UMYU Scientifica, Vol. 3 NO. 1, March 2024, Pp 129 – 143
https://doi.org/10.56919/usci.2431.015
ISSN: 2955 – 1145 (print); 2955 – 1153 (online)
A periodical of the Faculty of Natural and Applied Sciences, UMYU, Katsina

REVIEW ARTICLE

Occurrence of Carcinogens and their Potential Effects on Human Health – A Review

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ABSTRACT

The significant rise in cancer incidence and related deaths makes cancer one of the biggest threats to public health. Each year, there are about 10 million new cases of cancer and 6 million resultant deaths. In compliance with the disease triangle, the etiology of human cancer can be successfully traced to different environmental sources. Humans are continuously exposed to a wide range of different cancer-causing agents called carcinogens, such as household cleaners, solvents, pesticides, food additives, polluted air or environment, and other products. The Classification of Human Cancer by the International Agency for Research on Cancer (IARC) Monograph series was used as the primary data source for this review. We listed the cancer sites related to each agent based on the IARC review. Sources of these carcinogens were further grouped into classes in the IARC monograph. Home chemicals, environmental pollutants, occupational environments, environmental or medical radioactivity, drugs, microorganisms, contaminated air, and nutritional and behavioral choices are the sources of human exposure to carcinogens. The degree and frequency of exposure to carcinogens have a significant impact on their ability to cause cancer. The knowledge of carcinogens is crucial to creating awareness of cancer and advising the masses to reduce exposure to some environmental substances that are liable to cause cancer.

ARTICLE HISTORY

Received September 06, 2023.
Accepted March 15, 2024.
Published March 23, 2024.

KEYWORDS

Cancer, Carcinogenic agents, Genotoxic substance, Malignant cell, Neoplasia, Onchology

INTRODUCTION

A carcinogen is any substance, radiation, or agent that can potentially cause cancer. These substances can be inhaled, ingested, or come into contact with the skin, and they can cause changes or mutations in DNA that lead to the uncontrolled growth and division of cells, ultimately resulting in the development of cancer. Examples of carcinogens include certain chemicals, viruses, radiation, and some types of pollution. Suppose a substance leads to a significant rise in the incidence of one or more types of abnormal tissue growth in laboratory animals compared to those who are not exposed to the substance in a control group. In that case, it is considered to be carcinogenic (Rae *et al.*, 2015). According to a report by the International Agency for Research on Cancer IARC (2019), more than 1,000 substances have been identified as potential carcinogens to humans. These substances can be of biological, chemical, or physical nature and can occur naturally in the environment, such as UV rays from the sun and oncogenic viruses, or can be human-made, such as exhaust gases from vehicles and cigarette smoke (Lewandowska *et al.*, 2019). In recent decades, scientists have focused on identifying the environmental factors, including those present in homes and offices, which may contribute to cancer development. However, this has been challenging due to the widespread use of several substances in domestic cleaners, solvents, pesticides, sweeteners, lawn care products, and other consumer products.

Under certain conditions, a chemical that is classified as carcinogenic can trigger the formation of cancer in humans and animals by affecting one or more parts of the body (Siddiqui *et al.*, 2015). The body of an average individual contains over 100 trillion cells, and each could develop into a malignant cell if exposed to specific cancer-causing substances. These agents can be chemical (such as residues from decontamination), organisms (such as

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How to cite: Agboola, O. O., Emmanuel, A. O., Sabina, C. E., Anejo-Okopi, J., Naomi, A. I., Ene, U. I., & Olowoyo, J. O. (2024). Occurrence of Carcinogens and their Potential Effects on Human Health – A Review. *UMYU Scientifica*, 3(1), 129 – 143. https://doi.org/10.56919/usci.2431.015

cancer-causing microorganisms), or physical (such as UV rays or γ radiation) in nature (Rahman et al., 2022). The level of exposure to compounds known to cause cancer affects how quickly cancer develops after exposure. The likelihood that a person exposed to a carcinogen will acquire cancer is dependent on a number of variables, including the amount and length of exposure, exposure to other environmental factors, and the person's genetic makeup. (Carbone et al, 2020). Cancer-causing agents can cause genome damage, cell death, cellular oxidative stress, modified DNA, and prolonged inflammation in a variety of places all over the body. Most carcinogens act on the DNA of cells, causing mutations that can lead to cancer. Although the amount of exposure does not influence the development of cancer, the likelihood of cancer occurring does increase as the amount of exposure to carcinogenic compounds increases. This is similar to how a higher exposure to toxins can lead to more cases of poisoning in a population. However, once cancer has been diagnosed, the severity of the disease is not significantly affected by the amount of exposure to the carcinogenic agent (Gerba, 2019). Since carcinogens and toxic substances differ in this way, exposure standards for carcinogenic substances are much stricter than those for poisons (Karamertzanis et al.,2019).

Carcinogens have a huge potential to adversely affect health. About ten million additional cases of cancer are diagnosed each year, and approximately six million individuals die as a result. According to estimates, there are 102 thousand new instances of cancer in Nigeria, with 72 thousand deaths (Fatiregunet al. 2020). The incidence of cancer is rising on a global scale. Since 1990, the mortality rate has increased by eighteen percent while the incidence has increased by 19 percent (Kocarniket al 2022). At least one-third of these new instances may be avoided by making better use of the information already available. Understanding the causes of cancer can aid in its early detection or prevention. In the US, laws have been enacted to lessen workplace exposure to known carcinogens. In Nigeria, more study and awareness need to be conducted to boast the knowledge of safety precautions to take in the workplace, home and the living environment. People can lower their exposure to known carcinogens by quitting smoking, limiting their time in the sun, consuming less alcohol, and, for those who are old enough, getting the HPV and HBV vaccine. The objective of this research is to determine the substances that are responsible for causing cancer and to identify the sources through which individuals are exposed to carcinogenic compounds. This will assist individuals in being aware and in detecting the presence of carcinogens and their harmful consequences and aid them in avoiding/limiting activities that predispose them to these substances, hence minimizing the occurrence of cancer and the devastating effect of cancer in society.

METHODOLOGY

In this review, we gathered our research materials from various search engines such as PubMed, Scopus, Google Scholar, Science Direct, and Web of Science. The keywords used in the search included Carcinogens, Carcinogenic substances, cancer, and neoplasia. Our primary data on carcinogenic substances, their sources, classes, and mechanisms of action in humans were compiled from the published summaries of IARC review and final drafts created by Working Groups for IARC Monographs Volume 100. The agents that IARC classified as carcinogenic to humans and related each agent to cancer sites, sources, mechanism of action, and class were first listed. The carcinogens were classified into three types: chemical, physical, and biological, and analyzed their frequencies in causing cancer in various body sites, as well as the frequencies of their classes.

