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A COMPREHENSIVE REVIEW ON TYPES, MECHANISM AND NANOPARTICLE BASED TREATMENT OF BLOOD CANCER

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Abstract

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Hadiya Hassan

Blood cancer is a heterogeneous category of hematological malignancies that are caused by the impairment of genetic and epigenetic changes in hematopoietic stem and progenitor cells. The three main subtypes are leukemia, lymphoma and myeloma, which appear as a disruption to normal hematopoiesis and is caused by the uncontrolled growth of malignant blood cells due to the various lymphoid or myeloid lineages. Globally, the malignancies cause a significant disease burden in the form of morbidity and mortality associated with cancer that is especially clear in developing nations like Pakistan. The core of clinical treatment is made up of conventional therapeutic modalities, including chemotherapy, radiotherapy, immunotherapy, and blood transfusion; however, the efficacy of these modalities is often limited by systemic toxicity, multidrug resistance, relapse of the disease, and little specificity to malignant cells. The recent developments in nanomedicine have produced novel nanoparticle-based drug delivery systems that aim to enhance therapeutic effects whilst minimize off-target toxicity. Nanocarriers, including liposomes, dendrimers, quantum dots, carbon nanotubes, and metallic nanoparticles (including platinum, silver, palladium, and gold) have been shown to have potential anticancer activity due to their enhanced pharmacokinetics, targeted delivery, controlled drug release, and the ability to regulate molecular signaling pathways (including PI3K/AKT, p53 and caspase -mediated apoptosis). These nanosystems enable passive and active tumor targeting, increase drug bioavailability and provides great diagnostic and prognostic capabilities. It is a broad overview of modern literature review of the perspectives of blood cancer subtypes, the underlying molecular pathways, conventional treatment procedures, and novel nanoparticles-based interventions. The review by incorporating mechanistic knowledge

with the current technological breakthroughs highlights the translational promise of nanotechnology to enhance the accuracy of diagnostics, provide targeted treatment, and eventually increase the general clinical outcome in the treatment of hematological malignancies.

Introduction

Major Cancer in Pakistan

In Pakistan, cancer remains a significant public health concern, with nearly 150,000 new cases reported each year and mortality rates estimated between 60–80% (Yusuf et al., 2013). According to the Karachi Cancer Registry, lung cancer is the leading malignancy among men, largely attributed to cigarette smoking. Cancers of the oral cavity rank next in males and are strongly associated with both smoked and smokeless tobacco use, despite the nationwide smoking ban introduced in 2002 (Saqib et al., 2019; Hackshaw, 2010). Among women, breast cancer is the most frequently diagnosed malignancy, commonly peaking around 45 years of age. Oral cavity and ovarian cancers follow as the second and third most prevalent cancers in females, with oral cancers often appearing in younger age groups (Bhurgri et al., 2002). Similar to other low and middle-income countries, Pakistan has experienced a steady rise in breast cancer incidence over recent decades (Bhurgri et al., 2000; Hirabayashi and Zhang, 2009). Hospital-based studies further indicate that many Pakistani women present in their forties with locally advanced breast cancer, highlighting an increasing future healthcare burden (Kumar et al., 2016; Soomro et al., 2018). Data collected from a pathology-based cancer registry covering all districts of Karachi between 2010 and 2015 showed particularly high frequencies of breast, head and neck, and esophageal cancers among females, while lip, oral cavity,

and laryngeal cancers predominated among males patterns closely linked to tobacco exposure (Qureshi et al., 2016). Additionally, gastric cancer has been reported with notable frequency among younger Pakistani men (Daniyal et al., 2015). Quality of life has become an essential outcome measure in oncology, as evaluating it in patients with hematological malignancies can contribute to improved therapeutic planning and survival outcomes. According to the World Health Organization, 173,937 new cancer cases were recorded in Pakistan in 2018; among these, approximately 4.1% were leukemia, 3.4% non-Hodgkin's lymphoma, 0.92% Hodgkin's lymphoma, and 0.81% multiple myeloma. Efforts to effectively manage and prevent blood cancers in Pakistan are challenged by inadequate healthcare infrastructure, a shortage of trained oncologists, and limited access to advanced diagnostic technologies (Idrees et al., 2018).

MECHANISM OF BLOOD CANCER

Hematopoietic stem cells (HSCs) residing in the bone marrow are the fundamental source of all circulating blood cells and play a central role in the development of hematological malignancies (**Figure 1**). These pluripotent stem cells generate two principal progenitor pathways lymphoid and myeloid each of which is linked to specific categories of blood cancers (Ma et al., 2025; Filipek-Gorzała et al., 2024). Within the lymphoid lineage, progenitor cells differentiate into natural killer (NK) cells, T lymphocytes, and B lymphocytes, all of which are essential components of adaptive and innate immunity. Despite their protective physiological roles, these cells may acquire genetic and epigenetic abnormalities that drive malignant transformation. NK-cell–derived malignancies can manifest as NK-cell leukemia or lymphoma. Similarly, T lymphocytes may give rise to T-cell leukemias or lymphomas, while abnormal

proliferation of B lymphocytes can result in B-cell leukemia, various forms of lymphoma, or plasma cell disorders such as myeloma, depending on the differentiation stage and molecular alterations involved (Huntly et al., 2016). The myeloid lineage produces several mature blood elements, including monocytes, megakaryocytes, neutrophils, and erythroid cells. Malignant transformation at different stages of myeloid differentiation is associated with distinct disease entities. For instance, abnormal monocyte proliferation is linked to monocytic leukemia, whereas dysregulation of megakaryocyte development may lead to essential thrombocythemia or megakaryocytic leukemia. Neutrophil precursors can give rise to granulocytic leukemia, and erythroid progenitors may develop into erythroid leukemia, a relatively uncommon yet aggressive subtype (Al-Ani et al., 2025). Therefore, hematologic malignancies are classified according to their cellular origin, broadly distinguishing lymphoid from myeloid neoplasms. This lineage-based framework reflects the hierarchical and highly regulated nature of hematopoiesis and underscores the diverse molecular events that contribute to blood cancer development. A clear understanding of these cellular origins and differentiation pathways is essential for refining diagnostic strategies and designing targeted therapeutic interventions to improve clinical outcomes (Shimada, 2019).

