مجلة الدراسات التربوية والعلمية - كلية التربية - الجامعة العراقية
العدد السابع والعشرون - المجلد الثالث - علوم الحياة - آذار 2026 م
doi.org/10.52866/esj.2026.03.27.08

# The role of Cytotoxic pharmacological compounds in inhibiting the viability of cancer cell

Farah T.O. Al-Jumaili
Department of Molecular and Medical Biotechnology,
College of Biotechnology, Al-Nahrain University, Baghdad, Iraq

**Abstract:**

Cytotoxic medications hinder or stop the cell's ability to operate. The main application for cytotoxic medications is the treatment of cancer, usually in interaction with chemotherapy. Their applications have grown in recent years to include the treatment of rheumatoid and juvenile rheumatoid arthritis, psoriasis, and steroid-resistant muscular disorders.

The most widely used class of cytotoxic medications is called antineoplastics. It was common to use the terms cytotoxic and antineoplastic interchangeably. Cytotoxic medications can stop the cancer cells from proliferating and growing quickly. They may also have effect on the development of other quickly dividing cells in the body, such as the coating of the digestive tract and hair follicles. Along with the cancer cells many normal cells are also harmed by the treatment.

**Keywords: cytotoxicity; Chemotherapy; Antineoplastics; Rheumatoid.**

# الدور السمي الخلوي للمركبات الدوائية في تثبيط بقاء الخلايا السرطانية

أ.م.د فرح تركي عريبي الجميلي
كلية التقنيات الاحيائية / قسم التقنيات الحيوية الجزيئية والطبية / جامعة النهرين ، العراق - بغداد

**مستخلص:**

تُعيق الأدوية السامة الخلايا أو تُوقف قدرتها على العمل. ويتمثل الاستخدام الرئيسي لهذه الأدوية في علاج السرطان، عادةً بالتفاعل مع العلاج الكيميائي. وقد توسعت تطبيقاتها في السنوات الأخيرة لتشمل علاج التهاب المفاصل الروماتويدي والروماتويدي لدى الأطفال، والصدفية، واضطرابات العضلات المقاومة للستيرويدات تُسمى أكثر أنواع الأدوية السامة للخلايا مضادات الأورام. وكان من الشائع استخدام مصطلحي «سام للخلايا» و«مضاد للورم» بالتبادل. ويمكن للأدوية السامة للخلايا أن تمنع الخلايا السرطانية من التكاثر والنمو السريع. كما قد تؤثر على نمو خلايا أخرى سريعة الانقسام في الجسم، مثل غشاء الجهاز الهضمي وبصيلات الشعر. وإلى جانب الخلايا السرطانية، يتضرر العديد من الخلايا الطبيعية أيضًا بسبب هذا العلاج.

**الكلمات المفتاحية** : السمية الخلوية – العلاج الكيميائي– مضادات الأورام– التهاب المفاصل .

## Cytotoxicity

Cytotoxicity is the degree to which a chemical compound or biological agent can harm cells, leading to reduced cell viability, altered function, or cell death, means the characteristic of being cell-toxic. hazardous metals, chemicals, radiation particles, microbial neurotoxins, and certain neurotransmitters Examples of hazard agents are those that occur when the system is out of balance. In addition, convinced venoms are poisonous to cells, such as that of the brown recluse spider (*Loxosceles reclusa*) or puff adder (*Bitis arietans)* (1) .

## Cell physiology

is the area of biology that focuses on the activities and processes of cells, which are the fundamental structural and functional building blocks of all living things, It focuses on how cells adapt to their surroundings, communicate, and sustain life processes. The prognosis for cells treated with the cytotoxic chemical can vary. Death is the condition in which the cells lyse fast and lose their membrane integrity. The cells can also initiate apoptosis, a controlled cell death caused by a genetic mechanism, or they can cause actively proliferating and separating (a drop in cell viability). Necrosis-affected cells which usually enlarge quickly, lose their ability to form membranes, stop their metabolism, and leak their contents into the surrounding area. Rapidly necrotizing cells *in vitro* loss the energy or time to trigger the apoptotic apparatus and will not show apoptotic markers (2) .

