



**INTERNATIONAL JOURNAL OF
PHARMACEUTICAL SCIENCES**
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: <https://www.ijpsjournal.com>



Review Paper

Advances in Blood Cancer: Pathophysiology, Diagnosis and Emerging Therapeutic Strategies

Kiran Aher¹, Nandini Bagul¹, Manjusha Chavan¹, Gaurav Kasar^{*1}, Dipti Chavan¹,
Dr. Chandrashekhar Patil¹, Dr. Sunil Mahajan²

¹Department Of Pharmacology, Divine College of Pharmacy, Satana (Nashik), India

²Department Of Pharmaceutical Chemistry, Divine College of Pharmacy, Satana (Nashik), India

ARTICLE INFO

Published: 25 May. 2025

Keywords:

Blood cancer,
phytochemicals, Medicinal
plants

DOI:

10.5281/zenodo.15512403

ABSTRACT

Blood cancer or hematologic malignancy, comprises a range of disorders affecting the bone marrow, lymphatic system and blood circulation, leading to severe complications such as anemia, immune dysfunction and bleeding disorders. This review explores the underlying mechanisms of blood cancer, emphasizing genetic mutations, chromosomal abnormalities, dysregulated signaling pathways, epigenetic modifications and immune system evasion. Understanding these factors provides insights into targeted therapeutic strategies. Additionally, the role of natural products in blood cancer treatment is gaining recognition due to their bioactive compounds with potential anticancer properties. Various phytochemicals exhibit anti-leukemic effects through mechanisms such as apoptosis induction, oxidative stress modulation, and inhibition of key cancer-related pathways. Medicinal plants have demonstrated promising anticancer activity. This review highlights the significance of natural products in the development of novel blood cancer treatments and calls for further research and clinical validation to integrate these compounds into therapeutic regimens effectively.

INTRODUCTION

Blood cancer, also known as hematologic malignancy, is a group of disorders characterized by the uncontrolled proliferation of abnormal blood cells, affecting the bone marrow, lymphatic system, and blood circulation. These malignancies

disrupt normal hematopoiesis, impair immune function, and lead to severe clinical manifestations, including anemia, increased susceptibility to infections, and bleeding disorders. Blood cancers primarily originate from mutations in hematopoietic stem cells, resulting in the aberrant growth of leukocytes, erythrocytes, or

***Corresponding Author:** Gaurav Kasar

Address: Department of Pharmacology, Divine College of Pharmacy, Satana (Nashik), India

Email ✉: gauravkasar008@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



platelets [1]. The three major categories of blood cancer include leukemia, lymphoma, and multiple myeloma. Leukemia is a malignancy of the bone marrow and blood, wherein abnormal white blood cells proliferate uncontrollably, hindering the production of normal blood cells [2,3]. Lymphoma affects the lymphatic system, leading to the

abnormal growth of lymphocytes, which compromises immune function. Multiple myeloma, on the other hand, is characterized by the excessive proliferation of plasma cells in the bone marrow, resulting in complications such as bone lesions, kidney dysfunction and immunodeficiency [4].