RESULTS

Table 1 shows the correlation between the list of substances identified by IARC Monographs as having carcinogenic properties and their associated cancer sites in the body, including blood, bladder, breast, bile, bone, cervix, anus, lung, liver, lymph, embryo, endometrium, nasopharynx, oral cavity, ovary, larynx, pharynx, esophagus, penis, renal pelvis, skin, ureter, vagina, thyroid, pancreas, uterus, and brain. The table provides information on the sources of these agents, their mechanism of action, and their respective classification into chemical, biological, or physical classes of carcinogens. There were 82 carcinogens belonging to 52 chemical, 10 biological, and 20 physical classes of carcinogens, and their effects on the body were illustrated in Figure 1. Additionally, Figure 2 shows the frequency of the carcinogens causing cancer in different body sites, while Figure 3 presents the frequency of the carcinogens in their respective classes.

DISCUSSION

The carcinogenic substances linked to the formation of cancer in the body parts outlined in Table 1 are the agents whose accumulation above the permissible concentration for a long period could lead to the development of cancers in the various body parts that may have been exposed to them. According to the National Cancer Institute (NCI), the following cancers are the most common in 2020: breast cancer, lung and bronchus cancer, prostate cancer, colon and rectum cancer, melanoma of the skin, bladder cancer, non-Hodgkin lymphoma, kidney and renal pelvis cancer, endometrial cancer, leukemia, pancreatic cancer, thyroid cancer, and liver cancer. Figure 1 can deduce that 15% of the agents in Table 1 causes cancer of the blood, they include Busulfan, Chlorambucil, Methyl-CCNU, Cyclophosphamide, Etoposide, Melphalan, MOPP, Thiotepa, Treosulfan, Azathioprine, Epstein-Barr virus, Human immunodeficiency virus-1, Human T-cell

lymphotropic virus type-1, Internalized radionuclides that emit α-particles, Neutron radiation, radionuclides that emit β-particles, Tobacco smoking, Benzene, 1,3-Butadiene, Ethylene oxide, Iron, steel founding and Ciclosporin, 11% of these agents (Cyclophosphamide, Chlornaphazine, *Schistosoma haematobium*, Arsenic, X-radiation and gamma-radiation, smoking, 4-Aminobiphenyl, Dyes metabolized to benzidine, 4 ' –Methylenebis, 2-Naphthylamine, Ortho-Toluidine, Auramine, and auramine production Benzo[a]pyrene Magenta and magenta production, Coke production, and aluminum production) can cause cancer in the bladder. 3% of these agents (Diethylstilbestrol, X-radiation and γ-radiation, Alcoholic beverages, Ethanol, and Second-hand tobacco smoke) can cause breast cancer. 1% of the agents in Table 1 (*Opisthor chisviverrini*, *Clonor chissinensis*) can cause cancer in the bile. 2% of these agents (X-radiation and γ-radiation, α-particles and β-particles emitting Internalized radionuclides) can cause cancer of the bone. 1% of these agents in Table 1 (Diethylstilbestrol, Tobacco smoking) can cause cervical cancer. 1% of these agents cause (Human papillomavirus types) cause anal cancer. 16% of these agents (MOPP, Arsenic and arsenic compounds, Beryllium and beryllium compounds, Cadmium and cadmium compounds, Chromium (VI) compounds, Nickel compounds, Asbestos, Erionite, X-radiation and γ-radiation, Internalized radionuclides that emit α-particles, α-particles and β-particles emitting Internalized radionuclides, Tobacco smoking, Indoor emissions from household combustion of coal, Ortho-Toluidine Benzo[a]pyrene, Coal gasification, Coal-tar pitch Soot, aluminum production, Exposure as a painter, Rubber manufacturing industry, Diesel-engine exhaust, Trichloroethylene, Second-hand tobacco smoke) can cause lung cancer. 6% of these agents (hepatitis B virus, hepatitis C virus, α-particles and β-particles emitting Internalized radionuclides, Tobacco smoking, Alcoholic beverages, Ethanol, Aflatoxins, and Vinyl chloride) can cause cancer of the liver. 2% of these agents (Ortho-Toluidine, Benzo[a]pyrene) can cause cancer in the lymphatic system. 1% of these agents (Bis(chloromethyl) ether and chloromethyl methyl ether) can cause cancer in an embryo. 1% of these agents (Estrogen-only menopausal therapy) cause endometrial cancer. 3% of these agents (Epstein-Barr virus, Wood dust, Tobacco smoking, Chinese-style salted fish, Formaldehyde) cause nasopharyngeal cancer. 2% of these agents (Tobacco smoking, Smokeless tobacco, Betel quid, and areca nut and Alcoholic beverages) cause cancer in the larynx. 2% of these agents (Wood dust, Tobacco smoking, Betel quid and areca nut, and Alcoholic beverages) cause cancer of the pharynx. 6% of these agents (Kaposi sarcoma herpes virus, Wood dust, X-radiation and γ-radiation, Tobacco smoking, Smokeless tobacco, Betel quid and areca nut, Alcoholic beverages, Acetaldehyde, Ortho-Toluidine, Benzo[a]pyrene) cause cancer of the esophagus. 1% of these agents (Human papillomavirus types) cause penile cancer. 2% of these agents (Aristolochic acids and Phenacetin) cause cancer of the kidney (renal pelvis). 2% of these agents (Tobacco smoking, Smokeless tobacco, Betel quid and areca nut, and Alcoholic beverages) cause cancer of the mouth (oral cavity). 1% of these agents (Asbestos, Tobacco smoking) cause cancer of the ovary. 7% of these agents (Methoxsalen plus ultraviolet-A (UVA) radiation, Kaposi sarcoma herpes virus, Arsenic and arsenic compounds, Solar and ultraviolet radiation, X-radiation and γ-radiation, Shale oils, Untreated or mildly treated mineral oils, Soot, Sulfur mustard, Ciclosporin) cause cancer of the skin. 2% of these agents (Aristolochic acids, Phenacetin, Tobacco smoking) cause cancer of the ureter. 2% of these agents (Diethylstilbestrol, Human papillomavirus types) cause cancer of the vagina. 1% of these agents (X-radiation and γ-radiation) cause cancer of the thyroid. 2% of these agents (Tobacco smoking, Smokeless tobacco, ethanol) cause pancreatic cancer. 1% of these agents (Tamoxifen) cause cancer of the uterus. 1% of these agents (X-radiation and γ-radiation, Second-hand tobacco smoke) can cause cancer of the brain and central nervous system. The majority of the carcinogens outlined in Table 1 can trigger cancer in the blood, breast, skin, lung, and liver, while few others affect other sites in the body like the uterus, thyroid, lymph, penis, brain, and vagina.