The well-defined cytological and molecular processes that characterize apoptosis include nuclear condensation, cytoplasmic shrinkage, DNA fragmentation into regularly sized fragments, and a change in the cell's refractive index. Secondary necrosis eventually occurs in cultured cells after they undergo apoptosis. They will halt metabolism, lyse, and lose membrane integrity.(3) .

## Measurement

Cytotoxicity tests are usually used in the pharmaceutical sector to assess the cytotoxicity of chemical libraries. Scientists can search for cytotoxic

compounds or, otherwise, filter "hits" from early high-quantity drug screens for unfavorable cytotoxic effects if they are interested in developing a treatment that specifically targets fast dividing cancer cells. (1) .

Assessing the integrity of the cell membrane is typically how cytotoxic effects and cell viability are measured.

Cytotoxic compounds often erode the integrity of cell membranes. Important dyes, such as propidium iodide or trypan blue, are frequently prohibited from entering healthy cells. They can, however, penetrate and dye intracellular components when the cell membrane is compromised. As an alternative, the integrity of the membrane can be assessed by monitoring substances that are normally contained inside cells. The chemical commonly evaluated using the LDH assay is lactate dehydrogenase (LDH). A color shift results from LDH converting NAD to NADH when NADH interacts with a specific probe. (4).

Within a single cell population researchers can now evaluate the quantity of living and dead cells to identify the protease biomarkers. healthy cell membranes allow the live-cell protease to function if a cell is damaged or exposed to the outside world, the protease becomes inactive. Dead-cell protease is unable to traverse the cell membrane and can only be quantified in culture media subsequent to the loss of membrane integrity in the cells (5) .

The MTS assay or 2,3-bis-(2-methoxy-4-nitro-5-sulfophenyl)-2H-tetrazolium-5-carboxanilide (XTT), which produces a water-soluble product, or 3-(4, 5-Dimethyl-2-thiazolyl)-2, 5-diphenyl-2H-tetrazolium bromide (MTT) fig (1) can also be used to evaluate cytotoxicity. A colorimetric reaction is used in this assay to quantify the decrease of the cell. The MTS reagent will be transformed by living cells into a fluorescent dye and a colored (Formazan) product. In addition to employing dyes to indicate the redox potential of cells for viability monitoring, scientists have created tests that use ATP concentration as a viability marker. Among these ATP-based tests are bioluminescent assays, where ATP acts as the luciferase reaction's limiting reagent (6).

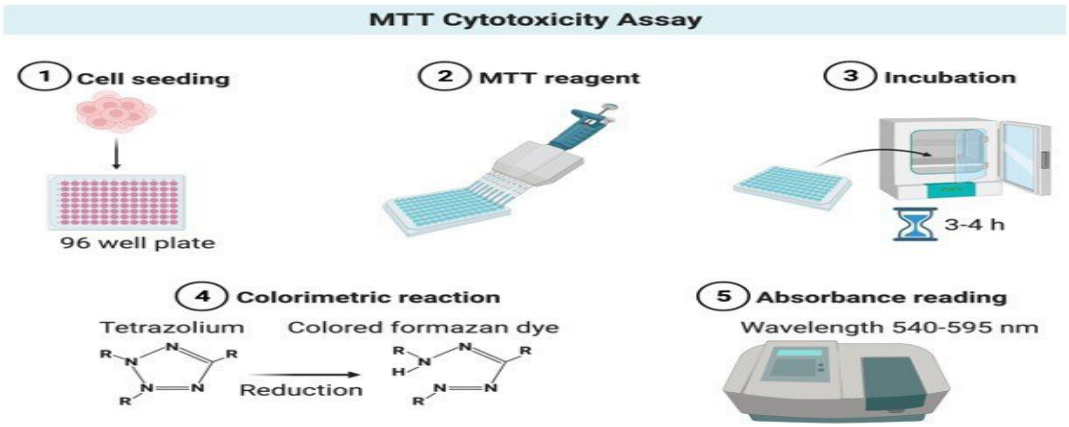


**Figure (1) : MTT assay (6)**

Cytotoxicity can be also monitored by (SRB) assay, WST assay and clonogenic assay (7)

