International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Effects of Cancer Drugs and Their Metabolism in Our Body

K.Malleswari[1],D.Rama Brahma Reddy[2],V.Prasanna Kumar[3], A.Sai Jagadeesh Babu[4],B.S.Santhosh[5]

[1]Associate Professor,Pharmaceutics, Nalanda institute of pharmaceutical sciences, Guntur
[2]Principal , Pharmaceutical chemistry, Nalanda institute of pharmaceutical sciences,Guntur
[3,4,5]Student,Pharmacy,Nalanda institute of pharmaceutical sciences,Guntur

ABSTRACT

Cancer is a genetic disorder that results from genetic or epigenetic alterations in the somatic cells and has abnormal cell growth which may be spread to other body parts. In 2018, 18 million cancer was recorded globally in which 9.5 million cancer cases in men, 8.5 million cases in women, and 9.6 deaths were also recorded in the same year. The most spreading cancer globally is prostate, breast, lung stomach, colorectal cancer, non-melanoma skin malignancies but there are 100 types of cancers that affect humans. The impact of cancer is increasing significantly day by day. Tobacco is 22% responsible for causing cancer, 15% cancer is caused due some infections like HIV, hepatitis b, Epstein-Barretc, and 10% is due to poor diet, obesity, excessive consumption of alcohol, exposure to ionizing radiation, etc. In this review article, we try to shed a light on various cancer-causing factors, type of cancer, how the cancer starts, sign or symptom of cancer, diagnosing tests, the treatments of cancer and problems related to cancer treatments. Nowadays, a lot of research is going on precision medicine for a better future of cancer treatments. The common therapies are given to patient's chemotherapy, radiation therapy, immunotherapy, surgery and hormone therapy and combinations of these therapies. Stem cell transplant is also the best therapy for cancer but it given after the common therapies to recover the patient from blood loss and help in making the patient healthy

Keywords: Etiological agents, pathophysiology,Anti-cancer drugs,metabolism

INTRODICTION

Cancer:

- Cancer is defined as uncontrolled growth of a group of cells disregarding the normal rule of cell division. Such cells are known as cancer cells.
- Normal cells are under direct supervision and their growth, proliferation and cell division are supervised through signal transduction. How ever cancer cells develop autonomous mechanism for its growth and proliferation.
- Cancer is diseases which turns the normal cell into cancer cell by the process called carcinogenesis.
- Clinically, there are many types of cancer, but biologically, the origin of cancer is similar, which is due to defect in gene expression.

- There are some factors which are responsible for change of normal cell into cancer cell. Those factors or agents are known as carcinogens.
- It is believed that all cells carry certain cancer producing oncogenes.
- Oncogenes are the genes that are responsible for induction of tumours. Under certain conditions these genes are triggered to multiply rapidly into malignant neoplasm.[(1)]

Etiological agents that induce cancer:

1. Environmental factors:

- tobacco, smokes, diets, environmental pollutants etc
- Heavy smoking cause lung, oral cavity and oesophagus cancer.
- Excessive intake of alcohol cause liver cancer.

2. Chemical carcinogen:

- Nickel compounds, cadmium, arsenic, nitrosamines, trichloroethylene, arylamines, benzopyrene, aflatoxins, reactive oxygen radicals etc

3. Physical carcinogen:

- UV rays (ultraviolet), ionizing radiation (x-rays and gamma rays)

4. Biological carcinog:

- Virus:
- Virus has also been associated with various types of cancers. These viruses are called oncoviruses.
- Rous sarcoma virus (RSV) is the first discovered retro-virus causing cancer.
- (Oncovirus**)**; Human papilloma virus (HPV), Epstein-Barr Virus, (EBV), Hepatitis B virus, Herpes virus
- Hepatitis B and C virus is casually related with hepato-cellular carcinoma.
- Cytomegalovirus (CMV) is associated with Kaposi ’s sarcoma.
- Human papilloma virus (HPV) is a chief suspect of cervix cancer.
- Bacteria; Helicobacter pylori,