Figure 2 indicates that the main sources of human exposure to cancer-causing agents can be attributed to various factors, including occupational exposures, medication, environmental exposures, and having multiple sexual partners. Of these factors, 45% of the sources listed in Table 1 were related to occupational exposures, 22% were from medication, 12% were from environmental exposures, and 7% were linked to having multiple sexual partners. Research has demonstrated that exposure to these agents at certain levels can lead to cancer. In addition to these sources, other factors that contribute to cancer include exposure to ultraviolet rays from the sun, indoor combustion of coal, and lifestyle choices such as smoking, alcohol consumption, and consumption of contaminated food or Chinese-styled salted fish. These lifestyle factors are responsible for 2-7% of the carcinogens in Table 1 (Figure 2).

The carcinogens listed in Table 1 were categorized into three groups: chemical, biological, and physical carcinogens. The chemical agents consist of compounds used in the manufacture of food commodities, such as color, flavor enhancers, household cleaners, insecticides, and drugs. The biological agents include oncogenic viruses and the physical agents consist of radionuclides and mineral fibers. 60% of the carcinogens in Table 1 are chemical agents. This implies that an individual may be exposed to a good number of these carcinogens at work, at home, or outdoors carelessly or unknowingly. 29% of the carcinogens were grouped as physical carcinogens, and 10% of them were biological carcinogens.

Table 1: Summary of carcinogens and the part of the body affected, their sources, effects, and classes

Carcinogens	Cancer Sites	Sources	Mechanism	CLASS
Busulfan	Blood	Medication	Genotoxic	Chemical
Chlorambucil	Blood	Medication	Genotoxic	Chemical
Methyl-CCNU	Blood	Medication	Genotoxic	Chemical
Cyclophosphamide	Bladder/Blood	Medication	Genotoxic	Chemical
Etoposide	Blood	Medication	Genotoxic	Chemical
L-phenylalanine mustard	Blood	Medication	Genotoxic	Chemical
Vincristine	Blood/lung	Medication	Genotoxic	Chemical
Nolvadex	Uterus	Medication	Genotoxic	Chemical
Thioplex	Blood	Medication	Genotoxic	Chemical
Ovastat	Blood	Medication	Genotoxic	Chemical
Diethylstilbestrol	Breast, Cervix, and Vagina	Medication	Epigenic effect	Chemical
Hormone replacement therapy (HRT) with estrogen	Endometrial and Ovarian cancer	Medication	Receptor-mediated effects/genotoxic	Chemical
Azathioprine	Blood/Skin	Medication	immunosuppressive/altered DNA effect	Chemical
Chlornaphazine	Bladder	Medication	Cytotoxic	Chemical
Aristolochic acids	Renal pelvis and Ureter	Medication	Genotoxic	Chemical
Methoxsalen plus ultraviolet-A (UVA) radiation	Skin	Medication	Genotoxic	Chemical
Phenacetin	Renal pelvis and Ureter	medication	Cytotoxic	Chemical
Epstein-Barr virus	Blood and nasopharynx	Multiple sexual partners, bodily fluid	Cytotoxic/genomic instability/receptor-mediated effect	Biological
Chronic infection with hepatitis B virus	Liver	Multiple sexual partners, bodily fluid	Cytotoxic/epigenetic effect/altered DNA	Biological
Chronic infection with hepatitis C virus	Liver	Multiple sexual partners, bodily fluid	Cytotoxic	Biological
Kaposi sarcoma herpes virus	skin, lymph nodes, lining of the mouth, nose, and throat, and other tissues of the body	Multiple sexual partners, bodily fluid	Cytotoxic/genomic instability/chronic inflammation	Biological
Human immunodeficiency virus-1	Blood	Multiple sexual partners, bodily fluid	Immunosuppressive	Biological
Human papillomavirus types	anal, cervical, vaginal, vulvar , and penile cancer	Multiple sexual partners, bodily fluid	Cytotoxic/genomic instability	Biological
Human T-cell lymphotropic virus type-1	Blood	Multiple sexual partners, bodily fluid	Cytotoxic	Biological
Opisthorchisviverrini	Bile duct	Eating raw or undercooked fish.	Cytotoxic/ chronic inflammation/oxidative stress	Biological
Clonorchissinensis	Bile duct	Eating raw or undercooked fish.	Cytotoxic/ chronic inflammation/oxidative stress	Biological
Schistosomahaematobium	Bladder	contaminated freshwater	Chronic inflammation/oxidative stress/genotoxic	Biological

Table 1 Continued

Arsenic and arsenic compounds	Lung, bladder, and skin.	Occupational exposure	Genomic instability/cytotoxic/oxidative stress	Chemical
Beryllium and beryllium compounds	lung	Occupational exposure	Oxidative stress/altered DNA/Cytotoxic	Chemical
Cadmium and cadmium compounds	lung	Occupational /Environmental exposure	Cytotoxic/genotoxic	Chemical
Chromium (VI) compounds	**lung**	Occupational /Environmental exposure	Genomic instability	Chemical
Nickel compounds	lung	Occupational /Environmental exposure	Altered DNA repair	Chemical
Asbestos	Lung, larynx, and ovary.	Environmental exposure	Genotoxic/chronic inflammation/epigenic effects	Physical
Erionite	Lung	Environmental exposure	Genotoxic/chronic inflammation/epigenic effects	Physical
Leather dust	Nasal and paranasal sinus	Occupational exposure	Genotoxic/cytotoxic	Physical
Wood dust	nasal cavity, paranasal sinuses, and nasopharynx	Occupational /Environmental exposure	Genotoxic/chronic inflammation	Physical
Solar and ultraviolet radiation	Skin	sunlight/occupational radiation	altered DNA repair/electrophilic	Physical
X-radiation and γ-radiation	Salivary gland, esophagus, stomach, colon, lung, bone, basal cells of the skin, female breast, kidney, urinary bladder, brain and CNS, and thyroid	Occupational exposure	altered DNA repair/electrophilic	Physical
Internalized radionuclides that emit α-particles	Lung, bone, blood, liver,	Occupational exposure	altered DNA repair/electrophilic	Physical
Neutron radiation	Blood	Occupational exposure	altered DNA repair/electrophilic	Physical
Internalized radionuclides that emit β-particles	Lung, bone, blood, liver,	Occupational exposure	altered DNA repair/electrophilic	Physical
Tobacco smoking	lung, oral cavity, nasooro- and hypopharynx, nasal cavity and accessory sinuses, larynx, esophagus, stomach, pancreas, colorectum, liver, kidney, ureter, urinary bladder, uterine cervix and ovary, blood	Smoking (lifestyle)	altered DNA repair/chronic inflammation/oxidative stress	Physical