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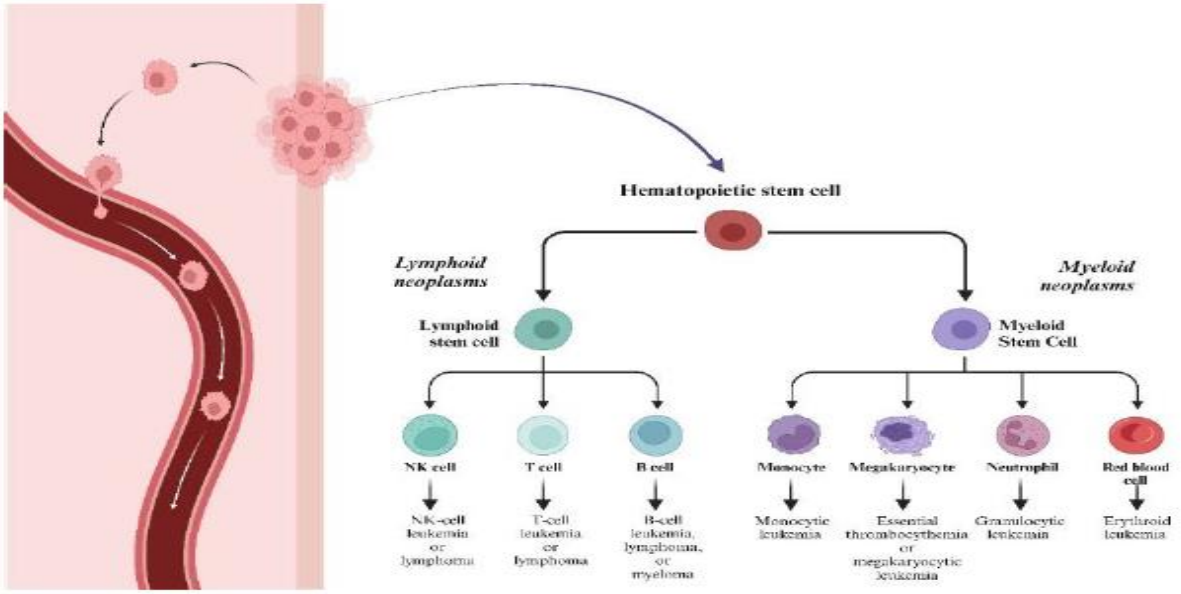

Figure 1: Haemopoietic stem cells develop into lymphoid and myeloid lineages, resulting in blood cancers. Lymphoid stem cells differentiate into NK, T, and B cells, which result in leukemia/lymphoma, T-cell leukemia/lymphoma, and B-cell leukemia/lymphoma/myeloma. Myeloid stem cells differentiate into monocytes, megakaryocytes, neutrophils, and red blood cells, resulting in monocytic, essential thrombocythemia/megakaryocytic, granulocytic, and erythroid leukaemias (Al-Ani et al., 2025).

MAJOR BLOOD CANCER TYPES

1. Leukemia Cancer: Leukemia is a hematologic malignancy typified by the clonal proliferation of genetically altered hematopoietic progenitor cells that is manifested by disruptions of normal hematopoiesis (**Figure 3A**). It is a proliferative disease that produces large active dysfunctional leukocytes that gradually increase in the bone marrow, peripheral blood, and, in some cases, the spleen (Ci et al., 2022). Since the dominance of the marrow microenvironment by malignant clones occurs, the production of normal erythrocytes, platelets, and functional leukocytes is inhibited, which leads to such clinical manifestations as anemia, bleeding diatheses, and increased susceptibility to the effects of infectious agents (Ci et al., 2022; Senapati et al., 2023).

Traditional treatment protocols include cytotoxic chemotherapy regimens, radiotherapy, and immunotherapeutic agent regimens. Despite these interventions being effective in improving clinical outcomes, survivors have not been able to survive optimally especially among adult patients with acute disease. The overall survival of acute leukemias with a 5-year follow-up is usually 3050percent, but it is lower in acute lymphoblastic leukemia with only around 17 percent and in acute myeloid leukemia with only 7 percent (Hodby and Marks, 2020). The outcome is often associated with low probability of success in treatment, failure to destroy all of the malignant clones, and relapse. One of the main limitations of the traditional chemotherapeutics is their unselective cytotoxicity, which preconditions the development of off-target adverse events and drug resistance (Ci et al., 2022). In addition, minimal residual disease (MRD) persistence during or after therapy significantly increases the likelihood of relapse in both children and adults, but MRD-positive patients have a relapse rate of 56% to 100% in five years. Such obstacles support the need to develop more specific treatment plans. Precision-targeted therapies aimed at destroying leukemic cells, but leaving normal tissue intact, have a high potential of deeper initial responses and reducing the risk of relap (Ci et al., 2022; Hodby and Marks, 2020). All in all, leukemia is mostly related to the circulatory system and bone marrow (Figure 2A) and is associated with the expenses of diagnostics and therapy (leukemia represents about 8 per cent of all cancers of all ages, which is very costly) (Rafiq et al., 2018).

Subtypes of leukemia: There are four major leukemic subtypes, which include acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and chronic myeloid leukemia (CML) (**Figure B**). Leukemia patients usually have a range of clinical manifestations, such as fatigue, myalgia, leukopenia,

anemia, and predisposition to most types of infections (Younas et al., 2018). Moreover, leukemia is a widespread childhood cancer, taking almost 30 percentage of all the malignancies in patients below 15 years (Siegel et al., 2024). Leukemia is a malignancy that develops into the bone marrow and the other hematopoietic tissues. The Philadelphia chromosome in chronic myeloid leukemia is the most salient chromosomal abnormality that has been directly implicated in the malignant transformation (Frei, 1985).

Acute Myelogenous Leukemia (AML): Acute myeloid leukemia also known as acute myelogenous leukemia is a condition that affects the myeloid lineage of the bone marrow that produces thrombocytes, erythrocytes, and leukocytes. In AML, the aberrant myeloid progenitors experience unregulated growth and accumulation thus interfering with normal hematopoiesis. Mutations in FLT3, NPM1, and CEBPA are some examples of genetic aberrations that predispose persons to AML. The increased risk of acquiring AML has been linked to prolonged exposure to some chemicals as well as the chemotherapeutic agents such as benzene (**Figure 2A**) (Cortes et al., 1996).

Acute Lymphocytic Lymphoma (ALL): Acute lymphoblastic leukemia (ALL) and acute lymphocytic lymphoma (ALL) are closely related malignancies, which are mainly targeted against lymphoid cells. In acute lymphocytic lymphoma, the malignant cells develop huge tumours in lymph nodes and other organs but in acute lymphoblastic leukemia they mostly affect bone marrow and the circulation (**Figure 2B**). Malignant lymphoblasts develop as the result of the pathological development and increase of immature lymphoid cells, usually those of the B-cell or T-cell lineage, causing acute lymphocytic lymphoma. The tumour masses may arise as a result of the malignancy cells penetrating the lymph nodes, the spleen, thymus, and other organs (Mahaja et al., 2014).

Chronic Myelogenous Leukemia (CML): Chronic myelogenous leukemia is a bone marrow and blood malignancy (**Figure 2C**). It is also marked by overproduction of myeloid cells, of which are the immature white blood cells (Mendez-Hernandez et al., 2023). A characteristic genetic defect in CML is the Philadelphia chromosome which is formed as a result of translocation between chromosomes 9 and 22. This translocation produces the BCR-ABL1 fusion gene, the aberrant expression of which is an aberrant, uncontrolled proliferation and division of myeloid precursors (Mendez-Hernandez et al., 2023).