5. Endogenous factors:

- Mutations, change in DNA replication, metabolic reactions generating, reactive oxygen radicals, Immune system defects, Ageing

Cancer pathophysiology

- Regardless of difference in types of cancer histologically and physiologically, there is existence of a common pathophysiological process of malignant tumours or cancer development in the organism.
- The commonly accepted basis of the pathogenesis of cancer is the damage to the genetic apparatus of cells (such as mutation, disturbance of gene expression, activation of tumour promoter gene, inactivation of tumour suppressor genes, etc.)
- It is believed that damage to the genetic apparatus of the cell along with inactivation of anti-tumour genes takes place and is essential for the development of malignant tumours. But it should be noted that the inactivation of tumour suppressor gene is one of the natural physiological reactions of the organism, and when this reaction becomes pathophysiological condition of an organism it results in cancer development.

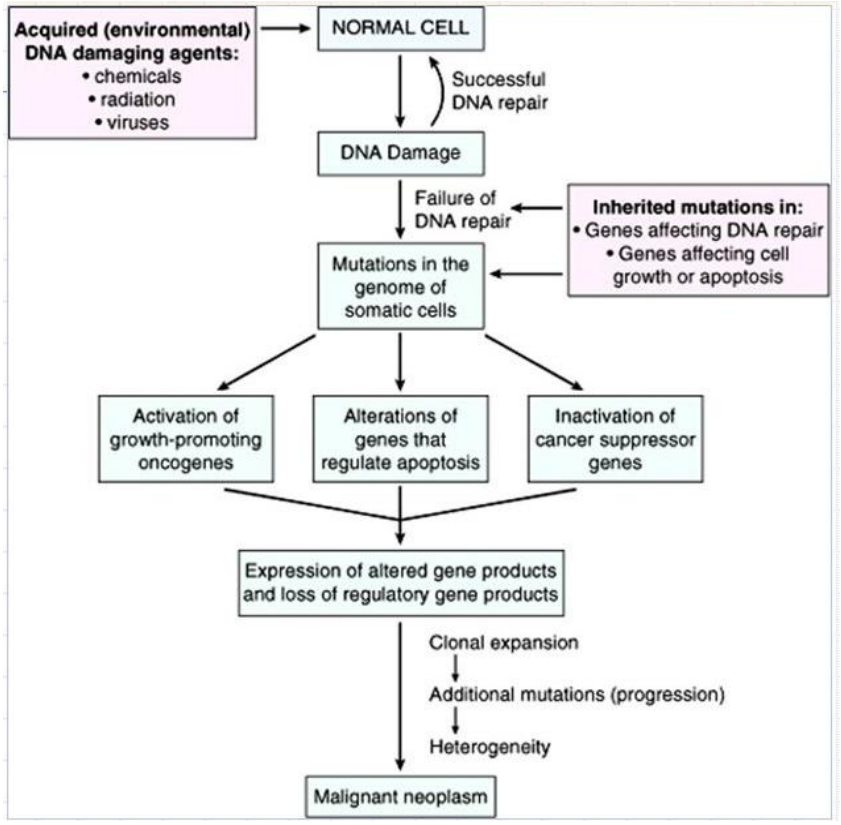

Figure:1Pathogenesis of cancer

At the cellular level, the development of cancer is viewed as a multi-step process involving mutation and selection for cells with progressively increasing capacity for proliferation, survival, invasion, and metastasis.

First step: Mutation and tumour initiation

- Genetic alteration leads to mutation in a single cell which results into abnormal proliferation of that cell known as tumour cell.