Table 1 Continued

Smokeless tobacco	oral cavity, esophagus, and pancreas	unburned tobacco (Lifestyle)	altered DNA repair/chronic inflammation/oxidative stress	Physical
N ' -Nitrosonornicotine (NNN) and 4-(methylnitrosam		Smoking (lifestyle)	altered DNA repair	Chemical
Betel quid and areca nut	Oral cavity, pharynx, and esophagus	Chewing betel quid with tobacco products	chronic inflammation/oxidative stress/altered DNA repair	Physical
Alcoholic beverages	Oral cavity, pharynx, larynx, esophagus, colorectum, liver and female breast	Alcohol consumption (lifestyle)	Cytotoxic/genotoxic	Chemical
Ethanol	Breast, liver, and pancreas.	Consumption of alcoholic beverages	Cytotoxic/genotoxic	Chemical
Acetaldehyde	Esophagus and other upper aero-digestive tract	Consumption of alcoholic beverages	Cytotoxic/genotoxic	Chemical
Shishamo	Nasopharyngeal	Consumption of Chinese-style salted fish	Cytotoxic/genomic instability/receptor-mediated effect	Physical
Indoor air pollution from coal burning.	Lung	Combustion of coal indoors	altered DNA repair	Physical
p-aminobiphenyl	Bladder	Occupational /Environmental exposure	Genotoxic/altered DNA repair	Chemical
Benzidine congeners	Bladder	Occupational exposure	Genotoxic/altered DNA repair	Chemical
MOCA (2-chlorobenzenamine)	Bladder	Occupational exposure	Genotoxic/altered DNA repair	Chemical
β-naphthylamine	Bladder	Occupational exposure	Genotoxic/altered DNA repair	Chemical
2-amino toluene	Lung, bladder, esophagus, and lymphatic system	Occupational exposure	Genotoxic/altered DNA repair	Chemical
Basic yellow 2 and auramine production	Bladder	Occupational exposure	Genotoxic/altered DNA repair	Chemical
Benzo[a]pyrene	Lung, bladder, esophagus, and lymphatic system	Environmental exposure	Genotoxic/altered DNA repair	Chemical
Magenta and magenta production	Bladder	Occupational exposure	No sufficient data	Chemical
Coal gasification	Lung	Occupational exposure	Genotoxic	Chemical
Coal-tar pitch	Lung	Occupational exposure	Genotoxic	Chemical
Coke production	Bladder	Occupational exposure	Genotoxic	Chemical
Shale oils	Skin	Occupational exposure	Genotoxic	Chemical
Untreated or mildly treated mineral oils	Skin	Occupational exposure	Genotoxic	Physical

Table 1 Continued

Soot	Skin and lung	Environmental exposure	Genotoxic/ altered DNA repair	Physical
Aflatoxins	Liver	contaminated food	Genotoxic/ altered DNA repair	Chemical
aluminum production	Bladder, lung	Occupational exposure	Genotoxic/ altered DNA repair	Physical
Benzene	Blood	Occupational /Environmental exposure	Genotoxic/ altered DNA repair	Chemical
Bis(chloromethyl) ether and chloromethyl methyl ether	Embryo	Occupational exposure	Genotoxic	Chemical
Biethylene	Blood	Occupational exposure	Genotoxic	Chemical
Dioxin, pentachlorodibenzofuran, pentachlorobiphenyl		Occupational exposure	receptor-mediated effect	Chemical
Epoxyethane	Lymph, blood	Occupational exposure	Genotoxic/ altered DNA repair	Physical
Formalin	Nasopharyngnx	Occupational exposure	Cytotoxic/genotoxic	Chemical
Mustard gas	Skin	Occupational exposure	altered DNA repair/cytotoxic	Physical
Vinyl chloride	Liver	Occupational exposure	altered DNA repair	Chemical
Isopropyl alcohol		Occupational exposure	altered DNA repair	Chemical
Strong acid mists	Larnynx	Occupational exposure	altered DNA repair	Chemical
Iron and steel foundry work	Blood	Occupational exposure	altered DNA repair	Physical
To be exposed as a painter	Lung	Occupational exposure	Genotoxic	Physical
Rubber manufacturing industry	Lung	Occupational exposure	Genotoxic	Physical
Diesel-engine exhaust	Lung	Occupational exposure	Reactive oxidative/altered DNA repair/chronic inflammation	Chemical
Trichloroethylene	Lung	Occupational exposure	Genotoxic	Chemical
Combined menopausal therapy estrogen–progestogen	cervix	Medication	Receptor-mediated/genotoxic	Chemical
Combined estrogen–progestogen oral contraceptives	Uterine Cervix	Medication	Receptor-mediated/genotoxic/oxidative stress	Chemical
Ciclosporin	Skin/blood	Medication	Immunosuppressive	Chemical
Crystalline silica dust in the form of quartz or cristobalite	Lung	Occupational /Environmental exposure	cytotoxic/genotoxic	Physical
Second-hand tobacco smoke	Lung, brain, breast	Smoking	Altered DNA repair/chronic inflammation/oxidative stress	Physical

Source: The International Agency for Research on Cancer (IARC) Monograph

Table 2: Characteristics of Carcinogens and Corresponding Toxicological End-points

SN	Characteristics of Carcinogens	Corresponding Toxicological End-points
1	Metabolically responsive to electrophiles or electrophilic	Metabolic activation, protein modifications, and differences in absorption, distribution, metabolism, and elimination can impact the effects of carcinogens.
2	Mutagenic	Effects on DNA, Chromosome damage, Alterations in genes
3	Disrupts DNA repair mechanisms or induces genomic instability	Genomic instability resulting from changes in DNA repair mechanisms.
4	Induces epigenic alterations	Epigenic alterations (DNA methylation, histone modification, and altered expression of microRNAs)
5	Causes oxidative stress	Reactive oxygen species (ROS) or free radicals.
6	Causes persistent inflammation.	Prolonged inflammation Prolonged irritation
7	Immunodepressive	Effects on the immune system
8	Alters the effects mediated by receptors	effects of hormones and other signaling molecules that bind to specific receptors on cells and trigger a cellular response
9	Causes immortalization	Immortalization Alterations in telomere length
10	Alters nutrient supply, the killing of cells, or cell growth	Effect on the cell-cycle Bystander effects Cell signaling pathways change Angiogenic outcomes Cell death Inhibition of gap-junctional intercellular communication

Source: Smith et al. (2016)