Chronic Lymphocytic Leukemia (CLL): Chronic lymphocytic leukemia is a neoplasm of lymphoid cells of the immune system (**Figure 2D**). CLL is diagnosed by the presence of mature and abnormal lymphocytes in bone marrow, lymph nodes, and peripheral blood, and other tissues (Nabhan and Rosen, 2014). A high risk of chronic lymphocytic leukemia has been linked to various inherited genetic disorders, such as familial CLL and chromosomal deletions, including 13q deletion (Genetic Factors) (Nabhan and Rosen, 2014). When one of the close relatives, e.g., a parent or a sibling, has chronic lymphocytic leukemia, the person is at a higher risk of having the disease; earlier the diagnosis made within the affected family member, the higher the risk (Family History) (Nabhan and Rosen, 2014).

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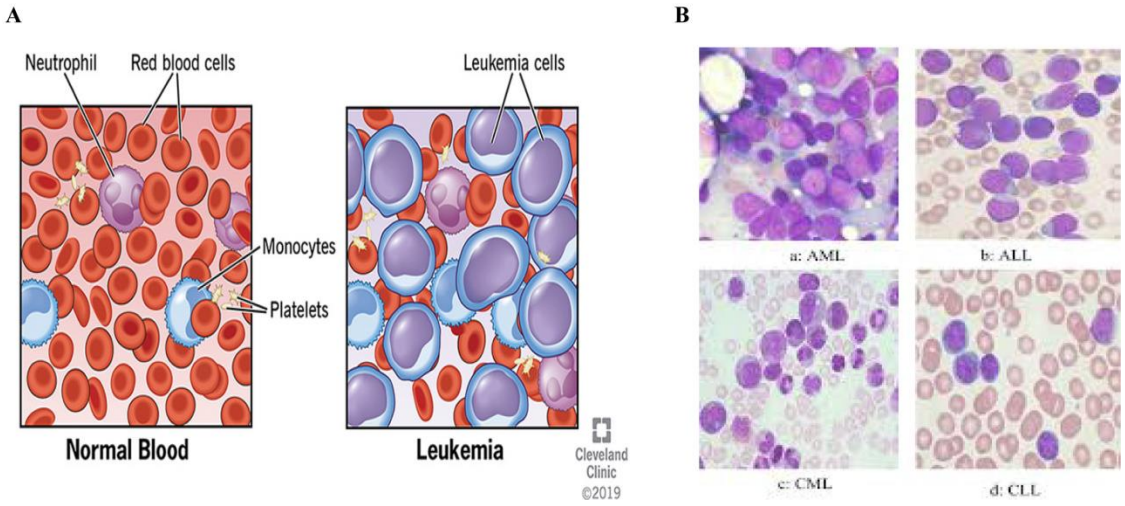

Figure 2: (A) Leukemia, (B) subtypes of leukemia.

2. Lymphoma: Lymphomas are among the most common hematological cancers and originate from the malignant transformation of developing or mature lymphocytes at various stages of differentiation (**Figure 3B**) (Etrych et al., 2022). Based on pathological and clinical characteristics, lymphomas are broadly divided into two principal categories: Hodgkin lymphoma and Non-Hodgkin lymphoma. Hodgkin lymphoma is comparatively less frequent and typically arises from B-cell lineage, whereas non-Hodgkin lymphomas comprise a diverse and more prevalent group of lymphoid malignancies (Swerdlow and Cook, 2020). Chemotherapy continues to serve as the cornerstone of initial lymphoma management, commonly employing cytotoxic agents such as alkylating compounds, nucleoside analogues, anthracyclines, topoisomerase inhibitors, and vinca alkaloids. Although therapeutic strategies have evolved over time, significant clinical challenges persist, limiting long-term treatment success (Ekpa et al., 2023). Even with improved protocols, many patients experience incomplete responses or disease recurrence. A major obstacle in lymphoma therapy is the emergence of drug resistance, whereby malignant cells acquire genetic alterations or modify intracellular signaling networks,

allowing them to survive chemotherapy and radiotherapy exposure (Ekpa et al., 2023). Such adaptive mechanisms substantially reduce treatment efficacy and contribute to unfavorable clinical outcomes

3. Myeloma: Myeloma is a malignant disorder of clonal plasma cells that primarily arises within the bone marrow and is clinically associated with features such as hypercalcemia, renal dysfunction, and osteolytic bone lesions (Chakraborty and Majhail, 2020). Despite significant therapeutic advances, the disease remains largely incurable, with relapse occurring in more than 90% of patients over the course of treatment (de la Puente and Azab, 2017). The persistent challenge in managing myeloma is largely attributed to its marked biological complexity. Both interpatient and intrapatient heterogeneity contribute to variable therapeutic responses and complicate the design of uniform treatment strategies (Vo et al., 2022). The presence of minimal residual disease (MRD) following therapy enables the survival of resistant cellular subclones, which can expand over time and drive disease recurrence. These resistant clones often acquire or possess mechanisms that reduce sensitivity to cytotoxic agents, ultimately diminishing the long-term effectiveness of currently available therapies. Consequently, relapse remains common even in patients who initially achieve clinical remission. In addition to tumor-intrinsic factors, the bone marrow microenvironment plays a pivotal role in disease progression. Interactions between myeloma cells and surrounding stromal components promote cellular proliferation, protect malignant cells from drug-induced apoptosis, and facilitate angiogenesis. Furthermore, the microenvironment can suppress antitumor immune responses, thereby contributing to therapeutic resistance and disease persistence (**Figure 3C**) (de la Puente and Azab, 2017).

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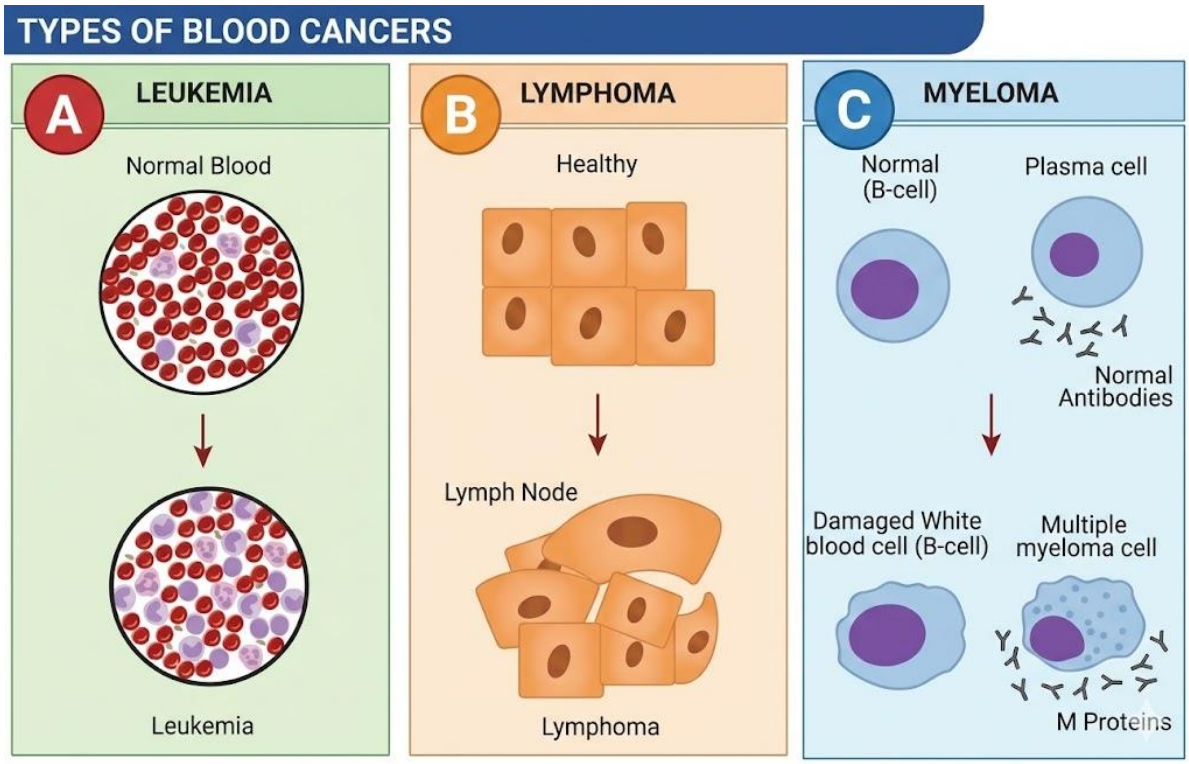