Second step: Cell proliferation and Tumour progression

- Tumour progression continues as additional mutations occur within cells of the tumour population.
- The mutated cells have some selective advantage over normal cell as such cells shows rapid growth and division. The descendants of a cell bearing such additional mutation will consequently become dominant within the tumour population

Third step: Clonal selection and malignancy

- Cell proliferation of tumour then leads to new clone of tumour cells with increased growth rate or other properties (such as survival, invasion, or metastasis) that confer a selective advantage. The process is called clonal selectio
- Clonal selection continues throughout tumour development, so tumours continuously become more rapid-growing and increasingly malignant.
- **For example:** In colon cancer, the earliest stage in tumour development is increased proliferation of colon epithelial cells. A clonal selection occurs in which, a single cell within these proliferative cell

population give rise to a small benign neoplasm. Further rounds of clonal selection lead to the growth of benign neoplasm with increase in size and proliferative potential resulting in malignant carcinoma. The cancer cells then continue to proliferate and spread through the connective tissues of the colon wall. Eventually the cancer cells penetrate the wall of the colon and invade other abdominal organs, such as the bladder or small intestine. In addition, the cancer cells invade blood and lymphatic vessels, allowing them to metastasize throughout the body.

Fourth step: Metastasis

- **Metastasis** is a complex process in which cancer cells break away from the primary tumour and circulate through the bloodstream or lymphatic system to other sites in the body.
- At new sites, the cells continue to multiply and eventually form additional tumours comprised of cells that reflect the tissue of origin.
- The ability of tumours, such as pancreatic cancer and uveal (iris, ciliary body, or choroid of eye) cancers, to metastasize contributes greatly to their lethality.
- Many fundamental questions remain about the clonal structures of metastatic tumours, phylogenetic relationships among metastases, the scale of ongoing parallel evolution in metastatic and primary sites, how the tumour disseminates, and the role that the tumour micro-environment plays in the determination of the metastatic site.[(2)]

Types of cancer

- Abnormal proliferation of any of the different kinds of cells in the body can result in Cancer. So there are more than a hundred different types of cancer varying on their behaviour, pathophysiology, site of origin and response to treatment or therapy.
- A tumour can be either benign or malignant**.**
- **Benign tumour:** A tumour that remains confined to its original location, neither invading surrounding normal tissue nor spreading to distant body sites is known as benign tumour. For examples; Skin wart
- **Malignant tumour:** A tumour which is capable of both invading surrounding normal tissue and spreading (metastasis) throughout the body via the circulatory or lymphatic systems is known as malignant tumour. Only malignant tumours are properly referred to as cancer.
- Pathologically, cancers are classified into three categories: Carcinomas, Sarcomas, Leukaemia

1. Carcinomas:

- This type of cancer arises from epithelial cells or ectodermal tissues lining the internal surface of the various organs.
- **For example:** breast cancer, lung cancer, skin cancer, brain cancer, cancer of pancreas and mouth, oesophagus, stomach and intestine.

2. Sarcomas:

- These cancers arise from connective and muscular tissue derived from mesoderm.
- **For examples**: bone tumours, muscle tumours, muscle tumours, cancer of lymph nodes.

3. Lymphomas or Leukaemia:

- It is the malignant growth of leucocytes (WBC).
- Persons affected with this cancer show the excessive production of leucocytes (blood cancer) and cancer of bone marrow.
- In addition, brain tumour, kidney tumour and eye tumour is seen in infants and children due to malignant growth of primitive embryonic tissues. Similarly, cervical cancer is common in women and prostate cancer common in men.[3]

Cancer Diagnosis (symptoms of disease)

- The early infection does not show significant symptom. Possible symptoms of cancer are as follows:
- A persistent cough or hoarseness in a smoker.
- A persistent change in digestive and bowel habits.
- Rapid change in the form, appearance and growth of a mole or wart.
- A hard area in the breast.
- Excessive loss of blood during monthly period in women.
- A swelling or sore throat that does not heal easily.
- Unexpected loss of weight.

Cancer Treatment

- Early treatment ensures that the cancer can be controlled. Some of treatments may control cancers.

1.Radiation or **Radiotherapy:**

- It involves the exposure the cancerous part of the body to high doses of radiation which can destroy rapidly growing cells and shrink tumours.

2.Surgery or Operation:

- Generally tumour and cancerous cells are surgically removed.

3. Chemotherapy:

- It involves some anticancer drugs to control cancer.
- Chemotherapy drugs are alkalyting agents (carboplatin, cisplatin, melphalan) and antibiotics (actinomycin, mythramycin).