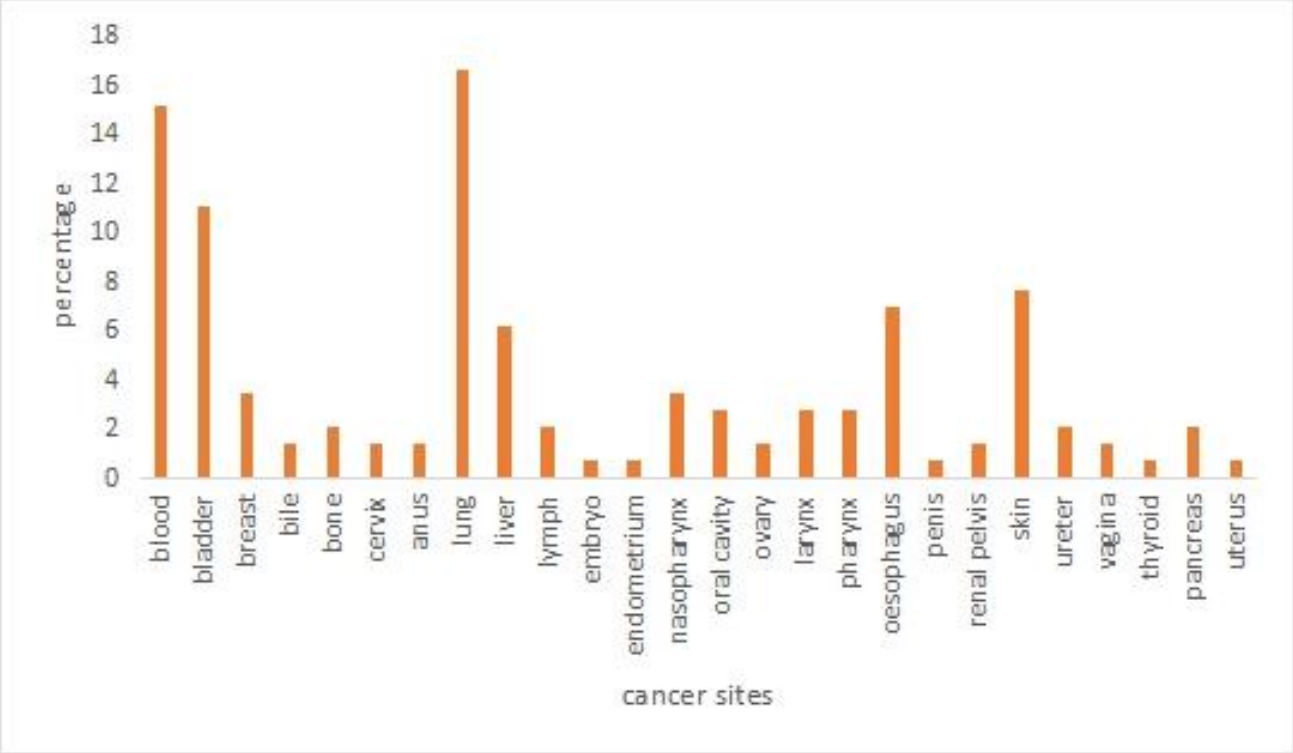

Figure 1: Body sites affected by carcinogens

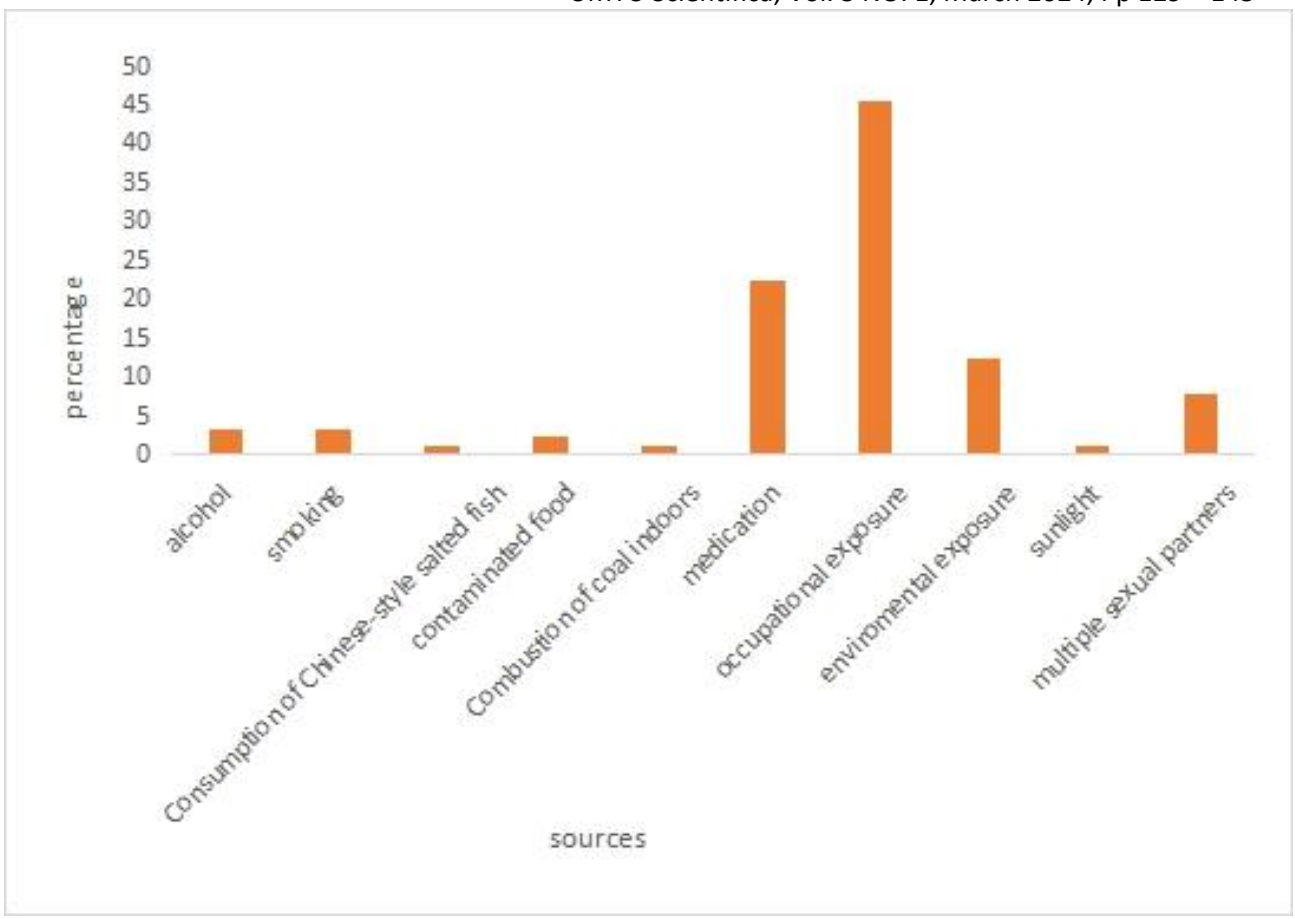

Figure 2: Sources of carcinogens

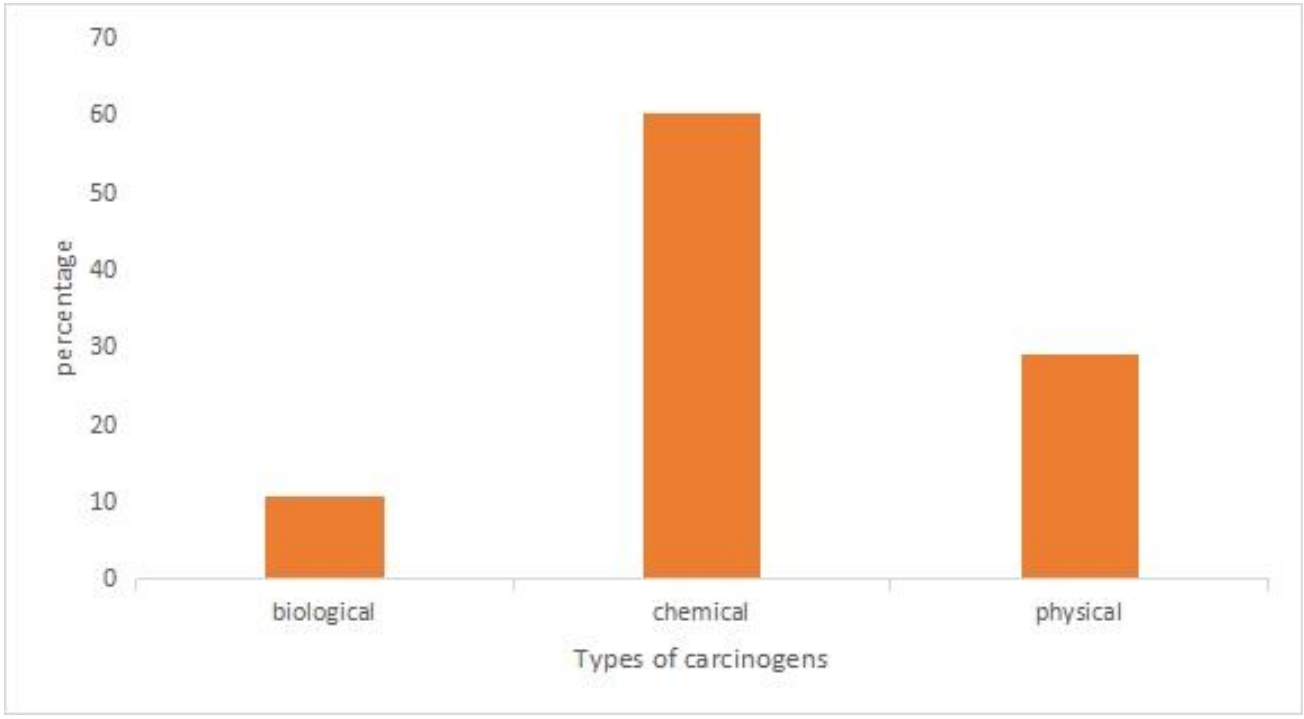

Figure 3: Classification of carcinogens

Classification of Carcinogens

According to the observed characteristics, carcinogens can be categorized as chemical, physical, or biological. Some researchers classify carcinogens based on the role that they perform in each phase of carcinogenesis; for example, incomplete carcinogens are mutagenic chemicals that cause irreversible DNA damage, while a complete

carcinogen exhibits characteristics that involve initiators and promoters at the same time depending on the dosage and exposure time. (Trosko, 2019).

Chemical Carcinogens

Chemical carcinogens are chemical compounds that can be present in a variety of substances, such as the smoke from cigarettes and some pesticides (Aljamali et al., 2022). Over 1000 chemical compounds have been labeled carcinogenic by the International Agency for Research on Cancer (Loomis et al., 2018). The IARC has identified various chemical waste products from industry and environmental contaminants from households, companies, and automobiles. A frequently used instance is acrylamide, which can cause human cancer and is produced by industrial processes, and the high-temperature heating of several foods via grout and soil stabilization products, as well as wastewater treatment, can release it into the environment. Other examples of chemical carcinogens include nitrosamines and polycyclic aromatic hydrocarbons, which are prevalent in tobacco smoke and have been linked to the emergence of lung cancer (Rifai et al., 2020).

Flavor enhancers, colors, preservatives, food fortifiers, and other chemical ingredients used in food production have a variety of negative health effects, especially when their concentration levels exceed the acceptable limits that are crucial to the composition of natural food. These result in mutations which alters the makeup of cells, increasing their propensity to develop into cancerous cells. (Goodall, 2021). Chemical carcinogens, which are substances that are found in food, may adversely affect cells through modifying their genetic makeup. These substances can be gases, liquids, or solids (Bhatia and Das, 2020). Both types of mutations—temporary and somatic—can result from these changes and may impact cell growth or result in cell death (Vijg and Dong, 2020).