## Drug toxicity

Is a drug's unwanted or detrimental effect on biological organs that results in cell death or functional abnormalities. Both acute (arising shortly after exposure) and chronic (arising after prolonged use) effects are possible Drug toxicity, which deals with the concept of "cell viability," which is commonly thought to be an aggregate characteristic describing the number and proportion of living and dead cells in the population, was one of the primary areas of focus in pharmacology. Additionally, it contributes to the loss of roughly one-third of therapeutic candidates and dramatically increases the expense of drug research..(8)

Cytotoxic medications are a component of several chemotherapy treatments, and their aim is to obstruct cell division. These medications aim to destroy tumors before they spread to the hosts, however they are unable to distinguish between normal and malignant cells.(8)

In the well-established and constantly growing field of cancer treatment, cytotoxic medicines play a significant role. Cytotoxic substances not only have the ability to destroy healthy cells but also have therapeutic effects

on cancerous cells. It is frequently not feasible for a patient to finish the entire course at the center due to financial limitations and great reserves from their home towns or villages because of the comparatively small number of cancer treatment centers.

Many patients find it convenient to complete the remaining treatment in their closest medical facility after the first one or two courses. Physicians at these non-specialized facilities might not be aware of the drug's local side effects, though. The infusion of cytotoxic medications is frequently entrusted to a junior house surgeon or intern, even in cancer institutions. This is because their lack of training in venipuncture and unawareness of the defenses involved in infusing a cytotoxic drug might result in the drug extravasation the body (9).

It speeches the idea of "cell viability," which is usually took as a broad characteristic that characterizes the number and proportion of living and dead cells in the population. The formation of reliable, available, and scalable viability assays based on the effects of biomarkers linked to cell death is crucial for the effective screening of drug toxicity.(10)

The first class of medications that were successfully utilized to treat neoplasms were cytotoxic ones. The first medication to be created was nitrosourea. These medications cause apoptosis (cytotoxicity) by attacking DNA or metabolic processes that are essential for cell division. Alkylating agents, antimetabolites, natural products, and other medications are the general categories into which they fall. DNA interstrand linkage is caused by alkylating chemicals through alkylation. Through the formation of DNA adducts, platinum compounds also result in inter- and intra-strand linking. Antimetabolites function by preventing the synthesis of pyrimidine, purines, or both. Natural products include antibiotics that create breaks in DNA strands fig (2) camptothecins and epipodophyllotoxins that interfere with topoisomerase function, and vinca alkaloids and taxanes, which damage microtubules (11).

Drugs in the miscellaneous group include those that work through completely distinct mechanisms, such as arsenic trioxide (ATO) and tretinoin

(ATRA), which both cause cell differentiation. Every drug class has a large number of more recent equivalents. Despite giving patients hope, cytotoxic chemotherapy comes with a multitude of adverse drug reactions (ADRs), mostly because these medications act on the body's normal, quickly dividing cells. Because tailored chemotherapy has a lower frequency of adverse drug reactions, it has recently acquired importance in research.