Figure 3: Types blood cancer.

CURRENT TREATMENT OF CANCER

Chemotherapy: Chemotherapy refers to the systemic use of cytotoxic and targeted pharmacologic agents that eliminates or suppresses malignant populations of cells. Regimens are often characterized as two or more agents that are administered simultaneously, having complementary mechanisms of action, and which, thus, will produce synergistic therapeutic effects, and will reduce the development of resistance. In certain haematological malignancies with agents that have a very low permeability rate across blood brain barrier, intrathecal administration of such drug directly into the cerebrospinal fluid is used to prevent or treat involvement of the central nervous system. Existing clinical practice includes a variety of classes of chemotherapeutic agents: antimetabolites, which interfere with the production of the nucleic acid by imitating the

endogenous metabolic products, inhibiting the production and mitosis process in tumour cells; antimitotic agents, which deactivate the dynamics of the microtubules, ultimately blocking cell proliferation; and other antitumour agents, which directly interact with nucleic acid, disrupting the processes of replication and transcription. This is because, the DNA structure is chemically modified by alkylating agents, and crosslinking is caused, and cell division is then inhibited. In some cancers, treatments that use aspranaginase reduce the amount of asparagine in circulation, thus restricting the ability of vulnerable cancer cells to produce protein. Other types of therapeutic agents include bisphosphonates used to treat bone complications, DNA repair enzyme inhibitors and histone deacetylases, and tyrosine kinase, among others, which have been used to complement the modern chemotherapeutic regimens (Thakur et al., 2021). Chemotherapy is also often used in conjunction with surgery or radiotherapy. It also plays a palliative role in the treatment of advanced or metastatic disease by relieving symptoms and slowing the growth of the tumour as well as enhancing survival. Nonetheless, the negative impacts and restrictions that have been well documented, chemotherapy is still a cornerstone in cancer management and still forms a basis of oncologic therapy (Frei et al., 1985).

Radiotherapy: Radiotherapy is aimed at killing most of tumor cells and leaving a residual population of normal cells. The level of technology has now led to the accurate distribution of radiation to the tumor site thus minimizing the collateral damage to healthy tissues. In addition, improved knowledge of the radiobiological differences in reaction of malignant and normal tissues has further honed the effectiveness of radiotherapy (Chen et al., 2017).

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Immunotherapy: Immunotherapy is a treatment paradigm, which expands the natural immune system of the patient to detect and destroy cancer cells. The defining approach entails the monoclonal antibodies- engineered proteins specific to tumor-associated antigens, hence leading to immune responses that help in clearance of the tumor cells. Also, another significant trend in this direction is the use of immune checkpoint blockers; they disrupt tumored immune evasion mechanisms. In cancer (malignancies like Hodgkin lymphoma) tumor cells can express the immune regulatory molecules (programmed death ligand-1 (PD-L1) and programmed death ligand-2 (PD-L2)). Checkpoint inhibitors block these pathways, and thus, restore immunological functions, especially where other conventional therapies have low efficacy. Moreover, cancer vaccines are currently being developed to prevent cancer or to treat the disease either to diminish the risk of oncogenes or increase the immune response to tumor cells. Therapies based on cytokines, including interferons and interleukins, stimulate the growth, activation and orchestration of antitumor activities by immune cells. Another innovative approach is the chimeric antigen receptor (CAR) T-cell therapy in which the T cells of a patient are genetically modified to identify and kill cancerous cells. These new forms of immunotherapeutic modalities enhance the innate ability of the immune system to identify aberrant cells. Though immunotherapy employs immunological knowledge with specific treatment modalities to overcome these resistance mechanisms, modern immunotherapy aims to overcome these obstacles by generating safe and effective tumor control (Thakur et al., 2021; Blattman et al., 2004).

Blood Transfusion: Therapeutic plasma exchange may be used in the treatment of cancer patients sometimes. Therapeutic plasma exchange is done to remove the circulating toxins in the plasma of an individual using specialised techniques but the

remaining plasma is retained in the patient to aid the recovery process. Even though therapeutic plasma exchange is a potential emerging treatment method in cancer care, available data is inconclusive due to a lack of large-scale clinical trials and an overwhelming predominance of observational studies (Yusafzai et al., 2017).

NANOPARTICLES STRATEGIES

Liposomes: Liposomes are spherical vesicles and are made of a single or more lipid layers that are enclosed by an aqueous core. They are usually produced through the dispersion of phospholipids in aqueous or other hydrophilic medium that allows spontaneous self-assembling bilayered nanoparticles. The wide range of fabrication modalities, including sonication, reverse phase evaporation, extrusion and solvent injection, provide accurate control of the particle sizes, which are usually between 50 and 500 nm. These procedures assist in effective encapsulation of aqueous based therapeutic agents into the aqueous core (Sun et al., 2014). Liposomal formulations are capable of reacting to external factors such as thermal, ultrasonic, microwave and radiofrequency exposures and hence they have a greater ability to control drug release (Frenkel, 2008). One can continue to control surface properties by conjugating various polymers or functional moieties to realize site-specific targeting (Sun et al., 2014). Liposomes are therefore widely used as drug-delivery vehicles, especially with regards to oncological target delivery (Torchilin, 2005). Active targeting is usually accomplished by functionalizing the surface; antibodies are conjugated to the liposomal surface in order to identify and bind the tumor-associated antigens. In cases where antibodies are not available or no longer applicable, high-affinity aptamers, which are short nucleic-acid ligands, would be useful as targeting agents. The monoclonal antibodies are also used in diagnostic imaging, drug delivery in a targeted manner and carrier systems

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(Brongersma, 2003; Crooke, 2004). Another interesting clinical use, also based on the use of liposomal vincristine, is the approval of a liposomal version of vincristine (Marqibo), measuring around 100 nm in diameter, which has been used in treatment of lymphoblastic leukaemia.