Alkyl or aryl epoxides, nitrosoureas, nitrosamides, and several sulfonate and sulfate esters are examples of substances that do not directly promote cancer development but can do so through their metabolites. These substances are transformed into electrophilic reagents that can either calcify or corrode the same living cell depending on how the carcinogenic ingredient has been subjected to enzymatic interaction. It develops a cancer-causing mutation (Das et al., 2020).

Chemical carcinogens can cause cancer by different mechanisms. For example, some chemicals can directly damage DNA, leading to mutations and chromosomal abnormalities. Others can interfere with normal cellular processes, such as cell division and apoptosis, leading to the uncontrolled growth and division of abnormal cells. The extent of damage and the risk of cancer may depend on factors such as the dose and duration of exposure, individual susceptibility, and the type of chemical carcinogen. Reducing exposure to chemical carcinogens is an important step in preventing cancer. For example, quitting smoking, avoiding exposure to occupational chemicals, and reducing exposure to environmental pollutants can help lower cancer risk. Additionally, regulatory measures and workplace safety protocols can help reduce exposure to chemical carcinogens in the environment and workplace.

Physical Carcinogens

Physical carcinogens can cause cancer through direct physical or mechanical action on cells or tissues. Physical carcinogens are widely varied in how they are composed, some of which are naturally occurring while others are man-made (Elgarahy et al., 2021). The method through which they cause cancer remains unclear. Many different mechanisms likely contribute to cancer development. The fact that some physical carcinogens combine with genetic elements and other environmental factors to cause cancer further complicates matters. When combined with exposure to cigarette smoke, asbestos, for instance, has a significantly larger potential to cause cancer than it does on its own alone (Machlowska et al., 2020). Depending on the type of radiation, the type of exposure, and the penetration depth, physical carcinogens such as UV rays from direct sunlight, ionizing radiation from X-rays, and radioactive elements in industry and the general environment can cause cancer. For instance, alpha radiation can cause cancer when inhaled or swallowed despite having a low surface penetration rate (Danho et al., 2022). Additionally, X-ray is a human carcinogen that is well-known for sticking around in various devices and emitting alpha particles continuously. Ionizing radiation has both direct and indirect impacts on living systems, including the breakdown of DNA molecules and the release of free ions into solutions (Gissela et al., 2015).