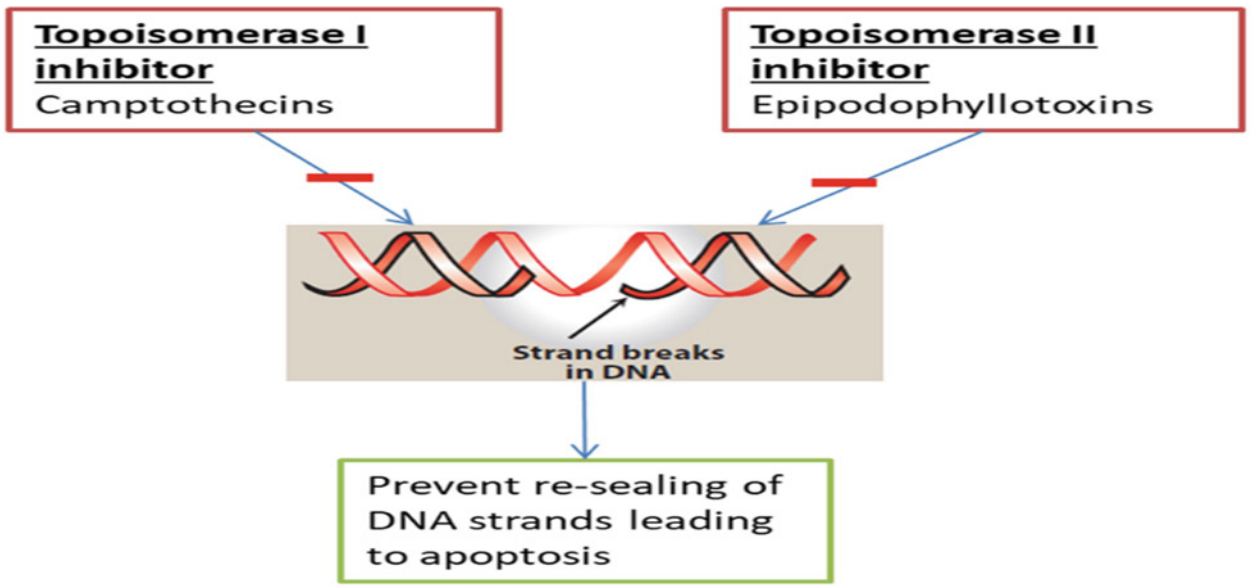


**Figure (2):Antibiotics that create breaks in DNA strands (11)**

Different cell fates can arise from treating cells with the cytotoxic chemical. The cells may experience necrosis, a condition in which cell lysis causes them to lose their membrane integrity and quickly perish. The cells can either initiate a genetic program of controlled cell death (apoptosis) or cease actively growing and dividing (a decrease in cell viability). (12).

A wide range of compounds can be harmful. Scientists and medical professionals need to be aware of the impacts and the extent to which they can harm an organism because certain substances are more poisonous than others. The property that makes a substance toxic or poisonous, such as a drug, is called toxicity. The dosage determines the toxicity. Toxicology is a more gener-

al term for a substance's detrimental effects on an organism, whereas cytotoxicity describes a substance's toxicity to cells. A cytotoxic substance can cause necrosis or apoptosis, which can damage or destroy cells. Because certain chemicals are more cytotoxic than others, researchers check a chemical's cytotoxicity levels to make sure it won't harm or kill people. Cytotoxic agents include, for example, several venoms and chemotherapy drugs.(13)

Cytotoxicity measurement finds application in the realm of chemotherapeutic medications and cancer research. It is critical to understand a drug's cytotoxic effects on malignant cells as well as any unintentional effects on normal, healthy cells. For instance, several chemotherapy medications are teratogenic, meaning they cause physical and functional abnormalities in fetuses or embryos(14).

Chemotherapy can be administered to relieve symptoms as well as with the goal of curing or extending life. Radiation and surgery are increasingly being combined with chemotherapy. This may be used as an adjuvant therapy or to shrink the tumor. Every cytotoxic medication has adverse effects, thus the patient's benefit and toxicity must be balanced (15).

Certain cancer treatments involve the use of medication combinations. Although these combinations usually have higher cytotoxic levels than individual medications, they offer the benefit of improving tumor treatment and improving patient survival. However, single-drug treatment is still the best option for certain malignancies (16).

Cytotoxic medicines are classified into various classes. Each has distinct areas of action, toxicity, and anti-tumor efficacy. The sites of metabolism and excretion are important factors to take into account before choosing a medicine since they may increase toxicity by impairing drug handling. In order to prevent any potential negative side effects, dosage is very crucial (17).

**Cytotoxicity and Nanoparticles**

Recently, there has been increased interest in the topic of nanotechnology. Although the quantity of these materials and their uses has expanded significantly over the past few decades, there is still a dearth of research on

the long-term effects of nanoparticles and nanomaterials on the human body. This suggests that they might be cytotoxic as well. An increasing number of medicinal and diagnostic instruments are utilizing nanoparticles (18) .

Variations in the physicochemical characteristics of nanoparticles can cause the body to unintentionally become cytotoxic. Knowing their cytotoxic effects is not limited to their usage in medicine. They also occur naturally as an unintentional byproduct of industrial research and development.

A number of routes exist for nanoparticles to enter the body, including injection, implantation, absorption, and ingestion. Once within the body, they may interact with lipids, proteins, DNA, and cell membranes, causing spontaneous adsorption of proteins and other potentially harmful effects. These may cause apoptosis, alteration of cell membranes, inflammation, and oxidative stress, among other bioeffects. Understanding their level of cytotoxicity is essential as they are utilized increasingly frequently across all industries (19).

