Recent Frontiers of

Phytochemicals

Applications in Food, Pharmacy, Cosmetics, and Biotechnology

Edited by
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Chapter 34

Modulation of drug resistance in leukemia using phytochemicals: *an in-silico, in-vitro, and in-vivo* approach

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34.1 Introduction

Leukemia is an uncontrolled proliferation of blood cells. Leukemia means "white blood" (leukos, "white"; haima, "blood"), because a delay in the maturation of the transit-amplifying cells causes a significant increase in immature white blood cells to circulate, turning the blood from red to creamy white. The hallmarks of leukemogenesis encompass recurrent nonrandom chromosomal translocations (Daga et al., 2018). Leukemia is classified clinically or pathologically into acute and chronic forms based on how rapidly the disease develops and the kind of blood cell involved (Vincent et al., 2001). There are mainly four types of leukemia: acute lymphocytic leukemia (ALL), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), and acute myelogenous leukemia (AML). Many of the outstanding triumphs in cancer treatment have resulted from novel investigations and trials in leukemia. These include combination chemotherapy, stem cell transplantation, "differentiation" therapy, monoclonal antibody therapy, and targeted treatment (Greaves, 2016). Doxorubicin, cytarabine, ibrutinib, idelalisib, rituximab, nilotinib, and imatinib are among the most commonly used chemotherapeutic drugs in the treatment of leukemia. The study shows that doctors are preferring to use chemotherapy or hematopoietic stem cell transplantation (HSCT), and the major issue with this treatment is that leukemia cells can easily relapse after the treatment. The characteristics of leukemia have become more advanced in recent years, and the treatment of this disease must also be more advanced. In addition, organ transplantation can be a good option, and they will have a lifelong risk of immunosuppression. Additionally, the effect of HSCT can be dangerous, and there is proof that "the donor-derived immune system" can easily attack the "recipient's leukemic cells." After the relapse of the HSCT, the chemotherapy control procedure is utilized to mitigate the effect. The killer immunoglobulin receptor and KIR ligand interact and allow the donor's T cells to recognize the antigens related to leukemia (Maacha et al., 2019). However, it happens much too often that leukemia escapes control after HSTC and uses chemotherapy to control the disease although acute leukemia shares several mechanisms of immune evasion that can be found in solid tumors. Unfortunately, hematological malignancies have less research in this area. A deeper understanding of this process is required to create an effective and reasonable immunotherapy for acute leukemia.

Resistance to chemotherapy is one of the most difficult challenges in cancer treatment. Ninety percent of cancer-related mortality is caused by the emergence of drug resistance, which renders chemotherapeutic drugs useless. Drug resistance is the ability of cancer cells to decrease the effectiveness and potency of chemotherapy agents (Nikolaou et al., 2018). Intrinsic resistance, which occurs in cancer when malignant cells develop resistance without having previously been exposed to chemotherapeutic drugs, causes a subpar response to initial therapy (Gottesman, 2002). In some situations, cancer cells initially respond well to chemotherapy but thereafter have a poor response because they have acquired resistance (acquired resistance). Prior studies on cell lines and animal models demonstrated that drug resistance in cancer may be gained by a variety of mechanisms, including drug efflux via the ATP-binding cassette (ABC) transporter, changing the expression of proteins targeted by anticancer medicines, drug detoxification, and evasion of apoptosis (Aris, 2000).

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