Physical carcinogens can cause cancer by damaging DNA, disrupting normal cellular processes, and promoting the growth and division of abnormal cells. The extent of damage and the risk of cancer may depend on factors such as the duration and intensity of exposure, individual susceptibility, and the type of physical carcinogen. Reducing exposure to physical carcinogens is an important step in preventing cancer. For example, wearing protective clothing and sunscreen can help reduce UV radiation exposure, while reducing exposure to particulate matter and air pollution can help prevent lung cancer. Additionally, regulatory measures and workplace safety protocols can help reduce exposure to physical carcinogens in the environment and workplace.

Biological Carcinogens

Biological carcinogens are agents that can cause cancer by directly or indirectly altering the genetic material (DNA) in cells, leading to the uncontrolled growth and division of these cells. Some numerous substances/organisms fall under the category of biological carcinogens that have the potential to result in malignancies like endometrial, breast, and prostate cancer. A number of bacteria, fungi, viruses, and parasites are examples of biological cancer-causing agents, and their persistent infection can result in cancer. Some bacterial species increase the risk of cancer, such as

Helicobacter pylori, which causes peptic ulcers and is a precursor to gastric cancer (Piscione et al., 2021). Helicobacter hepaticus also causes gastroenteritis (Deng et al., 2022). Aflatoxin B1 (AFB), a mycotoxin generated by *Aspergillus flavuns* and associated with several fungal infections on preserved foods, is a risk factor for liver and hepatocellular cancer (Marchese et al., 2018). The first virus found to cause cancer in animals was Ross sarcoma. Today, a number of viruses—referred to as oncogenic viruses—cause cancer. These viruses either clone viral cancer genes or inappropriately activate main tumor genes to induce cancer (Lawson and Glenn, 2022). The human papillomavirus (HPV), which is linked to cervical cancer and squamous cell carcinoma; the Ebstein-Bar virus (EBV), which is linked to more than 90% of cases of Burkitt's lymphoma and has also been linked to stomach cancer and cell-B lymphocytes, are just a few examples of the many types of these viruses (De Martel et al., 2020). Only a few parasites have been linked to cancer; the most significant of these is *Schistosoma haematobium*, which is linked to bladder cancer, as well as *Opisthor chisviverrinica*, which causes cholangiocarcinoma (Dheilly et al., 2019).

Biological carcinogens can cause cancer by different mechanisms. For example, viruses can insert their genetic material into the DNA of host cells, disrupting normal cellular processes and leading to cancer development. Bacteria and parasites can also directly damage DNA or induce chronic inflammation, promoting cancer cell growth. Hormones can stimulate the growth of certain cancer cells, while immunodeficiency can increase the risk of certain cancers by reducing the body's ability to fight infections and cancer cells.

It is important to note that not all infections will lead to cancer, and a combination of factors, including genetics, lifestyle, and environmental exposure often influences the development of cancer. Nonetheless, reducing exposure to biological carcinogens, such as through vaccination and infection control measures, can help to reduce the risk of certain types of cancer.

Sources of Carcinogens

Exogenous and endogenous factors are the two types of cancer-causing agents. The environment consists of the external conditions causing the development of people, animals, or plants. A distinction is frequently made between conditions over which individuals have no or only partial control and lifestyle choices that are unhealthy, such as the inhalation of tobacco and related products, the consumption of certain foods, and their contamination by mycotoxins. Exposure to pollutants in the air and water may occur at the workplace, whereas "lifestyle" factors such as eating a high-fat diet, processed meat, smoking, and drinking alcohol may occur in the latter. Carcinogens can enter the environment through a variety of activities and paths. Daily, humans are exposed to a wide spectrum of potentially hazardous natural or man-made toxins, as well as a plethora of complex combinations that may be carcinogenic. Aflatoxin B1, produced by the fungus *Aspergillus flavus*, is an example of a naturally occurring microbial carcinogen. Human cancer has been linked to viruses such as hepatitis B and the human papillomavirus (Liu, 2020). Some bacteria (e.g., *Helicobacter pylori*) and helminths (e.g., *Opisthor chisviverrini* and *Clonor chissinensis*) are also known to cause cancer in humans (Pakharukova et al 2021).

Many chemicals used in home or workplace construction materials or products are carcinogenic. Numerous household products contain these substances, and they are frequently present in composite wood products (such as hardwood plywood, particleboard, and medium-density fiberboard), which release chemicals into the surrounding air, as demonstrated by research on laboratory rodents and employees who have been exposed to formaldehyde while at work. (Rietjens *et al*, 2022). Formaldehyde can be released through smoking and cigarette smoke. On the other hand, asbestos is a known carcinogen supported by human and animal studies. It is composed of tiny, strong fibers commonly used to reinforce building materials such as ceiling tiles, roof shingles, and car parts. Asbestos can be present in old pipe insulation, attic insulation, textured ceilings, or floor tiles. When these materials are disrupted, they release microscopic asbestos fibers into the air. The inhalation of these fibers can cause mesothelioma, a type of lung cancer, and the fibers can become trapped inside the lungs.

The skin can suffer damage from UV rays, whether from the sun or a tanning bed, as they are absorbed into the skin. Skin cancer cases are primarily caused by exposure to UV ray pollution, which can be exacerbated by climate change. Radon is a type of environmental radiation commonly found; it is produced by the natural decay of uranium in soil and can accumulate in homes. Radon is the second most common cause of lung cancer after smoking. It is gaseous, and inhalation of the gas can damage the lining of the lungs. Certain medical procedures, such as computed tomography (CT scan) and radiation therapy used to treat cancer, can also lead to carcinogenic radiation exposure. Women who receive radiation therapy after a mastectomy have been reported to have a higher risk of developing lung cancer due to the radiation targeting the chest (Schlosser *et al*., 2020).

Cancer can be caused by various viruses that damage healthy cell DNA. Chronic viral infections such as human papillomaviruses (HPV) can lead to cancers of the mouth, throat, cervix, and genital regions (penile, vaginal, and vulvar). Hepatitis B and C infections can cause liver scarring (cirrhosis) and ultimately lead to liver cancer. Human T-lymphotropic virus type 1 (HTLV-1) is a form of blood cancer that can cause leukemia. Epstein-Barr virus, which causes mononucleosis, has been linked to an increased risk of nasopharyngeal cancer and lymphomas. Human immunodeficiency virus (HIV) has been associated with Kaposi sarcoma, lymphomas, genital and ocular malignancies, and non-melanoma skin cancers (De Martel *et al*., 2020).