**Cytotoxic Agents in Humans and Animals**

Cytotoxic constituents can also be originate in humans and animals:

**Cytotoxic T-cells**

Cytotoxic T-cells, also known as cytotoxic T-lymphocytes, are produced by our bodies. These T-cell types look for, locate, and eliminate virus-infected cells. They are also capable of killing cancer cells .

Utilizing the body's own cytotoxic cells to combat cancer is an intriguing field of cancer research. For instance, the immune system's own cytotoxic cells are natural killer lymphocytes and CD8+ cells .

These therapies function differently. Some enable T-cells to "see" previously concealed cancer cells, while others collect and multiply the cells. (20).

**Cytotoxic Venom**

The presence of cytotoxic T-cells is not unique to humans. Vipers, cobras, and violin spiders, for instance, have cytotoxic venoms .

There are other cytotoxic compounds in nature, such as snake venom. Even your own cytotoxic cells, which are essential to your immune system,

are produced by your body (21).

It's informal to confuse the "cytotoxic" with "genotoxic." If a chemical harms cells, it is deemed cytotoxic. If a chemical directly damages the DNA of cells, it is deemed genotoxic. Death may or may not follow DNA damage. Damage to a cell's DNA results in mutations. If the mutated cells are not fixed, cancer may develop.(22)

Cancer often happens when there are mutations in two kinds of genes

- Oncogenes mean the genes that produce the proteins that propel cell division
- The genes encoding the proteins that repair damaged DNA or, in the event that the DNA cannot be repaired, kill the cell (tumor suppressor genes) One example of this type of gene is the BRCA gene.(23).
-

**Dangers of Cytotoxic Substances**

Although cytotoxic medications destroy cancer cells, they can also harm healthy, normal cells. This procedure is connected to a number of the adverse effects of chemotherapy.Those who handle cytotoxic drugs or substances must use extreme caution. Depending on how they might be exposed to a drug, different actions must be taken. (24).

Protections a person might need to take when handling cytotoxic substances include:

- Gloves with their shirt manacles inserted under the gloves
- Long cover clothing
- Disposable dresses
- Safety glasses
- Protecting the respiratory system

Cytotoxic safety measures may need to be followed at home by cancer patients undergoing treatment. These precautions safeguard their relatives in case they inadvertently come into contact with bodily fluids containing cells that are harmful to humans.(25)

## Conclusion

In an attempt to find the perfect medication that would destroy the tumor without endangering healthy tissue, there was a massive rush of research into novel anticancer drugs following the initial encouraging outcomes of cytotoxic treatment in the 1940s. Although this ambition remains unfulfilled forty years later, the hunt for

novel cytotoxic agents has produced thousands of molecules with potential medicinal uses. Nowadays, a little fewer than forty of these are regularly utilized.

## References

**1-**Gavanji S, Bakhtari A, Famurewa AC, Othman EM (January 2023). "Cytotoxic Activity of Herbal Medicines as Assessed in Vitro: A Review". *Chemistry & Biodiversity*. 20 (2): 3–27.

**2-**Bertheloot D, Latz E, Franklin BS. Necroptosis, pyroptosis and apoptosis: an intricate game of cell death. *Cellular Mol Immunol.* 2021

**3-**Riss TL, Moravec RA (February 2004). "Use of multiple assay endpoints to investigate the effects of incubation time, dose of toxin, and plating density in cell-based cytotoxicity assays". Assay Drug Dev Technol. 2 (1): 51–62.

**4-**Chan FK, Moriwaki K, De Rosa MJ. Detection of necrosis by release of lactate dehydrogenase activity. Methods Mol Biol. 2013;979:65-70

**5-**Capoor, Malini R; Bhowmik, Kumar Tapas (2017). "Cytotoxic Drug Dispersal, Cytotoxic Safety, and Cytotoxic Waste Management: Practices and Proposed India-specific Guidelines". Indian Journal of Medical and Paediatric Oncology. 38 (2): 190–197

**6-**Fan F, Wood KV (February 2007). "Bioluminescent assays for high-throughput screening". Assay Drug Dev Technol. 5 (1): 127–36.