4. Hormone therapy:

- Hormone therapy is a treatment that slows or stops the growth of breast and prostate cancers that use hormones to grow.

5. Stem cell transplant:

- Stem cell transplants are procedures that restore blood-forming stem cells in cancer patients who have had theirs destroyed by very high doses of chemotherapy or radiation therapy.

6. Precision medicine:

- Precision medicine helps doctors select treatments that are most likely to help patients based on a genetic understanding of their disease.

7. Target therapy:

- Targeted therapy is a type of cancer treatment that targets the changes in cancer cells that helpthemgrow,divide,andspread

Herbal- therapy:

- Certain medicinal plants have anti- cancer property

Causes of Cancer:

- here are many causes which may cause cancer in different body parts like mainly 22% deaths are due to tobacco consumption, 10% of deaths are due to poor diet, obesity, lack of physical activity, excessive drinking of alcohol or other facts include certain exposure to ionizing radiation, environmental pollutants, and infection
- About 15% of cancer in the world is due to some infections like hepatitis b hepatitis c human papillomavirus infection, helicobacter pylori, and immunodeficiency virus (HIV)Epstein - Barr virus. These factors are at least partly responsible for changing the genes
- Inherited genetic defects froparents are also responsible for 5-10% of Cancer is caused by the interaction betweegenetic factors and 3 categories of agentswhich we consume externally including:
- Inherited genetic defects from patient's Inherited genetic defects from patients parents are also responsible for 5-10% of cancer.
- Cancer is caused by the interaction between genetic factors and 3 categories of agents which we consume externally including

Physical Carcinogens:

Ionizing radiation such as radon, ultraviolet rays from sunlight,uranium, radiation from alpha, gamma, beta, and X-ray-emitting sources.

Chemical Carcinogens:

Compounds like n-nitrosamines, asbestos, cadmium, benzene, vinyl chloride, nickel, and benzidine and contains about 60 known potent cancer-causing toxins or chemicals in cigarette smoking or tobacco consumption, a drinking water contaminant (arsenic), a food
contaminant (aflatoxin

Biological Carcinogens:

Infections fromcertain bacteria, viruses, or parasites and Pathogens like human papillomavirus (HPV),EBV or Epstein-Barr virus, hepatitis B and CKaposi's sarcoma-associated herpesvirus(KSHV), Markel cell polyomavirus, Schistosoma spp., and Helicobacter pylori

Aging is also the cause of cancer. Age is the common incidence of cancer, which dramatically rises.

Genetics:

Genetics is the commonest cause for cancer or tumor-like Ovarian, breast, prostate, skin cancer, colorectal cancer. Individuals that eat heaps of cooked meat can also increase risk because of compounds fashioned at high temperatures. Proving that a substance doesn't cause or isn't associated with hyperbolic cancer risk is tough.[4]

Anti-cancer drugs – discovery, development and therapy:

Themost widely used treatments for cancer are surgery, radiotherapy andchemotherapy. Chemotherapy is the only option for metastatic cancers, where the treatment has to be systemic. The most frequently used chemotherapy drugs have been identified empirically without an pre-existing knowledge regarding the molecular mechanism of action of the drugs. Despite the remarkable progress achieved in cancer care and research over the past several decades, the treatment options for the majority of epithelial cancers have not changed much.However, a critical mass of knowledge has been accumulated that may transform cancer treatments from cytotoxic regimens towards the rapidly dividing cells into personalized targeted therapies. This chapter will provide an overview of currently used chemotherapeutics and will explore the impact of the molecular understanding of cancer on modern drug discovery, drug development and cancer therapy[(5)]