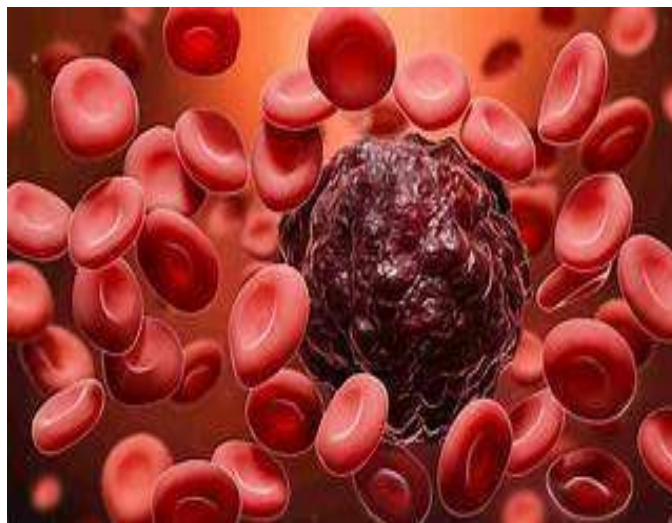


Figure 1: Blood cancer

The exact etiology of blood cancer remains multifactorial, with genetic predisposition, environmental factors, viral infections, and exposure to carcinogens playing significant roles. Genetic mutations in key regulatory genes, such as TP53, JAK2, and BCR-ABL, have been implicated in the pathogenesis of hematologic malignancies. Additionally, factors such as ionizing radiation, exposure to benzene, and viral infections (e.g., Epstein-Barr virus, human T-cell leukemia virus) contribute to the development of blood cancers [5]. Advancements in diagnostic modalities, including molecular profiling, cytogenetics, and next-generation sequencing, have enhanced our understanding of blood cancer pathophysiology. Early detection through hematological tests, bone marrow biopsy, and flow cytometry has improved patient prognosis and treatment outcomes. Conventional therapies such as chemotherapy, radiotherapy, and hematopoietic

stem cell transplantation (HSCT) remain the cornerstone of blood cancer treatment. However, recent advancements in targeted therapy, immunotherapy, and CAR-T cell therapy have revolutionized treatment approaches, offered improved survival rates and reduced adverse effects [6,7]. Despite significant progress in blood cancer research, challenges persist in treatment resistance, disease relapse, and managing therapy-induced complications. Further exploration of precision medicine, novel biomarkers, and gene-editing technologies holds promise in overcoming these obstacles and enhancing patient outcomes [8]. This review aims to provide a comprehensive overview of blood cancer, covering its epidemiology, pathophysiology, diagnostic approaches, and recent advancements in therapeutic strategies. By elucidating the current understanding of hematologic malignancies, this article seeks to contribute to the ongoing efforts in

developing more effective and personalized treatment modalities for patients battling blood cancer.

Types of Blood Cancers

Blood cancers are broadly classified into three main types: leukemia, lymphoma, and multiple myeloma. Each type has subcategories that vary in pathophysiology, clinical presentation, and treatment approaches.

1. Leukemia Leukemia is a cancer of the blood and bone marrow characterized by the excessive production of abnormal white blood cells. It is classified into four main types:

- **Acute Lymphoblastic Leukemia (ALL):** A rapidly progressing leukemia that primarily affects children, though it can also occur in adults. It arises from immature lymphocytes and leads to severe immune system impairment.
- **Acute Myeloid Leukemia (AML):** Affects the myeloid lineage of blood cells, leading to the accumulation of immature white blood cells (blasts) in the bone marrow, disrupting normal blood cell production.
- **Chronic Lymphocytic Leukemia (CLL):** A slow-growing leukemia that affects B lymphocytes. It is more common in older

adults and may not show symptoms for a long time.

- **Chronic Myeloid Leukemia (CML):** Characterized by the presence of the Philadelphia chromosome (BCR-ABL fusion gene), leading to uncontrolled proliferation of myeloid cells [9].

2. Lymphoma Lymphoma originates in the lymphatic system and primarily affects lymphocytes. The two main types are:

- **Hodgkin Lymphoma (HL):** Marked by the presence of Reed-Sternberg cells, this lymphoma typically originates in the lymph nodes and spreads in an orderly manner. It is highly treatable, especially in early stages.
- **Non-Hodgkin Lymphoma (NHL):** A diverse group of lymphomas that vary in aggressiveness and originate from either B cells or T cells. Examples include diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma [10].

3. Multiple Myeloma Multiple myeloma is a plasma cell malignancy that affects the bone marrow, leading to excessive production of abnormal antibodies (paraproteins). This condition results in bone damage, kidney dysfunction, and immune suppression. It is often diagnosed using serum protein electrophoresis and bone marrow biopsy [11].