Certain chemotherapy and hormonal therapy drugs may elevate the likelihood of cancer. For instance, chemotherapy drugs like Ellence (epirubicin) and Cytoxan (cyclophosphamide) used to treat early-stage breast cancer may trigger leukemia. Oral contraceptives may increase the risk of breast or cervical cancer, but they may reduce the risk of endometrial, ovarian, and colorectal cancer (Aggarwal *et al.*, 2021).

Both indoor and outdoor air can contain cancer-causing agents. Lung cancer is highly associated with common outdoor air pollutants from industrial or power plants, motor vehicle exhaust, dust and metal and solvent residues, and smoke from fires. Indoor air pollutants can come from various sources, including building materials, paint fumes, fire retardants, cleaning chemicals, and dust. These indoor air pollutants can also contribute to the development of lung cancer and other types of cancer. According to studies, the chemicals mentioned above are believed to be potential causes of lung cancer and other types of cancer (Turner *et al.*, 2020).

Various lifestyle factors can lead to genetic mutations that increase the risk of cancer. For instance, smoking or exposure to secondhand smoke is linked to at least seventy compounds in tobacco that alter DNA and cause cancer. Additionally, not smoking tobacco but using other tobacco products can also increase the risk of cancer. Drinking alcohol is also known to increase the risk of several cancers, including those affecting the head and neck, esophagus, breast, liver, and colon, due to the presence of carcinogenic substances produced during brewing (Kassim *et al.*, 2020).

When crispy, brown foods and vegetables, such as potatoes, are heated to high temperatures, they emit a chemical called acrylamide; studies have shown that rats who consumed acrylamide in their drinking water developed cancer; acrylamide is also found in many products and tobacco smoke (Rifai and Saleh, 2020). Findings from more than 800 studies have shown that processed meat (Bacon, salami, pepperoni, sausage) and any meat that is being preserved or flavored can raise the risks of getting colon cancer (Libera *et al.*, 2021).

Cancer can be caused by various lifestyle factors such as obesity, lack of physical activity, and poor dietary habits, specifically consuming processed meat, smoked, salted, or fermented food items. High-temperature cooking of meat, such as grilling or pan-frying, can also lead to the formation of carcinogenic compounds known as heterocyclic amines, including 2-amino-3,8-dimethylimidazo, quinoxaline, 2-amino-3,4,8-trimethylimidazo, quinoxaline, and 2-amino-1-methyl-6-phenylimidazo pyridine. Studies on rodents have linked heterocyclic amines to lung cancers, and one of them, 2-amino-1-methyl-6-phenylimidazo pyridine, has been found to cause breast tumors in rats and increase the risk of breast cancer in humans according to dietary epidemiology studies (Dolan *et al.*, 2021; Murphy, 2022; Bellamri *et al.*, 2021).

Research has revealed that the long-term consumption of food contaminated with heavy metals poses a significant risk to human health and can increase the incidence of cancer and mental illnesses. Studies have further suggested that heavy metals like Cd and Pb can increase the risk of gastric cancer and colon cancer, respectively, and the risk may be even higher when multiple metals are combined. These heavy metals can enter the body through various routes, such as dietary intake, skin contact, and breathing. Pesticides are also widely used in food production, and the potentially harmful effects of pesticide residues in food concern the public (Cui *et al.*, 2022).

It should be emphasized that exposure to carcinogens does not always lead to cancer, and the risk of developing cancer can be influenced by various factors, including the length and severity of exposure, as well as individual aspects like genetics and lifestyle. However, minimizing exposure to recognized carcinogens is a critical measure in decreasing cancer risk.

Risk of Exposure to Carcinogens

According to the National Cancer Institute (NCI, 2023), most cancer-related factors and preventive measures are identified through epidemiological research, in which scientists analyze large populations and compare those who develop cancer with those who do not. These studies may reveal that individuals who develop cancer are more or less likely than the general population to engage in certain behaviors or be exposed to certain substances. Both the presence of certain behaviors and exposure to chemicals and other substances can increase the risk of developing cancer. The risk of developing cancer varies amongst demographic groups and is related to lifestyle variables and habits, according to epidemiological studies on cancer incidence. Exposure to natural carcinogens (asbestos) and environmental chemical carcinogens (polycyclic aromatic hydrocarbon, aromatic amines, amino azo dyes, N-nitro compounds, etc.) may cause a significant share, if not the majority, of human malignancies, according to estimates (Kayamba and Kelly, 2022).

People who work in certain areas, such as mining, agriculture, and manufacturing, where exposure to hazardous chemicals and substances is more common, should be especially concerned about the danger of exposure to carcinogens. Carcinogen exposure, however, is not confined to the workplace; it can also occur at home, in public places, and in the general environment. Decreasing exposure to known carcinogens is a crucial step in lowering the chance of acquiring cancer. This can involve abstaining from tobacco products, limiting exposure to dangerous substances and chemicals, and implementing the necessary safety precautions at work and home. Furthermore, living a healthy lifestyle that includes regular exercise, a balanced diet, and limiting exposure to environmental chemicals will help lower the risk of developing cancer. The danger of being exposed to carcinogens cannot be disregarded because it poses

serious harm to human health and may raise the possibility of getting cancer. People should be aware of possible carcinogenic exposures in their environment and take the necessary precautions to lower their risk of exposure.

CONCLUSION

Numerous scientific studies used in this review have found strong evidence that the carcinogens highlighted in Table 1 are exposed to through home chemicals, workplace pollutants, environmental or medical radiation, medications, viruses, polluted air, dietary and lifestyle choices, and other sources. Additionally, the degree and frequency of exposure to carcinogens have a significant impact on their ability to cause cancer. When adequately exposed to humans, carcinogens—which can be biological, chemical, or physical agents—can have severe effects such as genotoxicity, cytotoxicity, oxidative stress, altered DNA, cell death, and chronic inflammation. These outcomes lead to mutations, which occasionally transform into the numerous tumors displayed in diverse human body regions.

The main preventable risk factors for cancer that have been identified thus far are tobacco, nutrition, drugs, infections, and high-dose exposures in the workplace and environment. Some cancer-causing exposures, such as tobacco smoke, UV light, lifestyle choices that raise the risk of contracting a biological agent, as well as employment and environmental conditions, can be avoided. The materials used in jobs, the water we drink, the food we eat, and the air we breathe are among the more difficult to avoid. However, some of them cannot be avoided because they are a part of daily life. However, practical measures like using gloves, reading labels, and quitting smoking should be taken to assure protection. This review should be helpful for scientific purposes in determining research priorities and understanding carcinogens, their occurrence, and their effect, as well as for regulatory or precautionary purposes.

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