Dendrimeric nanoparticles: Dendritic nanomaterials are highly branched macromolecules whose size and shape can be conveniently tuned to maximise interaction with cancer cells (Namazi and Adeli, 2004). Their main benefits are the ability to adjust flexibility, density, and solubility in aqueous, thus allowing targeted delivery and release of drugs (Sun et al., 2014).

Quantum dots: Quantum -dots nanocarriers are currently being used to improve the efficacy of anticancer therapeutics. Recent reports have determined a natural flavonoid antiproliferative natural flavonoid that, on conjugation with cadmium-telluride quantum dots of diameter 4 nm, causes apoptosis in the malignant tumor cells (Li et al., 2004). The use of quantum dots as nanocomposite formulations with wogonin also shows efficacy in the treatment of multidrug-resistant leukaemia through its interaction with aberrant signalling pathways.

Carbon nanotubes: Carbon nanotubes are used to bind drugs as well as to be taken up through endocytosis into cells. They are typically made into nano-suspensions and single-walled nanotube (SWCNTs) is a more stable suspension than multi-walled nanotube (MWCNTs) (**Figure 4**). When exposed to enzymes, CNTs disulfide bond, and thus the encapsulated drug is released (Liu et al., 2013). They may cause photochemical injury to the tumour cells and may also be used to image the tumours using Raman spectroscopy (Rao et al., 1997).

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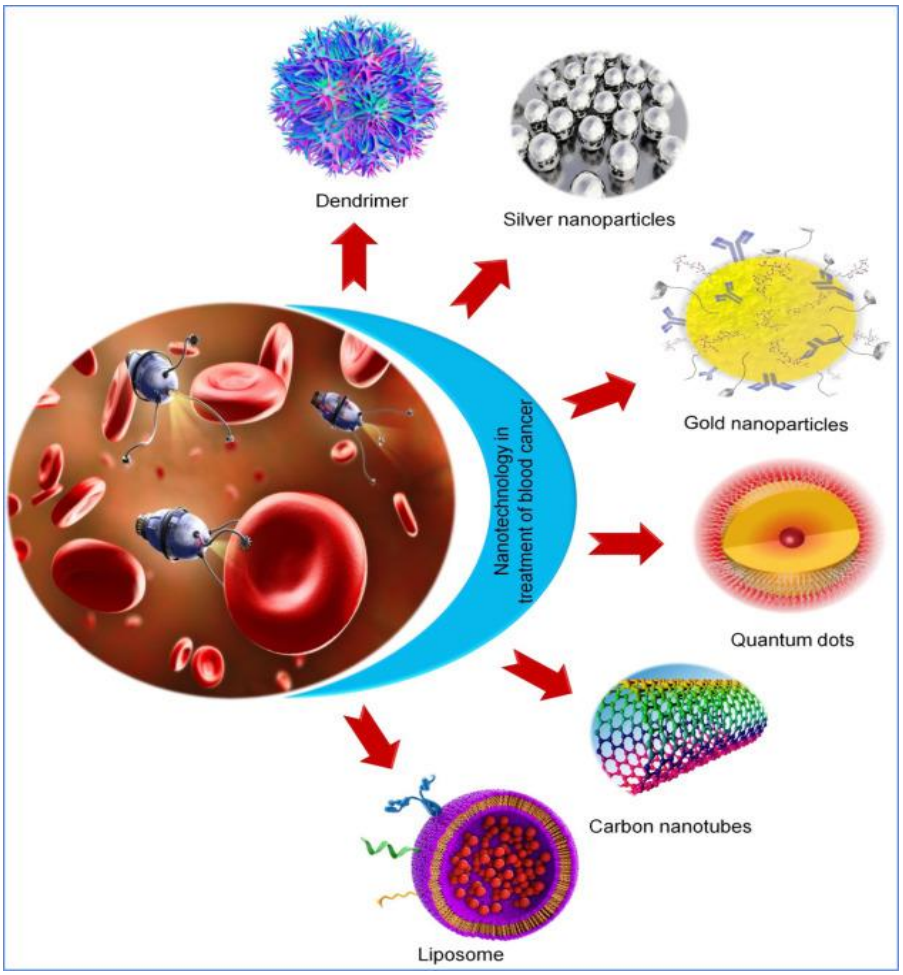

Figure 4: Nanotechnology in treatment of blood cancer.

Metallic nanoparticles

Metallic nanoparticles, ranging in size from 1 to 100 nm, are classified into nanoparticles, nanowires, nanoplatelets, and nanostructures. Higher surface energy levels contribute to their ability to aggregate and create macroscopic structures. To maintain stability in a liquid environment, two major strategies are used. Static stabilisation includes the formation of an electrical double layer by collecting negative ions, which prevents nanoparticle agglomeration via repulsion. Another way is steric

stabilisation, which involves wrapping metallic nanoparticles in polymers, surfactants, or ligands to prevent them from becoming unstable.

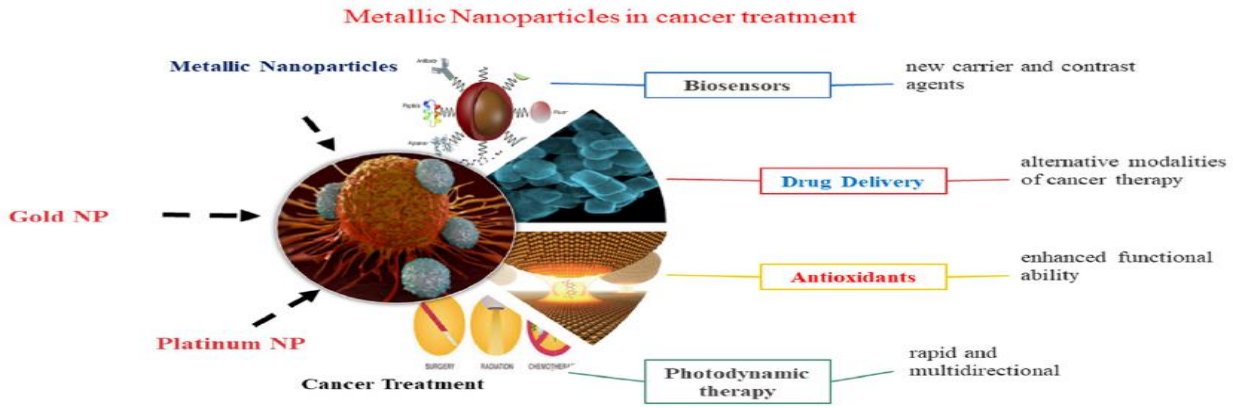

Figure 5: Metallic nanoparticles in cancer treatments.