Despite significant progress in the understanding of cancer biology there is a persistent lack of progress in curing most metastatic forms of cancer. Among the standard treatment options for human cancers which include surgery, radiation therapy, immunotherapy and chemotherapy, the latter one is often the only option for treatment of metastatic disease where treatment has to be systemic throughout the entire body. Chemotherapy is the use of chemical agents for the treatment of cancer. Most chemotherapeutic agents exert their cytotoxic effect by modifying DNA, by acting as fraudulent mimics of DNA components, by inhibiting enzymes involved in DNA synthesis or by blocking cell division. Traditional chemotherapy kills cells that are rapidly dividing, regardless if they are cancer cells or not. Therefore standard chemotherapy damages healthy tissues, especially those that display a high replacement rate. Over the past few decades efforts in cancer research has paved the way for better therapies that interfere with specific targeted molecules. These treatments are called targeted therapies and hold promise to improve clinical outcomes without the toxicity associated with traditional chemotherapy. The transformation of the accumulated knowledge in cancer biology into clinical practice represents a major challenge for the scientific community and pharmaceutical industry.[(6)]

The classification of traditional chemotherapy:

Nowadays, many different alkylating agents are given as part of anticancer therapy regimes. In addition a broad range of non-alkylating drugs have been developed to treat cancer. All current chemotherapeutic drugs can be classified into several categories according to their mechanism of action:

1. DNA-modifying agents (alkylating agents and alkylating-like agents)
2. anti-metabolites (that imitate the role of purines or pyrimidines as building blocks of DNA),
3. spindle poisons (typically plant alkaloids and terpenoids that block cell division by inhibiting microtubule function),
4. topoisomerase inhibitors (preventing transcription and replication of DNA) and
5. cytotoxic antibiotics (for example anthracycline, that inhibit DNA and RNA synthesisthus block topoisomerase.[(7)]

Table 1 shows examples of each category Chemotherapy agents can also be classified into cell cycle specific and cell cycle non-specific drugs. Most chemotherapeutic drugs are cell cycle-specific and act on cells undergoing division. Cell cycle-specific drugs can be subdivided into S-phase- G1-phase-, G2 phase- and M-phase-specific agents according to the phase of the cell cycle in which they are active.

Antimetabolites are most active during the S phase of cell cycle because they exert their cytotoxic activity by inhibiting DNA synthesis. Conversely, vinca alkaloids which inhibit spindle formation and alignment of chromosomes are M-phase specific. Cell cycle-specific drugs are most effective for high growth fraction malignancies (e g: hematologic cancers). Their capability to kill cells displays a dose-related plateau and does not increase with further increased dosage, because at a certain time point only a subset of cells is fully drug sensitive. In contrast, cell cycle non-specific drugs such as alkylating agents have a linear dose-response curve and affect cells regardless whether they are proliferating or resting. They are effective for both low and high growth fraction tumours[8]

The limitations of traditional chemotherapy:

The success of cancer chemotherapy is limited by problems with toxicity, efficacy and drug resistance. As most conventional chemotherapeutic agents also affect rapidly dividing cells in healthy tissues they can cause severe side effects, in particular myelosuppression, immunosuppression, alopecia, mucositis, nausea and vomiting, diarrhea and flu-like symptoms. The cytotoxic effect of conventional chemotherapy affects resting cells, e g . cancer stem cells less effectively. Therefore, the drug might be very efficient against cells that form the bulk of the tumour, that are not able to form new cells but does not affect the rare subpopulation of cancer cells which can repopulate the tumour and cause relapse.[7] In addition, traditional chemotherapeutic agents target cell proliferation with little effect on other important hallmarks of cancers such as angiogenesis, invasion and metastases. A major problem associated with anticancer drugs (traditional and targeted therapies) is drug resistance. Some tumours, in particular pancreatic cancer, renal cell cancer, brain cancer and melanoma exhibit absence of response on the first exposure to standard agents (primary resistance). Conversely, some drug-sensitive tumours acquire resistance during the course of the treatment (acquired resistance) Drug resistance can be classified into drug-specific resistance and multi-drug resistance. Whereas drug-specific resistance is usually mediated by specific genetic alterations, the multi-drug resistant phenotype is often associated with increased expression of P-glycoprotein which expels drugs from the cell[9]

Table:1 Conventional chemotherapeutic agents classified according to their mode of action

