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PHYTOCHEMICAL POTENTIAL IN LEUKEMIAS: A MINI REVIEW

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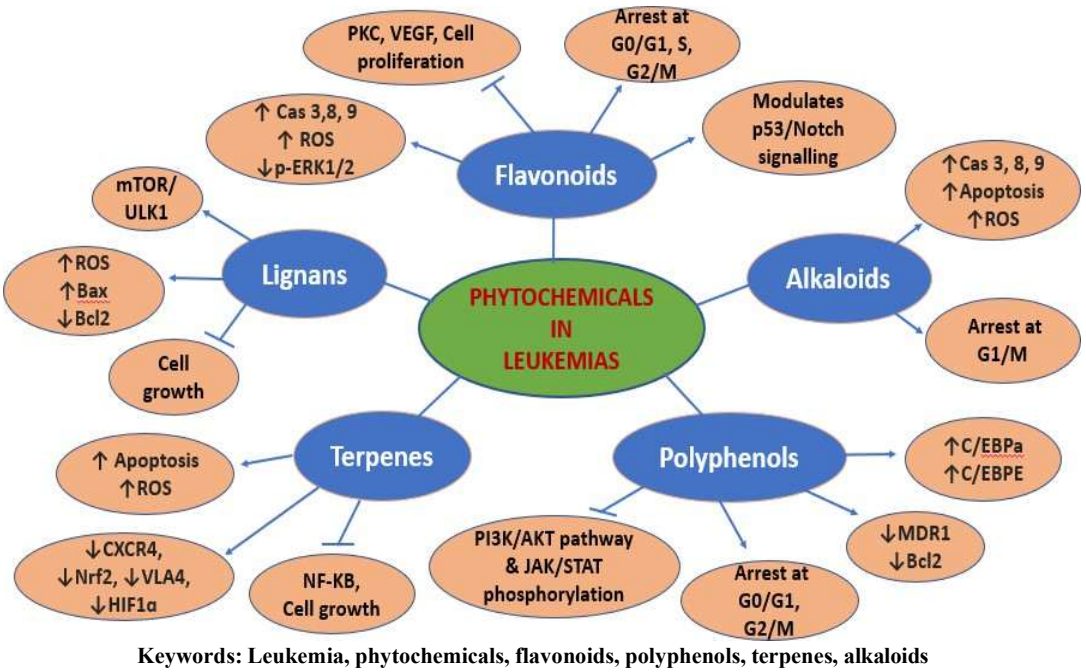
ABSTRACT

Leukemia still remains a challenge inspite of advancements in drug discovery. The major reasons are the genetic aberrations and relapse that can occur due to very few leukemic cells. Natural compounds are still underestimated with respect to treatment of cancer. In the present review, the role of natural compounds in treating various leukemias through targeting different pathways have been documented.

Graphical Abstract:



Keywords: Leukemia, phytochemicals, flavonoids, polyphenols, terpenes, alkaloids

1. INTRODUCTION

The uninhibited growth of hematopoietic cells within bone marrow defines leukemia **[1]**. High doses of synthetic drugs are capable of killing cancer cells but also have life- threatening side-effects. These side-effects and multi-drug resistance of cancer cells to synthetic drugs draw attention to the role of plants as a source of medicine. Natural compounds have shown anti-cancer effects and drug discovery and development from plant-based compounds are comparatively less time-consuming, inexpensive and safe in comparison to conventional synthetic compounds. Even our previous studies succeeded in determining that phytochemicals like Silibinin and Hesperidin shows synergistic potential with Cytarabine (anti- leukemic drug) in AML cells **[2, 3, 4]**.

2. Flavonoids

Flavonoids are secondary metabolites derived from plants and have multiple anticancer effects **[5]**. In CLL cells HG3 and EHEB, luteolin activates caspase-3 and - 9, resulting in an endogenous mechanism of apoptosis. Flavonoid gardenin-B increases caspase-3, -8, and -9 activation as well as PARP levels (which are critical for DNA repair and activity) in AML cells HL60 and U937 **[6]**. Oroxylin A induces apoptosis by elevating caspase-9 regulation and decreasing survivin, pro-caspase-9 and p-ERK1/2 expressions **[7]**. Quercetin supresses expression of anti-apoptosis protein Bcl-2 and manages the protein expression of pro-apoptosis Bax and also activates caspase-3, that initiates caspase-3 dependent mitochondrial pathway to induce apoptosis **[8]**. Baicalein initiates apoptosis by inducing ROS **[12]**. Acacetin induces apoptosis on CLL B-lymphocyte through targeting mitochondria, by increasing reactive oxygen species (ROS) formation, release of cytochrome-c and caspase-3 activation **[9]**. Flavonoid myricetin synchronizes Bcl-2 proteins, Wnt/β-catenin and MAPK signalling, and enhances DNA damage, ROS-mediated stress and ER stress **[10]**. Myricetin, raises mitochondrial cytochrome-c release and impels apoptosis in T- ALL Jurkat cells **[6]**.

