the humans, there is a list of pesticides issued by the government which are banned. WHO issued some guidelines for the use of pesticides to decrease the risk of cancer in humans, there are some guidelines as explained earlier, in my opinion we all should follow these guidelines to protect the environment and the humans. Pesticides are of different types so they are classified on the basis of origin and also on the basis of mode of entry.

Different types of pesticides have different mechanism of action when they entered into the body, important classes of synthetic pesticides are explained like Organophosphates, Carbamates, Organochlorines, Pyrethroids. Naturally obtained pesticides are not harmful for the human beings, heavy metals used as pesticides are very harmful for the humans as they causes cancer and some other toxic effects in the human body.

There should be some other guidelines which should be there for the proper use of pesticides. Some more research should there on the cancer causing pesticides and there should be a proper guidance for the use of pesticides.

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