Platinum nanoparticles: The biomedical applications of nanoscale platinum have increased considerably due to its notable antioxidant properties and anticancer potential, which contribute to tumor growth inhibition. When platinum nanoparticles are functionalized with specific targeting ligands, their ability to selectively accumulate in tumor tissues is enhanced. These modified nanoparticles can also support controlled drug release and improve overall drug delivery performance. However, some recent investigations have reported possible adverse effects, including the accumulation of nanoparticles in vital organs and cellular systems. On a global scale, platinum-based chemotherapeutic drugs such as cisplatin, carboplatin, and oxaliplatin continue to be extensively used in cancer therapy (Wang et al., 2018). Despite their effectiveness, the lack of precise targeting in conventional cancer treatment may lead to unwanted side effects and increased drug resistance (Mochida et al., 2019). Platinum nanoparticles are actively studied across biotechnology, nanomedicine, and pharmaceutical research fields. Nevertheless, clinical trials evaluating inorganic platinum nanoparticle

formulations in humans are still limited. It has been suggested that extending the systemic circulation time of platinum nanoparticles could enhance their therapeutic benefits (Jeyaraj et al., 2019). One proposed strategy to achieve this is surface modification with a biocompatible polymer such as polyvinylpyrrolidone (PVP), which may improve stability and compatibility (Jeyaraj et al., 2021).

In an experimental study, doxorubicin (DOX) was used as a model anticancer drug to develop PVP-functionalized platinum nanoparticles. The synthesized nanoparticles demonstrated an octopod structure with consistent dispersion. This nanoplatform was designed to improve drug distribution while reducing toxicity. The platinum–DOX conjugate system enhanced drug release efficiency and biocompatibility. Its anticancer activity was tested on two breast cancer cell lines, MCF-7 and MDA-MB-231. The findings indicated that the system promoted activation of the tumor suppressor gene PTEN, leading to suppression of the PI3K/AKT signaling pathway (**Figure 2**) (Patel et al., 2021).

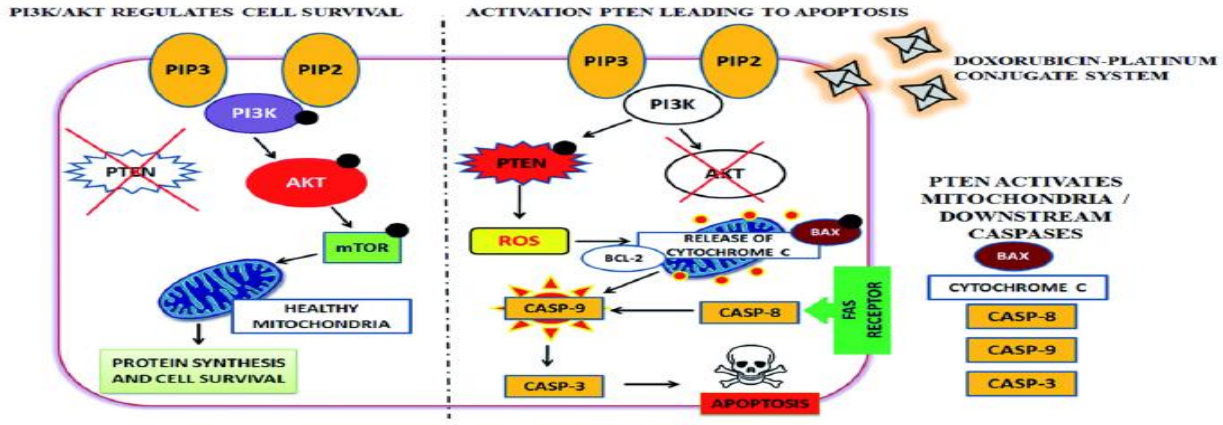

Figure 6: Using a doxorubicin-platinum conjugate system enhances PTEN expression and inhibits the PI3K/AKT pathway. Reproduced with permission from Patel et al. (2021). Copyright (2021) RSC.

Kankala et al. (2020) proposed that platinum nanoparticles possess the ability to penetrate deeply into tumor tissues and produce enhanced therapeutic effects through their capacity to generate reactive free radical species. In their strategy, ultrasmall platinum nanoparticles were incorporated into a chitosan matrix and subsequently assembled onto zinc-doped mesoporous silica nanocarriers using a self-assembly approach. The inclusion of zinc within the silica framework improved the loading and release efficiency of doxorubicin in the acidic tumor microenvironment, thereby reducing the need for additional surface modification (Dhavale et al., 2021). Furthermore, the therapeutic performance was strengthened by destabilizing the coordination interactions between the drug molecules and the carrier system, leading to more efficient drug release and tumor targeting, as demonstrated by Dhavale et al. (2021). Overall, this nanoplatform enhanced tumor suppression by facilitating deeper penetration into malignant tissues while simultaneously generating cytotoxic free radicals, which proved particularly effective against multidrug-resistant cancer cells (Kankala et al., 2020).

Silver nanoparticles: Silver nanoparticles are widely applied in biomedical fields, including antimicrobial wound dressings, infection-control formulations, and anticancer therapies, due to their versatile biological activities (Sondi et al., 2004). Their anticancer potential is primarily associated with the induction of oxidative stress, elevated reactive oxygen species (ROS) production, and subsequent DNA damage. While ROS play a normal role in maintaining cellular balance and intracellular signaling, excessive ROS generation triggered by silver nanoparticles disrupts this equilibrium, leading to damage of DNA, proteins, and lipids. This oxidative imbalance ultimately contributes to cellular dysfunction and cytotoxicity (Jain et al., 2021).

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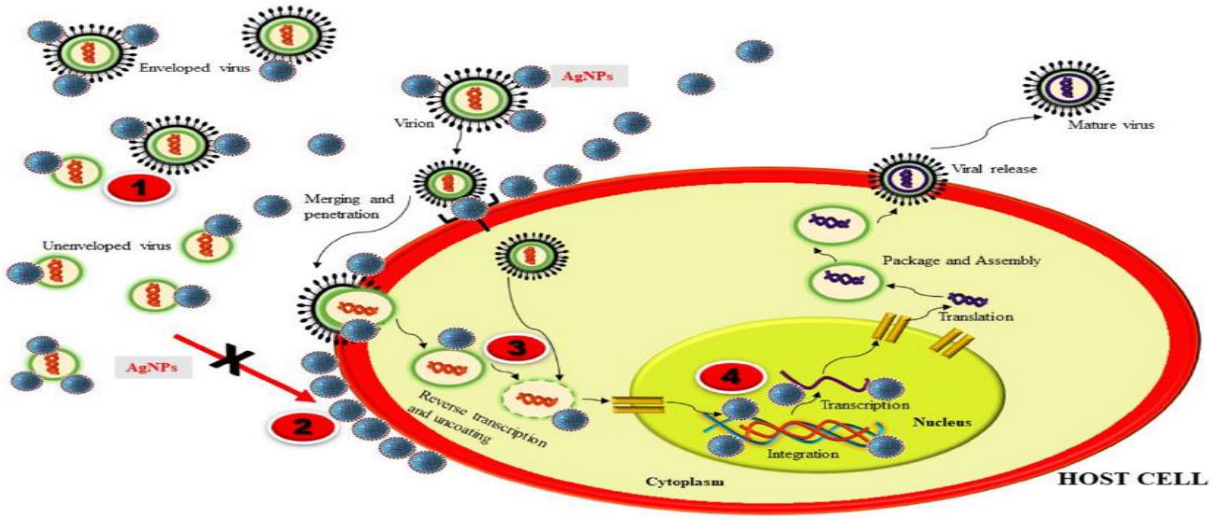

Figure 7: (1) Both encapsulated and unenveloped viruses interact with Ag nanoparticles via their surface protein (gp120). (2) Ag nanoparticles prevent viruses from infecting host cells. (3) Ag nanoparticles prevent viruses from entering the nucleus of cells. (4) By interfering with viral DNA, AgNanoparticles limit viral replication. Reproduced with permission from Jain et al. (2021). Copyright (2021) Springer.