K562 cells treated with fisetin are arrested in the S and G2/M phases, but those treated with hesperetin are arrested in the G0/G1 phase **[11]**. Myricetin, in K562 leukemic cells arrests cells in S phase by impeding purine nucleotides generation via cohesion of inosine 5′-monophosphate dehydrogenases. Myricetin impedes DNA topoisomerase I and II by enhancing the binding of topoisomerase-DNA complexes **[10]**. Baicalein suppresses AMKL cell proliferation by arresting cell cycle at G1/G0 phase and differentiation and it can even induce megakaryocyte differentiation and stop cell proliferation by modulating Notch

signalling in AMKL cells **[12]**. Wogonin initiates G1 phase cell cycle arrest, apoptosis via mitochondrial pathway, inhibits angiogenesis, invasion and PKC pathway; modulates p53 signalling pathways, induces differentiation, obstructs VEGF and hence anti- tumor angiogenesis. Wogonin, apigenin, chrysin, and luteolin, prohibits cyclin-dependent kinase 9 (CDK9) and obstructs phosphorylation of carboxy-terminal domain of RNA polymerase II. This mechanism leads to reduced RNA synthesis and then rapid down- regulation of anti-apoptotic protein Mcl-1 resulting in apoptosis induction in cancer cells **[9, 12, 13]**.

In U-937, HL60, and K-562 cells, kaempferol causes chromatin constriction and apoptosis. It causes G1 phase cell cycle arrest in U937 and K562 cells, and G2/M phase cell cycle arrest in HL-60 cells. In relapsed CLL with del(17p3), flavopiridol inhibits cell cycle progression, causing in p53-independent apoptosis. In chronic or acute leukemia, flavopiridol as an adjuvant to chemotherapeutic medicines has shown promise. Alvocidib inhibits CDK9 and suppresses Mcl-1, Myc, and cyclin D1 transcription. In numerous clinical trials, alvocidib showed good therapeutic results in patients with relapsed/refractory (R/R) AML **[7, 14, 15]**. Apigenin halts cells in S, G2/M and/or G0/G1 phases in different leukemias and suppresses the growth of K562 cells. Combined doses of doxorubicin, etoposide, and apigenin reduces ATP levels, elevates apoptosis, and blocks the cell cycle **[16]**. Genistein blocks the cell cycle in G0/G1 and G2/M phase in HL-60 cells, at G2/M phase in NB4 cells and at S and G2/M in Jurkat cells **[17]**. Butein subsides c- Myc expression at transcriptional level, deaccelerates DNA-binding activity, represses regulation of Akt, hence stops hTERT phosphorylation and translocation into the nucleus, accelerates CD11b expression in leukemia cells, inhibits telomerase activity, deprives proliferation, and induces cell death **[18]**.

3. Polyphenols

Resveratrol prohibits growth and initiates apoptosis by down-regulation of Bcl-2; causes cell cycle arrest in G1 phase, in ALL L1210 cell line **[19]**. Curcumin prohibits JAK- STAT3 phosphorylation by suppressing JAK2 and cyclin D1 in K562 CML cells; initiates caspase-dependent apoptosis by inhibiting PI3K/AKT pathway in CEM, HSB2, Jurkat, and MOLT-4 cell-lines **[20, 21]**.

EGCG treatment decreases G0/G1 and G2/M population in K562 cells. It reduces the cell viability and initiates DNA damage, which then progresses to apoptosis by a non-cell cycle specific pathway that occurs due to modulation of gene via oxidative stress pathway in K562 cells **[22]**. Curcumin causes G1 phase cell cycle arrest due to its

pro-oxidant nature in KG1a, Kasumi-1, HL60, and MV4-11 cells, followed by caspase-dependent apoptosis. In contrast, some studies states that curcumin causes a G2/M arrest in HL-60 cells **[23]**.