**7-**Easty, A.C.; Coakley, N.; Cheng, R.; Cividino, M.; Savage, P.; Tozer, R.; White, R.E. (February 2015). "Safe handling of cytotoxics: guideline recommendations". Current Oncology. 22 (1): e27–e37.

**8-**Guengerich FP. Mechanisms of drug toxicity and relevance to pharmaceutical development. Drug Metab Pharmacokinet. 2011;26:3–14.

**9-**Thakur JS, Chauhan CG, Diwana VK, Chauhan DC, Thakur A. Extravasational side effects of cytotoxic drugs: A preventable catastrophe. Indian J Plast Surg. 2008 Jul;41(2):145-50. doi: 10.4103/0970-0358.44923. PMID: 19753254; PMCID: PMC2740528.

**10**-Preventing Occupational Exposures to Antineoplastic Drugs in Health Care Settings, Thomas H. Connor and Melissa A. McDiarmid, CA Cancer Journal for Clinicians 2006;56;354-

365

**11**-Antonia S. J., Villegas A., Daniel D., Vicente D., Murakami S., Hui R., (2017). Durvalumab after chemoradiotherapy in stage III non-small-cell lung cancer. *N. Engl. J. Med*. 377, 1919–1929.

**12**- Eesha Shukla, Divya Dhatri Kara, Tanvi Katikala and Mahalaxmi RathnanandJournal: Drug Development and Industrial Pharmacy, 2023, Volume 49, Number 1, Page 1.

**13**- Çelik, T. A. (2018). Introductory Chapter: Cytotoxicity. *InTech*.

**14**- Gilbert S., Oliphant C., Hassan S., et al. ATP in the tumour microenvironment drives expression of nfP2X7, a key mediator of cancer cell survival. *Oncogene*. 2019;38(2):194–208

**15**- Janssen L.M.E., Ramsay E.E., Logsdon C.D., Overwijk W.W. The immune system in cancer metastasis: friend or foe? *J Immunother Cancer.* 2017;5(1):79.

**16**-Emon B., Bauer J., Jain Y., Jung B., Saif T. Biophysics of tumor microenvironment and cancer metastasis - a mini review. *Comput Struct Biotechnol J.* 2018;16:279–287

**17**- Edwardson DW, Narendrula R, Chewchuk S, Mispel-Beyer K, Mapletoft JP, Parissenti AM. Role of Drug Metabolism in the Cytotoxicity and Clinical Efficacy of Anthracyclines. Curr Drug Metab. 2015;16(6):412-26

**18**- Sun, H . (2019) Cytotoxicity-Related Bioeffects Induced by Nanoparticles: The Role of Surface Chemistry *Front. Bioeng. Biotechnol.* Vol. 7

**19**- Riss, T . (2019) Cytotoxicity Assays: *In Vitro* Methods to Measure Dead Cells Assay *Guidance Manual* . National Institute for Health and Care Excellence (Website) Cytotoxic Drugs [Accessed online 26th May 2021]

**20**-Papaioannou NE, Beniata OV, Vitsos P, Tsitsilonis O, Samara P. Harnessing the immune system to improve cancer therapy. *Ann Transl Med*. 2016;4(14):261. doi:10.21037/atm.2016.04.01

**21**-Bracci L, Schiavoni G, Sistigu A, Belardelli F. Immune-based mechanisms of cytotoxic chemotherapy: implications for the design of novel and rationale-based combined treatments against cancer. *Cell Death Differ*. 2014;21(1):15–25.

**22**- Casey SC, Vaccari M, Al-Mulla

F,. The effect of environmental chemicals on the tumor microenvironment. Carcinogenesis. 2015;36 Suppl 1(Suppl 1):S160–S183.

**23**- Szikriszt B, Póti Á, Pipek O,. A comprehensive survey of the mutagenic impact of common cancer cytotoxics. Genome Biol. 2016;17:99.

**24**- Sun, H (2019) Cytotoxicity-Related Bioeffects Induced by Nanoparticles: The Role of Surface Chemistry *Front. Bioeng. Biotechnol.* Vol. 7 .

**25**- Piccinini F, Tesei A, Arienti C, Bevilacqua A. Cell counting and viability assessment of 2d and 3d cell cultures: expected reliability of the trypan blue assay. Biological procedures online. 2017;19 (1):8.