Type of agent	**examples**	**Mode of action**	**Affected cell cycle phase**
DNA-modifying agents			
Alkylating agents	Chlorambucil	Alkylation of DNA	Phase nonspecific
	Cyclophosphamide	Alkylation of DNA	Phase nonspecific
	Carmustine	Alkylation of DNA	Phase nonspecific
	Lomustine	Alkylation of DNA	Phase nonspecific
	Dacarbazine	Alkylation of DNA	Phase nonspecific
	Temozolomide	Alkylation of DNA	Phase nonspecific
Platinum complexes	Cisplatin	DNA adduct formation	Phase nonspecific
	Oxaliplatin	DNA adduct formation	Phase nonspecific
	Carboplatin	DNA adduct formation	Phase nonspecific
Anti-metabolites			

	Methotrexate	Folic acid antagonist	S-phase
	6-Mercaptpurine	Inhibitnucleotide synthesis	S-phase
	Fluorouracil	Inhibit synthesis ofnucleic acids	S-phase
	Gemcitabine	IncorporatedintoDNA/interfere with DNA synthesis	S-phase
Spindel poisons			
Vinca alkaloids	Vinblastine	Prevent microtubule assembly	M-phase
	Vincristine	Prevent microtubule assembly	M-phase
Taxanes	Paclitaxel	Prevent microtubule disassembly	M-phase
	Docetaxel	Prevent microtubule disassembly	M-phase
Topoisomerase inhibitor			
Topoisomerase inhibitor	Camptothecin	Cause strand breaks/inhibit DNA synthesis	G2 phase
Topoisomerase inhibitor	Etoposide	Inhibit DNA replication	M-phase
	Topotecan	Inhibit DNA replication	M-phase
Antitumor antibiotics:			
	Bleomycin	CausesDNA fragmentation	G2 phase
	Daunorubicin	Intercalate with DNA/inhibit topoisomerase II	G2 phase
	Doxorubicin	Intercalate with DNA/inhibit topoisomerase II	G2 phase

Pre-clinical development:

Preclinical development is the process of taking an optimized lead through the stages necessary to allow human testing. Preclinical development includes in vitro and in vivo experiments to determine safety and efficacy of the drug candidate. During preclinical development, researchers must work out how to make large enough quantities of the drug for clinical trials. Efficacy evaluation of an anticancer drug candidate involves testing the impact on the viability of a broad variety of cancer cell lines xenograft experiments in nude mice and experiments in more sophisticated genetically engineered mouse models. One of the major challenges in drug development is the accurate prediction of drug toxicity in humans. The standard approach to toxicity testing includes acute, sub chronic, chronic exposure in three animal species. Regulatory authorities usually require that drugs are tested in both a rodent and a non-rodent mammalian species. Usually, these tests are carried out in mice, rats and dogs. Drugs with toxicity only in humans and not in non-human animals should be detected in the clinical trials. Unfortunately, due to several limitations in the design of clinical trials this is not always the case. That is one of the reasons why 2.9% of the marketed drugs were withdrawn from the market during the last four decades. Pre-

clinical studies must be conducted according to stringent good laboratory practices (GLPs), which require meticulous control and recording of processes. Before any clinical trial can begin, the sponsor, usually a pharmaceutical company must obtain permission to test the candidate drug in humans filing an Investigational New Drug (IND) application. The application is reviewed by regulatory authorities to make sure people participating in the clinical trials will not be exposed to unreasonable risk Studies in humans can only begin after IND is approved.[10]

Clinical development:

Clinical trials serve as the basis for evidence-based medicine and are conducted in three phases of development before a new drug can be approved for commercialization.