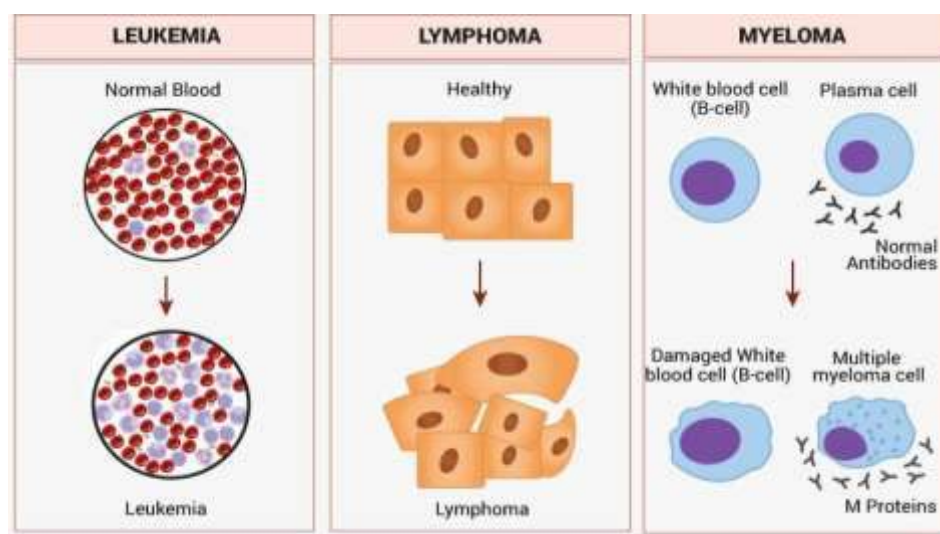


Figure 2: Types of Blood cancer

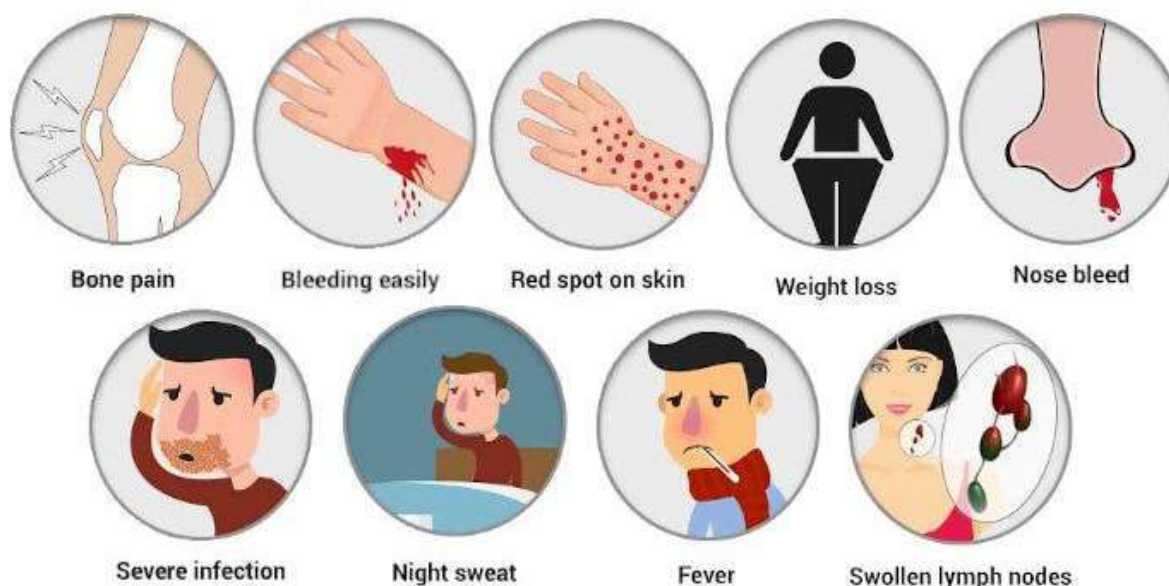


Figure 3: Symptoms of Blood cancer

Causes of Blood Cancer

Blood cancer arises from a combination of genetic, environmental and lifestyle factors.

Genetic Mutations

Inherited mutations in genes like TP53, BRCA1, and BRCA2 increase susceptibility. Somatic mutations, such as BCR-ABL translocation in CML, drive malignant transformation, leading to

uncontrolled cell growth and impaired regulation of normal blood cell production.

Exposure to Radiation and Chemicals

Ionizing radiation from medical treatments or environmental exposure significantly raises the risk of developing blood cancers. Carcinogens like benzene and formaldehyde are well-documented contributors to DNA mutations, leading to hematologic malignancies.