After cellular internalization, silver nanoparticles can undergo processing within the acidic intracellular environment, where they may exert cytotoxic effects. Their interaction with essential cellular components can interfere with metabolic activities and cell proliferation, which has been associated with enhanced oxidative stress and potential cellular damage (De Matteis et al., 2015). However, when strategically engineered, silver nanoparticles can also improve anticancer drug performance. For instance, Muhammad et al. (2021) reported that incorporating silver nanoparticles into paclitaxel nanocrystals significantly enhanced the overall anticancer activity against human cancer cells. In this design, the chemotherapeutic agent paclitaxel was combined with silver nanoparticles to form a hybrid nanocrystal system. Paclitaxel nanocrystals functioned as a structural

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template for polydopamine (PDA) coating. The PDA layer acted as a platform for the in-situ formation and attachment of silver nanoparticles (RGDARF) and was further modified with the tumor-targeting peptide NR1. This multifunctional formulation improved cellular uptake, increased in vitro anticancer efficacy, and reduced cancer cell migration. The combined effects of silver nanoparticles and paclitaxel enhanced receptor interaction, enabled pH-responsive drug release, and benefited from the nanoscale size, resulting in synergistic therapeutic outcomes. The NR1/AgNP-functionalized paclitaxel nanocrystals demonstrated improved selectivity while maintaining biocompatibility. Mechanistically, these nanocrystals promoted apoptosis through membrane disruption, mitochondrial dysfunction, elevated reactive oxygen species (ROS) generation, and DNA damage, including double-strand breaks (Muhammad et al., 2021). Furthermore, Umapathi et al. (2020) and Muhammad et al. (2020) suggested that activation of apoptotic pathways, particularly p53 and caspase-3 signaling, along with modulation of the Bax/Bcl-2 ratio, may contribute to the observed anticancer effects of these nanocrystal systems (Umapathi et al., 2020).

Palladiumnano particles: Palladium-based nanomaterials possess distinctive catalytic and optical characteristics that make them promising candidates for theranostic applications. They have been explored as prodrug activators, photothermal agents, and anticancer therapeutics, as well as for antimicrobial purposes. Biosynthesis approaches, including the use of natural resources such as Saudi propolis, have been investigated for cost-effective production of palladium nanoparticles. Al-Fakeh et al. (2021) demonstrated that palladium nanoparticles exhibited significant cytotoxic activity against MCF-7 breast cancer cells, with an IC50 value of 104.79 µg/mL, indicating notable therapeutic potential. Further surface modification using polyvinylpyrrolidone

(PVP) enhanced their stability and biological performance. Increasing concentrations of PVP-functionalized palladium nanoparticles resulted in a dose-dependent reduction in MCF-7 cell viability. The proposed mechanism of action involves activation of caspase-3/7 pathways, leading to mitochondrial membrane disruption and nuclear DNA damage, ultimately inducing apoptosis (Ramalingam et al., 2020).

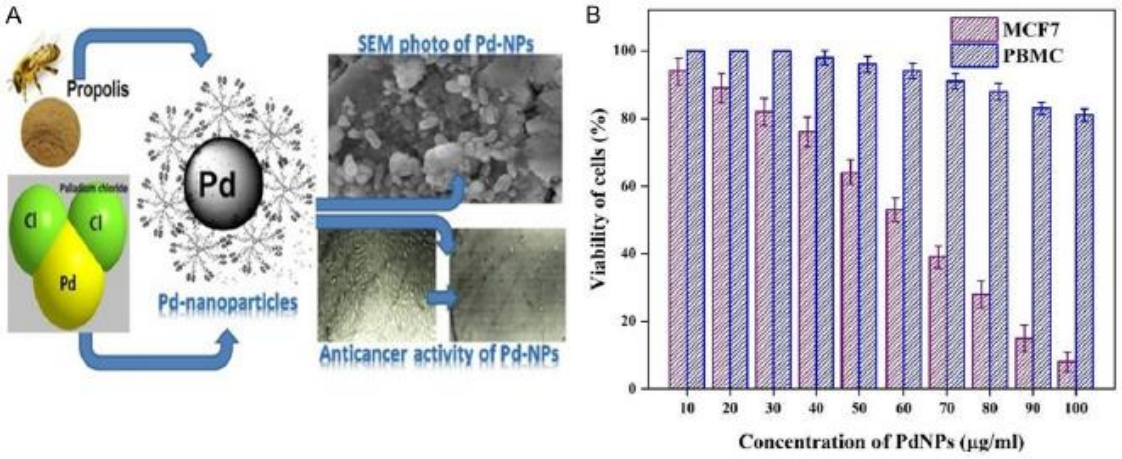

Figure 8: A. Mechanism of palladium nanoparticles' anti-cancer action. Reproduced with permission from Al-Fakeh et al. (2021). Copyright (2021) MDPI. B. PVP-Pd nanoparticles were tested for cytotoxicity against breast cancer cell lines using the MTT assay. Reproduced with permission from Ramalingam et al. (2020). Copyright (2020), RSC.

Gold Nanoparticles: Gold nanoparticles possess distinctive physicochemical characteristics that make them highly valuable in biomedical applications, particularly in medical imaging and cancer diagnostics. Their prolonged circulation time in the bloodstream improves tumor accumulation and enhances diagnostic precision. These nanoparticles are widely explored for drug delivery systems, gene and nucleic acid transport, radiotherapy enhancement, and photothermal cancer therapy. The ability to synthesize gold nanoparticles in different sizes and shapes increases their clinical potential, while their generally low toxicity and strong biocompatibility further support

their biomedical use. Several gold nanoparticle–based diagnostic platforms have already received regulatory approval, and many additional formulations are currently under development and evaluation (Aygun et al., 2020). Recent studies have demonstrated that gold nanoparticles functionalized with curcumin (CUR) and isonicotinic acid hydrazide (INH) can effectively target cancer cells (Umapathi et al., 2020). These modified nanoparticles showed significant cytotoxic effects against LK-2 lung cancer cells and TIG-120 epithelial cells. The anticancer mechanism was associated with increased reactive oxygen species (ROS) production, leading to enhanced apoptosis. Morphological changes consistent with programmed cell death were also observed in treated cells. Moreover, comparative analyses indicate that these functionalized gold nanoparticles may exhibit anticancer activity comparable to or synergistic with conventional chemotherapeutic agents such as cisplatin (Botteon et al., 2021).