Phase 1 clinical trials:

A phase 1 clinical trial (also called first in humans, FIH) is the first step in testing a new investigational drug or new use of a marketed drug in humans. Oncology phase 1 trials typically involve 20-80 patients with advanced cancer that has not responded to standard cancer treatments. In phase 1 clinical studies emphasis is put on drug safety. A principal goal of this phase is to establish a dose and/or schedule of a candidate drug for testing its efficacy in phase 2 trials. Trial participants are divided into small groups, known as cohorts. The first cohort receives a low dose of the new drug. In the absence of any major adverse side effects, the dose is escalated until pre-determined safety levels are reached, or intolerable side effects start showing up. Drug induced toxicity is analysed relative to the dose and unexpected side effects are explored. Furthermore, researchers characterize the metabolism and routes of excretion of the candidate drug. Phase 1 clinical trials last about 1 year. About 70% of drugs pass this phase.

Phase 2 clinical trials:

In Phase 2, the candidate drug is tested to see if it has any beneficial effect and to determine the dose level needed for this effect. Phase 2 clinical trials are clinical studies on a limited scale focused on efficacy. They typically involve 100-300 individuals who have the target disease and may be done at multiple sites to enhance recruiting. As the success of targeted anticancer treatments depends on the presence of a specific molecular target, the selection of suitable patients is key for testing these agents in phase 2 clinical trials. Patients receiving the drug are compared to similar patients receiving a placebo or another drug. The efficacy of a candidate drug in clinical trials is measured by means of certain predetermined endpoints such as overall survival or progression free survival. An increasingly important aspect in phase 2 trials for targeted agents is the development of mechanism-based biomarker to determine if the candidate drug affects the intended target. Phase 2 clinical trials last about 2 years. About 33% of drugs pass this phase.

Phase 3 clinical trials:

Phase 3 clinical trials are comparative studies on large number of patients to demonstrate that the candidate drug works. In order to generate statistically significant data about safety and efficacy phase 3 clinical trials are conducted as multi-center (conducted at more than one medical center), randomized (patients are randomly allocated to receive one or other of the alternative treatments) and double-blind (neither the participants nor the researchers know who is receiving a particular treatment) controlled studies. Phase 3 clinical trials typically involve 1000-3000 patients. The drug candidate is compared

with existing treatments focused on safety and efficacy. Phase 3 clinical trials should characterize the effect of the candidate drug in different populations considering patient variations in genetics, life style and concomitant conditions such as liver impairment or pregnancy using different dosages as well as combined treatment with other drugs. Phase 3 clinical trials should confirm therapeutic efficacy in the target population and determine the safety profile. It also provides the basis for labelling instructions to ensure proper use of the drug. Phase 3 clinical trials last about 3 years. About 25 - 30% of drugs pass this phase.[11]

EFFECTS OF ANTICANCER DRUGS:

Majority of the cytotoxic drugs have more profound effect on rapidly multiplying cells, because the most important target of action are the nucleic acids and their precursors, and rapid nucleic acid synthesis occurs during cell division. Many cancers (especially large solid tumours) have a lower growth fraction (lower percentage of cells are in division phase) than normal bone marrow, epithelial linings, reticuloendothelial (RE) system and gonads.These tissues are particularly affected in a dose-dependent manner by majority of drugs; though, there are differences in susceptibility to individual members.[12]

METABOLISM OF ANTICANCER DRUGS:

In cancer cells, metabolism is dysregulated to support the demands of uncontrolled proliferation. This rewiring of cellular metabolism leads to characteristic metabolic phenotypes that can be used for earlier cancer diagnosis, patient selection strategies for clinical trials, and/or as biomarkers of treatment response.Altered metabolism also results in unique metabolic dependencies that, in some cases, can be targeted with precision medicine and nutrition, including drugs that selectively target metabolic enzymes. Cancer and cancer therapies can also alter metabolism at the whole-body level and interact with the metabolic effects of diet and exercise in complex ways that may affect cancer outcomes and impact a patient's quality of life[13]