Viral Infections

Certain viruses are closely linked to the development of blood cancers. Epstein-Barr virus (EBV) is associated with Burkitt's lymphoma and Hodgkin lymphoma, while Human T-cell leukemia virus (HTLV-1) has been implicated in adult T-cell leukemia/lymphoma.

Weakened Immune System

Individuals with compromised immune function, such as those with autoimmune disorders or undergoing immunosuppressive therapy (e.g., organ transplant patients), have an increased likelihood of developing blood cancers due to reduced immune surveillance.

Lifestyle Factors

Smoking has been linked to an elevated risk of acute myeloid leukemia (AML) and other hematologic malignancies. Additionally, poor dietary habits, obesity, and a sedentary lifestyle contribute to overall cancer risk and progression.

Family History

A family history of leukemia, lymphoma, or multiple myeloma significantly raises an individual's predisposition to developing blood cancer. Genetic predisposition plays a crucial role in determining susceptibility to hematologic malignancies [12-14].

Mechanism of Blood Cancer

The development of blood cancer is driven by a series of genetic, molecular, and environmental factors that disrupt normal hematopoiesis and immune regulation. The primary mechanisms involved in the pathogenesis of blood cancers include:

1. Genetic Mutations and Chromosomal Abnormalities

Genetic alterations play a crucial role in the initiation and progression of blood cancer. Mutations in tumor suppressor genes (e.g., TP53, RUNX1) and oncogenes (e.g., JAK2, BCR-ABL) lead to uncontrolled cellular proliferation, apoptosis resistance, and impaired differentiation of hematopoietic cells. Chromosomal translocations, such as the Philadelphia chromosome (t [9;22]) in chronic myeloid leukemia (CML), result in the formation of fusion proteins that drive cancerous growth [15].

2. Dysregulation of Cell Signaling Pathways

Aberrant activation of signaling pathways such as JAK-STAT, PI3K-AKT, and NF- κ B contributes to sustained cell survival, proliferation, and evasion of immune surveillance. These pathways promote the expansion of malignant blood cells while suppressing normal hematopoietic differentiation.

3. Altered Epigenetic Regulation

Epigenetic modifications, including DNA methylation, histone acetylation, and chromatin remodeling, affect gene expression in hematologic malignancies. Dysregulation of epigenetic regulators such as DNMT3A and TET2 leads to aberrant stem cell self-renewal and leukemic transformation [16].

4. Microenvironmental Influences

The bone marrow microenvironment provides critical support for hematopoietic cells through cytokines, growth factors, and stromal cell interactions. In blood cancer, the microenvironment becomes altered, favoring the proliferation and survival of malignant cells while inhibiting normal hematopoiesis. In multiple myeloma, for example, bone marrow stromal cells



secrete interleukin-6 (IL-6), which promotes myeloma cell growth and drug resistance [17].

5. Immune System Evasion

Cancerous blood cells employ multiple mechanisms to evade immune detection, including downregulation of major histocompatibility complex (MHC) molecules, production of immunosuppressive cytokines, and induction of regulatory T cells (Tregs). This immune evasion facilitates the unchecked growth of malignant cells.

6. Deregulated Apoptosis Mechanisms

Apoptosis, or programmed cell death, is a crucial process in maintaining normal cell populations. Blood cancers often involve mutations in pro-apoptotic (e.g., BAX) or anti-apoptotic (e.g., BCL-2) genes, leading to resistance against cell death and enhanced survival of malignant cells.

7. Viral Involvement in Oncogenesis

Certain viruses, such as the Epstein-Barr virus (EBV) and human T-cell leukemia virus type 1 (HTLV-1), contribute to blood cancer development by integrating their genetic material into host cells, leading to oncogenic transformation. For instance, EBV is strongly associated with Burkitt's lymphoma and Hodgkin's lymphoma [18-20].

Diagnosis of Blood Cancer

Blood cancer is diagnosed through a combination of laboratory tests, imaging studies, and biopsies. Common diagnostic methods include:

- **Complete Blood Count (CBC):** Measures red blood cells, white blood cells, and platelets to detect abnormalities.

