

# Pharmacodynamics of Chemotherapeutic agents

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## Abstract

A variety of compounds natural and synthetic in origin can be enlisted as chemotherapeutic agents. Their nature and role can be designed on the basis of tumor size, shape, age etc. The knowledge of pharmacokinetic and pharmacodynamic parameters of drug compounds are very much required to design a dosage form and many compounds are regularly being added into the list. A multidisciplinary approach is required to have the relevant data (both *in vitro* and *in vivo* studies) on the new molecules for better understanding the transport and mechanism of these compound in living systems. In this research article, a little effort has been made to study different historical development and pharmacodynamics of already used chemotherapeutic agents.

## Introduction

The chemical compounds used in the treatment/inhibition of tumor are chemotherapeutic agents or antineoplastic agents [1]. As per their mechanism of action these are categorized as mitotic inhibitors, topoisomerase inhibitors, antimetabolites and alkylating agents. Many adverse effects are also associated with this therapy which mainly includes (e.g. impaired growth of healthy cells nausea, enhanced infection risk of, and vomiting), and with some agents, an increased risk of secondary neoplasms. Symptomatic management of associated side effects is recommended to improve tolerance. Pharmacokinetics and pharmacodynamic are two important branches of pharmacology. One must have the knowledge of both to design a pharmaceutical dosage form. The former deals with the transport of drug compound in the living system to reach to target site in effective concentration while the later deal with the mechanism of action of drug. This is a list of chemotherapeutic agents most commonly used to treat any kind of cell growth [2] are; antibacterial compounds (prokaryotes)-antimycobacterials, antiparasitic agents (eukaryotes), antifungal compounds (eukaryotes), antiviral compounds and anticancer compounds

In particular, Pharmacodynamics drug mechanism that how a drug shows its therapeutic effect in living system and pharmacokinetics deals with the transport of drug compound in the system to reach to target site [3]. Both together influence dosing, benefit, and adverse effects. Pharmacodynamics is sometimes abbreviated as PD and pharmacokinetics as PK, especially in combined reference (for example, when speaking of PK/PD models). Some types of cancer can be cured effectively by the techniques of chemotherapy[4]. A revolution in medicine took place about 1825 when a group of doctors in Boston and London experimented to see what would happen if such treatments were withheld from diseases patients. Surprisingly, they found the survival rate essentially the same and, in some cases, better. Over the next few decades, the lessons from their experiments spread, and as the worst features of heroic therapy disappeared, doctors adopted a conservative, non-meddling approach to disease. It became the doctor's job to diagnose the illness, explain it to the family, predict what would happen in the next several days, and then stand by the care for the patient within the limits of what was known. The antimicrobial drugs that have become mainstays of our health-care delivery system. We shall explore their discovery and examine their uses, while noting the important side effects attributed to many of them. When Pasteur performed his experiments a hundred years ago, he implied that microorganisms could be destroyed and that someday, a way would be found to successfully treat many diseases. Only since the 1940s has Pasteur's prophecy become reality. Synthetically or semisynthetically manufactured drugs are commonly used these days which are fall in the category of "chemotherapeutic agents." Our discussion of chemotherapeutic agents will begin with a brief review of their developments.

### **Groups of Chemotherapeutic Agents:**

#### **Sulfanilamide and Other Sulfonamides:**

Sulfonamides are class of chemotherapeutic compounds and sulfanilamide is the first member of the class [5]. The mechanism of action of these agents seems to be competitive inhibition. According to the mechanism of competitive inhibition, folic acid is produced in the body of certain bacteria used further for the production of nucleic acid. Humans cannot synthesize folic acid for use in nucleic acid production. Folic acid cannot be synthesized in human body so it has to be supplied by food by bacteria synthesize it by themselves. In the production of folic acid, one part is PABA (para-aminobenzoic acid), which is structurally similar to

sulfanilamide in chemical structure. So, if sulpham drug is present in atmosphere, bacteria will be absorbed sulpham drug instead of PABA and it will be used in the manufacture of folic acid and consequently the DNA. In this way the bacterial DNA having sulpham drug as a part results to malfunctioning and consequently death of the bacterial cell

Modern sulfonamides are typified by sulfamethoxazole [6]. This drug is frequently used to treat gram -ve bacteria of urinary tract. Frequently the drug is combined with trimethoprim, a drug that inhibits another step in folic acid synthesis.

Commercially the drug combination is known as Bactrim. It is frequently used to treat Pneumocystis pneumonia. Another common sulfonamide, sulfisoxazole, is marketed as Gantrisin cream for vaginal infections due to Gram-negative bacteria. In some patients, a drug allergy to sulfonamides develops, with a skin rash, gastrointestinal distress, or type II cytotoxic hypersensitivity.

### **Other Chemotherapeutic Agents:**

The discovery and development of sulfanilamide led to the development of numerous other chemotherapeutic agents, many of which are currently in wide use. One example is the antituberculosis drug isoniazid (isonicotinic acid hydrazide, INH). Biochemists believe that isoniazid inhibits the folic acid synthesis required for the cell-wall formation in Mycobacterium species.

Isoniazid is prescribed along with ethambutol and rifampin. Ethambutol is a synthetic, well-absorbed drug that is tuberculocidal. Visual disturbances limit its use to treatment of tuberculosis.

Another chemotherapeutic agent, a quinolone called **nalidixic acid**, acts against the block's gram -ve bacteria of infection by altering DNA synthesis. Fluoroquinolones are nalidixic acid developed in lab used against the infection of urinary tract and intestinal tract. Examples of the fluoroquinolone drugs are ciprofloxacin (Cipro), enoxacin, and norfloxacin.

**Nitrofurantoin** is a drug actively excreted in the urine for urogenital infections. Metronidazole (Flagyl) has been used for decades **against trichomoniasis, amebiasis and giardiasis**. However, evidence that the drug

causes tumors in mice has prompted physicians to prescribe it with caution. The treatment of malaria has long depended upon the consumption of quinine.

When the tree bark used in its production became unavailable during World War II, researchers quickly set to work to develop two alternatives – **chloroquine and primaquine**. Chloroquine is effective for terminating malaria attacks; primaquine destroys the malaria parasites outside red blood cells.

Two other chemotherapeutic drugs, both inhibitory to mycobacterium species, bear brief mention. The first is para-aminosalicylic acid (PAS), a drug that closely resembles sulfonamides and is used for tuberculosis. The second agent is diaminodiphenylsulfone, or dapsone, used to treat leprosy.

The drugs mainly used are; alkylating drugs attack DNA to kill cancer cell e.g. cyclophosphamide, antimetabolites drugs inhibit with the making of DNA e.g.5-fluorouracil (5-FU), antitumor antibiotics drugs alter vital working of cell and making of genetic materials and peptones. It includes doxorubicin and bleomycin; plant alkaloids stop division of cells. For example, vinblastine and vincristine, steroid hormones retard hormones cancers e.g. tamoxifen in breast cancer.

## Conclusion

The drug compounds used to control the growth of tumor or inhibition are termed as chemotherapeutic agents as many of them are synthetic in origin. Although many natural counterparts also present in the list. As per their mechanism of action these are categorized as mitotic inhibitors, topoisomerase inhibitors, antimetabolites and alkylating agents. Chemotherapy embraces the use of drugs that target tumors and, in fact, has now come to be associated specifically with that branch of pharmacology (Oncology). The mechanism of these drugs is complex associated with many risks but still many time proves to quite hopeful in critical cases. Many new drugs are being synthesized and are under trial worldwide.

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