PROPERTIES OF NANOCARRIERS

The therapeutic performance of nanocarriers can be optimized by tailoring their physicochemical characteristics, including particle size, geometry, and surface properties. Appropriate control of particle size enhances systemic distribution and promotes efficient accumulation at target sites. Likewise, particle shape influences fluid dynamics in the bloodstream, which can improve cellular interaction and internalization by cancer cells. Surface charge also plays a crucial role in nanoparticle behavior; neutral or mildly positive nanoparticles generally demonstrate improved diffusion and cellular uptake (Stylianopoulos et al., 2010). In addition, surface functionalization with specific ligands can modify charge characteristics, extend blood circulation time, and enhance targeted delivery, while simultaneously improving drug solubility, stability, and controlled clearance.

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Poorly soluble drugs are often rapidly eliminated before reaching tumor tissues; therefore, encapsulation within hydrophilic nanocarriers can enhance solubility and increase bioavailability, ultimately improving therapeutic efficacy (Wicki et al., 2015). The reticuloendothelial system (RES) naturally recognizes and clears foreign or hydrophobic particles through uptake by the liver and spleen. To overcome this limitation, nanoparticle surfaces are frequently coated with polyethylene glycol (PEG), which increases hydrophilicity and reduces immune recognition, thereby prolonging systemic circulation (Bregoli et al., 2016). Opsonization by proteins secreted by macrophages further facilitates clearance of unmodified particles, reducing drug accumulation at tumor sites. Consequently, the incorporation of targeting ligands on nanoparticle surfaces is a key strategy to achieve selective delivery and improve therapeutic specificity.

LEUKEMIA RISK FACTORS

Several environmental, occupational, genetic, and lifestyle-related factors have been consistently linked to an increased risk of developing leukemia. These include exposure to ionizing radiation (whether therapeutic, occupational, or related to wartime events), prior chemotherapy treatment, inherited genetic mutations or syndromes, contact with certain chemicals in residential or workplace settings, and behaviors such as tobacco use. While some risk factors are more strongly associated with particular leukemia subtypes, many contribute broadly across different forms of the disease. For instance, exposure to high levels of ionizing radiation, such as that experienced by survivors of atomic bomb detonations in Japan, has been associated with elevated mortality from non-chronic lymphocytic leukemia (non-CLL), including acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), and chronic myeloid leukemia (CML) (Preston et al.

1994; Richardson et al. 2009; Hsu et al. 2013). Similarly, increased leukemia risk has been reported among individuals exposed to occupational radiation, including nuclear industry workers and radiology personnel, particularly in earlier decades (Mohan et al. 2003; Yoshinaga et al. 2004; Metz-Flamant et al. 2012). Therapeutic radiation administered for the treatment of pelvic malignancies or certain benign conditions has also been associated with subsequent development of leukemia (Boice et al. 1987; Wright et al. 2010; Sakata et al. 2012).

In addition to radiation, exposure to formaldehyde—commonly used in industrial processes, construction materials, and disinfectants has shown a significant relationship with the development of myeloid leukemias (Beane Freeman et al. 2009; Zhao et al. 2009). Although these risk factors vary in nature and source, they may promote leukemogenesis through overlapping biological mechanisms that contribute to genetic damage and malignant transformation, a topic that extends beyond the scope of this review.

PREVENTION OF BLOOD CANCER:

Preventing blood cancers, including multiple myeloma, remains difficult because their exact etiological factors are not fully clarified. Nevertheless, several evidence-based strategies may help reduce overall risk and support general cancer prevention.

Healthy Lifestyle Practices: Adopting and maintaining a healthy lifestyle can contribute to lowering the risk of various cancers, including hematological malignancies. Avoiding all forms of tobacco use, including cigarettes and smokeless tobacco, is strongly recommended, as smoking has been associated with an increased risk of certain blood cancers, such as acute myeloid leukemia (AML). A well-balanced diet rich in fruits, vegetables, whole grains, and lean protein sources may support immune function and

overall health, while limiting red and processed meat intake is advisable. In addition, regular physical activity approximately 150 minutes of moderate-intensity exercise or 75 minutes of vigorous activity per week can help maintain a healthy body weight and strengthen immune defense mechanisms (Kapoor and Rajkumar, 2023; Willard et al., 2009).

Reduction of Occupational and Environmental Exposures: Limiting exposure to harmful environmental and workplace agents may also help decrease blood cancer risk. Benzene exposure, common in industries such as chemical manufacturing, rubber production, and petroleum refining, has been linked to increased leukemia risk; therefore, adherence to workplace safety standards and protective measures is essential. Similarly, minimizing unnecessary exposure to ionizing radiation whether from occupational sources, medical imaging, or radiotherapy when avoidable can contribute to risk reduction. Patients should consult healthcare professionals regarding the benefits and risks of diagnostic or therapeutic radiation procedures (Iwasaki et al., 2023).

Genetic Screening and Counseling: Certain inherited genetic abnormalities are associated with a higher susceptibility to blood cancers. Individuals with a family history of hematological malignancies or known genetic predisposition may consider genetic counseling and, when appropriate, testing to evaluate their risk profile and explore preventive strategies (Singh et al., 2023). Although these measures may reduce risk, they cannot guarantee complete prevention. Therefore, regular medical check-ups, early detection, and timely treatment remain critical components in improving outcomes for blood cancer patients (Edsjö et al., 2023).

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CONCLUSION

In conclusion, blood cancers such as leukemia, lymphoma, and multiple myeloma are a diverse category of hematological neoplasias beginning with genetic and epigenetic disturbances of hematopoietic progenitor and stem cells. The complex pathogenesis of them is the dysregulation of cellular proliferation, the lack of the apoptotic process, and disturbed molecular signaling pathways, which lead to gradual impairment of normal hematopoiesis and immune activities. Though traditional therapeutic options (chemotherapy, radiotherapy, immunotherapy etc) are still the focus of clinical treatment, they are often limited by a number of systemic toxicity, multidrug resistance, limited residual disease, and high relapse rates. New nanotechnology-based approaches can provide a way out of these shortcomings by improving drug bioavailability, providing targeted delivery, and improving therapeutic selectivity at minimal off-target effects. Several nanosystems, such as liposomes, dendrimers, quantum dots, carbon nanotubes, and metallic nanoparticles, such as platinum, silver, palladium, and gold, have a great potential in regulating important oncogenic pathways and inducing apoptosis in malignant cells. Altogether, incorporation of mechanistic knowledge of hematological malignancies with the progress in nanomedicine offers a strong basis to innovative, more specific, and efficient treatment methods. Further translational studies and well-conceived clinical trials are needed to capitalize the clinical potential of nanoparticle-based therapy in enhancing survival and quality of life of blood cancer patients.

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