- **Bone Marrow Biopsy:** Examines bone marrow samples to identify cancerous cells.
- **Flow Cytometry:** Analyzes cell surface markers to classify leukemia and lymphoma subtypes.
- **Cytogenetic and Molecular Tests:** Detect genetic mutations such as BCR-ABL in CML.
- **Imaging Studies (CT, MRI, PET scans):** Identify tumor spread and organ involvement [21,22].

Role of Natural Products in Blood Cancer

Natural products, especially plant-based medicines and remedies have been studied since time immemorial due to their therapeutic effectiveness against various maladies and illnesses. This prompted the exploration and isolation of numerous phytoconstituents with clinical benefits and these compounds have had profound impacts in medical science. For cancer therapy, up to 60% of anticancer candidates in clinical use that exhibited significant efficacy are natural product derivatives [23]. They serve as good sources of lead molecules and offer affordable materials in modern drug discovery. Plant-based natural products cause fewer undesirable side effects probably due to their similarity with chemical entities found in the human diet that have significant tolerance induction ability. The secondary metabolites of plants such as flavonoids, tannins, alkaloids and terpenoids are well known to possess substantial anticancer capabilities. They trigger, promote or modulate the metabolic pathways that can alter proliferation, migration and apoptosis in cancer cells via a multitude of biological mechanisms. Thus, not surprisingly phytoconstituents are the principal sources of chemotherapeutic drug investigations in preclinical and clinical studies of



cancer. For instance, paclitaxel, a plant alkaloid was discovered in 1962 while screening natural products for treatment of cancer. It is commercially marketed in the name of Taxol® and has become one of the most effective drugs till date against breast and ovarian cancer [24]. The drug development process from its source to a finished product is an extremely costly and complex process that can take 12–15 years. The toxicity of natural products and isolated compounds is a major concern in drug discovery and development. Therefore, an in-depth investigation for safer natural drugs is always a prerequisite. Preclinical and clinical phases for the new chemical entities (NCEs) are important obligatory steps in drug development to assess the safety and efficacy of the test compound with an aim to predict any potential adverse events that may result after treatment. Toxicity tests are also imperative to identify the relationship between a dose, its potential side effects, anomalies on genetic material and on vital organs as well as to estimate toxicokinetic profiles. Besides, some of the major challenges encountered during drug development are low solubility, functional group reactivity, molecular complexity, and instability of investigational new drugs [25]. Therefore, the current review is an attempt to summarise a few plant extracts and phytoconstituents that are in the limelight in the past decade for significant anticancer activity.

1. Vincristine

Vincristine is a potent anticancer alkaloid derived from the Madagascar periwinkle plant (*Catharanthus roseus*). It belongs to the vinca alkaloid class and plays a crucial role in cancer therapy, particularly for hematological malignancies. Vincristine works by binding to

tubulin proteins, which are essential for microtubule formation. By inhibiting microtubule polymerization, it prevents the proper formation of the mitotic spindle, leading to cell cycle arrest in metaphase and ultimately inducing apoptosis in rapidly dividing cancer cells. Due to its mechanism of action, vincristine is widely used in the treatment of acute lymphoblastic leukemia (ALL), Hodgkin's lymphoma, and non-Hodgkin's lymphoma. It is often included in combination chemotherapy regimens such as CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) for lymphomas. However, vincristine's clinical use is limited by dose-dependent neurotoxicity, which can cause peripheral neuropathy, making careful dose adjustments necessary [26].

2. Vinblastine

Vinblastine is another vinca alkaloid derived from the Madagascar periwinkle plant (*Catharanthus roseus*), sharing a similar mechanism of action with vincristine. It disrupts microtubule formation by binding to tubulin, inhibiting spindle fiber assembly during mitosis, and thereby halting cancer cell proliferation. However, vinblastine exhibits a slightly different toxicity profile compared to vincristine, with more pronounced myelosuppression but less neurotoxicity. This makes it an important chemotherapeutic agent in the treatment of Hodgkin's lymphoma, non-Hodgkin's lymphoma, and multiple myeloma. It is commonly used in the ABVD regimen (Adriamycin, Bleomycin, Vinblastine, Dacarbazine) for Hodgkin's lymphoma. Due to its bone marrow-suppressing effects, careful monitoring of white blood cell counts is required to avoid severe neutropenia and infection risk [26,27].