In the past, much of the assessment of metabolic changes has been limited to measuring individual hormones and metabolites using imaging modalities and standard clinical laboratory tests. In contrast, metabolomics involves the systematic measurement of many metabolites, including nutrients, drugs, signaling mediators, and the metabolic products of these small molecules in blood, urine, tissue extracts, or other body fluids.Metabolomics is a powerful tool that can identify cancer biomarkers and drivers of tumorigenesis.The objective of this review is to provide an overview of current and future opportunities of metabolomics to improve the diagnosis, monitoring, and treatment of cancer. We begin with a review of how metabolism and cancer interact at the level of cells, tissues, and the whole body.We then introduce general technical aspects of metabolomics, instrumentation, and source material, including the pros and cons of different approaches. In the final section, we provide examples of how metabolomics has been used in the clinical and translational research setting as a way to guide potential future applications. Because the role of metabolism in cancer has been extensively covered, the reader is referred to other excellent reviews cited throughout this article for a more in-depth discussion of specific topics.[14]

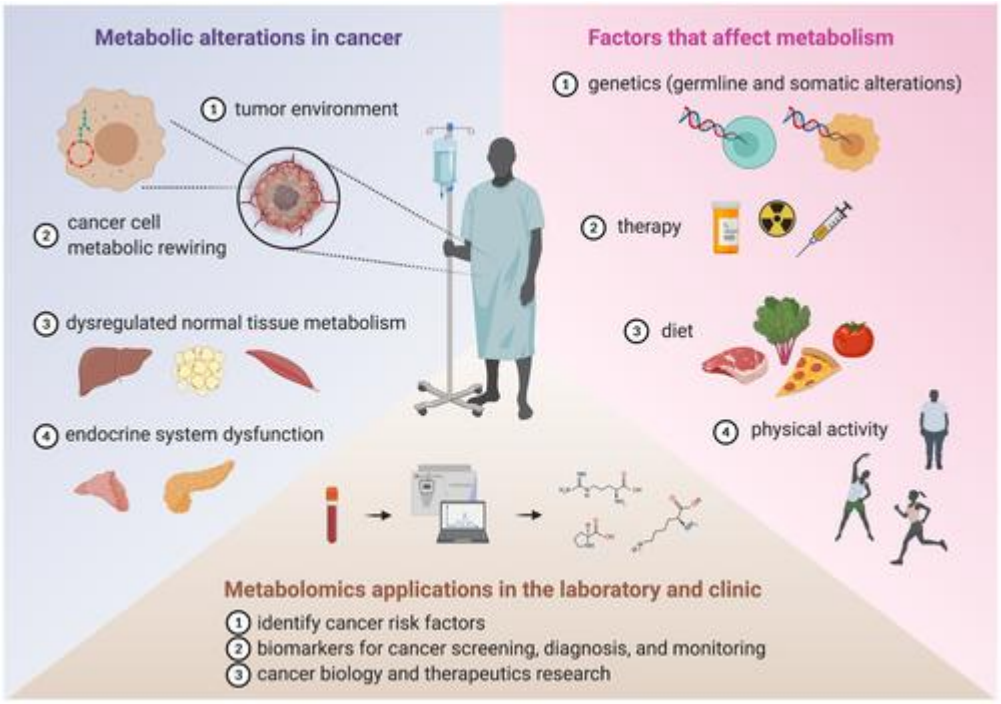

Figure:2 metabolic alterations in cancer and factors that effect metabolism

Cancer and metabolism interact at many levels. Cancer causes metabolic alterations in cancer cells and normal tissues, which, in turn, interact with intrinsic and extrinsic factors to affect systemic metabolism. Metabolomics is a systems-based approach used to define these complex metabolic interactions for diagnostic and therapeutic gain. See text for details.[(15)]

CONCLUSION:

Although it is used less compared with the other omics approaches, metabolomics has the potential to significantly impact core areas of oncology, including screening, diagnosis, and therapy. However, such applications require a better understanding of how these measurements are connected to human physiology and cancer biology. In biofluids that are readily accessible clinically, most notably plasma, our understanding of which metabolites can be measured to reflect cancer status is in its very early stages. Although some inroads have been made, it is still unclear to what extent a metabolite profile in plasma reveals the metabolic activity of the cancer. Additional studies conducting metabolomics experiments in fluids that harbour the cancer and connect these measurements to both metabolism and the biology of the tumour is a promising new direction. Much remains to be learned about how to interpret cancer metabolism from these measurements.

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