Figure 4: *Catharanthus roseus*

3. Etoposide

Etoposide is a semi-synthetic derivative of podophyllotoxin, originally extracted from the American Mayapple plant (*Podophyllum peltatum*). This drug is classified as a topoisomerase II inhibitor, meaning it interferes with the enzyme responsible for relaxing supercoiled DNA during replication. By stabilizing the DNA-topoisomerase II complex, etoposide causes double-stranded DNA breaks, which leads to the accumulation of DNA damage and eventual apoptosis of cancer cells. It is a key

component in the treatment of acute myeloid leukemia (AML) and Hodgkin's lymphoma, often used in combination with other chemotherapeutic agents [28]. Etoposide is administered either orally or intravenously, and its effectiveness depends on cell cycle specificity, primarily targeting cells in the S and G2 phases of the cell cycle. However, one of its major drawbacks is bone marrow suppression, which can lead to anemia, leukopenia, and increased infection risk. Long-term use is also associated with an elevated risk of secondary leukemias.



Figure 5: *Podophyllum peltatum*

4. Homoharringtonine (Omacetaxine Mepesuccinate)

Homoharringtonine, also known as Omacetaxine mepesuccinate, is a plant alkaloid derived from the Chinese plum yew (*Cephalotaxus harringtonia*). It

functions primarily as a protein synthesis inhibitor, disrupting the elongation phase of mRNA translation. This leads to a depletion of short-lived survival proteins, particularly affecting leukemic cells that rely on continuous protein synthesis for survival. Homoharringtonine has shown remarkable efficacy against chronic myeloid leukemia (CML), including cases that have developed resistance to tyrosine kinase inhibitors (TKIs) such as imatinib. This makes it a valuable

treatment option for patients who have failed conventional targeted therapies. Unlike vinca alkaloids and etoposide, its primary toxicity is related to hematological side effects, including thrombocytopenia and neutropenia, rather than neurotoxicity. Despite these side effects, it remains a vital option for refractory CML cases, particularly in patients who do not respond to BCR-ABL inhibitors [29].



Figure 6: *Cephalotaxus harringtonia*

CONCLUSION

Natural products have played a pivotal role in the treatment of blood cancers, with these four drugs demonstrating remarkable efficacy and unique mechanisms of action. Vincristine and vinblastine target microtubules, etoposide inhibits topoisomerase II, and homoharringtonine disrupts protein synthesis, all leading to cancer cell death. While these drugs are highly effective, they come with distinct toxicity profiles that require careful management. As research progresses, new derivatives and combination therapies continue to improve survival outcomes and minimize side effects in hematological malignancies.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021; 71: 209–249.
2. Ganesh K and Massagué J. Targeting metastatic cancer. Nat Med 2021; 27: 34–44.
3. Merriel SWD, Ingle SM, May MT, et al. Retrospective cohort study evaluating clinical, biochemical and pharmacological prognostic factors for prostate cancer progression using primary care data. BMJ Open 2021; 11: e044420.
4. GlobalSurg Collaborative and National Institute for Health Research Global Health Research Unit on Global Surgery. Global variation in postoperative mortality and complications after cancer surgery: a multicentre, prospective cohort study in 82 countries. Lancet 2021; 397: 387–397.
5. Roy A and Li SD. Modifying the tumor microenvironment using nanoparticle



- therapeutics. *Wiley Interdiscip Rev Nanomed Nanobiotechnol* 2016; 8(6): 891–908.
6. Bayat Mokhtari R, Homayouni TS, Baluch N, et al. Combination therapy in combating cancer. *Oncotarget* 2017; 8: 38022–38043.
7. Abbas Z and Rehman S. An overview of cancer treatment modalities. *Neoplasm* 2018; 1: 139–157.
8. El-Hussein A, Manoto SL, Ombinda-Lemboumba S, et al. A review of chemotherapy and photodynamic therapy for lung cancer treatment. *Anticancer Agents Med Chem* 2021; 21(2): 149–161.
9. Ghanghoria R, Kesharwani P, Tekade RK, et al. Targeting luteinizing hormone-releasing hormone: potential therapeutics to treat gynecological and other cancers. *J Control Release* 2018; 269: 277–301.
10. Charmsaz S, Collins DM, Perry AS, et al. Novel strategies for cancer treatment: highlights from the 55th IACR annual conference. *Cancers* 2019; 11: 1125.
11. Arruebo M, Vilaboa N, Sáez-Gutierrez B, et al. Assessment of the evolution of cancer treatment therapies. *Cancers* 2011; 3: 3279–3330.
12. Moses MA, Brem H and Langer R. Advancing the field of drug delivery: taking aim at cancer. *Cancer Cell* 2003; 4(5): 337–341.
13. Shapira A, Livney YD, Broxterman HJ, et al. Nanomedicine for targeted cancer therapy: towards the overcoming of drug resistance. *Drug Resist Updat* 2011; 14(3): 150–163.
14. Mondal J, Panigrahi AK and Khuda-Bukhsh AR. Conventional chemotherapy: problems and scope for combined therapies with certain herbal products and dietary supplements. *Austin J Mol Cell Biol* 2014; 1: 10.
15. El-Readi MZ and Althubiti MA. Cancer nanomedicine: a new era of successful targeted therapy. *J Nanomater* 2019; 2019: 4927312.
16. Naji A, Eitoku M, Favier B, et al. Biological functions of mesenchymal stem cells and clinical implications. *Cell Mol Life Sci* 2019; 76(17): 3323–3348.
17. Takahashi K and Yamanaka S. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. *Cell* 2006; 126: 663–676.
18. Li Y, Hermanson DL, Moriarity BS, et al. Human iPSC-derived natural killer cells engineered with chimeric antigen receptors enhance anti-tumor activity. *Cell Stem Cell* 2018; 23: 181.e5–192.e5.
19. Ouyang X, Telli ML and Wu JC. Induced pluripotent stem cell-based cancer vaccines. *Front Immunol* 2019; 10: 1510.
20. Trujillo-Alonso V, Pratt EC, Zong H, et al. FDA-approved ferumoxytol displays anti-leukaemia efficacy against cells with low ferroportin levels. *Nat Nanotechnol* 2019; 14(6): 616–622.
21. Lin W, Huang L, Li Y, et al. Mesenchymal stem cells and cancer: clinical challenges and opportunities. *Biomed Res Int* 2019; 2019: 2820853.
22. Chu DT, Nguyen TT, Tien NLB, et al. Recent progress of stem cell therapy in cancer treatment: molecular mechanisms and potential applications. *Cells* 2020; 9: 563.
23. Chang JC. Cancer stem cells: role in tumor growth, recurrence, metastasis, and treatment resistance. *Medicine* 2016; 95(1 Suppl. 1): S20–S25.
24. Sullivan CB, Porter RM, Evans CH, et al. TNF α and IL-1 β influence the differentiation and migration of murine MSCs independently of the NF- κ B pathway. *Stem Cell Res Ther* 2014; 5: 104.
25. Vakhshiteh F, Atyabi F and Ostad SN. Mesenchymal stem cell exosomes: a two-edged sword in cancer therapy. *Int J Nanomedicine* 2019; 14: 2847–2859.



26. Reddy RL. Mobilization and collection of peripheral blood progenitor cells for transplantation. *Transfus Apher Sci* 2005; 32: 63–72.
27. Copelan EA. Hematopoietic stem-cell transplantation. *N Engl J Med* 2006; 354: 1813–1826.
28. Casper J, Wolff D, Knauf W, et al. Allogeneic hematopoietic stem-cell transplantation in patients with hematologic malignancies after dose-escalated treosulfan/fludarabine conditioning. *J Clin Oncol* 2010; 28: 3344–3351.
29. Sage EK, Thakrar RM and Janes SM. Genetically modified mesenchymal stromal cells in cancer therapy. *Cytotherapy* 2016; 18(11): 1435–1445.

HOW TO CITE Kiran Aher, Nandini Bagul, Manjusha Chavan, Gaurav Kasar*, Dipti Chavan, Dr. Chandrashekhar Patil, Dr. Sunil Mahajan, *Advances in Blood Cancer: Pathophysiology, Diagnosis and Emerging Therapeutic Strategies*, *Int. J. of Pharm. Sci.*, 2025, Vol 3, Issue 5, 4218-4228. <https://doi.org/10.5281/zenodo.15512403>