Activity loss of transcription regulators C/EBPa and C/EBPE has a role in pathogenesis of AML. EGCG upregulates C/EBPa and C/EBPE and it also intensifies the binding of H4 hyperacetylated histone and acetylated H3K14 histone to the promoter regions of C/EBPa and C/EBPE genes **[24]**. Resveratrol shows high potential in adjuvant therapy for leukemia by modulating autophagy and induce apoptosis in MOLT4 and HL60 human leukemia cells. It reduces drug resistance in HL60/ADR cells by regulating PI3K/Akt/Nrf2 signalling pathway and MRP1 expression. Resveratrol, when combined with prednisolone, reduces MDR1 protein expression **[25]**.

4. Alkaloids

Alkaloids possess strong anticancer activity both *in vitro* and *in vivo*, and can act as CDK or protein kinase inhibitors and can be transformed as novel anticancer agents **[26]**. Canthin-6-one elevates caspase-3, -8, -9 cleavage, ROS, apoptosis signal-regulating kinase 1,

p16, p27, p38, p53, c-Jun N-terminal kinases, Ki-67 negative population, checkpoint kinase 2, H2A histone family member X (H2A.X), INK4A and Kip1, while decreases mitochondrial membrane potential and p- retinoblastoma protein in Kasumi-1 cells **[27]**.

Curine is a bisbenzylisoquinoline alkaloid and is orally active at non-toxic doses **[28]**. It induces damage to the plasma membrane, influences cyclin expressions involved in G1 phase regulation of cell cycle, causes G1 phase arrest in HL60 cells. Curine depolarizes mitochondrial potential and it triggers apoptosis via intrinsic pathway in HL60 cells **[29]**.

Vinca alkaloids are the second-most-used class of cancer drugs with cytotoxic effects from the plant *Catharanthus roseus* **[30]**. Vinblastine, a vinca alkaloid is a stathmokinetic oncolytic agent and arrests growing cells in metaphase *in vitro* and initiates myelosuppression in xenograft mouse models of leukemia. Another vinca alkaloid, vincristine is a mitotic inhibitor, useful in cancer chemotherapy. Liposomal vincristine has been given FDA approval for treating acute leukemias. Vindesine is an anti-mitotic vinca alkaloid used in chemotherapy **[31, 32]**.

5. Terpenes

Terpenes with antioxidative and anti-inflammatory properties are valued as possible anticancer agents **[33]**. Terpene eucalyptol initiates apoptosis in leukemic cell- lines. Nerolidol inhibits cell growth through alterations in cell cycle as well as increases proportion of apoptotic cells **[34]**.

Triptolide is a diterpene triepoxide which induces apoptosis of KG1a cells by initiating ROS production via down-regulation of CXCR4, Nrf2, VLA4, and HIF-1α. Minnelide down-regulates the transcription and translation of Myc and stem cell surface markers. Parthenolide, a sesquiterpene lactone molecule, binds to IκB kinase and modifies p50 and p65 NF-κB subunits to prohibit NF-κB and thus demotes LSCs proportion in primary AML cells and it also interdicts mitochondrial glutathione system and hence increases ROS levels **[15, 35]**. Terpene myrcene shows cytotoxicity in leukemic cells, while bisabolol shows inhibitory effects in B-CLL and primary lymphoid leukemias **[34]**.

6. Lignans

Lignans are plant metabolites obtained from oxidative coupling of phenylpropanoids and possess antioxidant properties **[36]**. Enterolactone, a flaxseed lignan, engenders intrinsic pathway of apoptosis in AML cells, upregulates Bax and downregulates Bcl-2 **[37]**. Sesamin from *Sesamum indicum L.* inhibits MOLT4 and NB4 cell proliferation, initiates caspase-3 and mTOR/ULK1 signalling and therefore regulates apoptosis and autophagy **[38]**. Schisandrin, in THP-1 cells, accelerates intracellular ROS proportions **[39]**.

p16, p27, p38, p53, c-Jun N-terminal kinases, Ki-67 negative population, checkpoint kinase 2, H2A histone family member X (H2A.X), INK4A and Kip1, while decreases mitochondrial membrane potential and p- retinoblastoma protein in Kasumi-1 cells **[27]**.

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Hinokinin and cubebin potently obstructs U937 cell proliferation and induces apoptotic morphology in HL60 and U937 cells possibly via stimulating effector caspases **[40]**. Justicidin B possess strong anti-proliferative and pro-apoptotic activity at low doses and it also sensitizes LAMA-84, K562 and SKW3 leukemia cells, commences intrinsic mitochondrial cell death signalling pathway via caspase-3 and -9 in HL60 cells and drives redox homeostasis by way of degenerating ROS deletion in K562 cells **[41]**.

Natural compounds have enough potential to suppress various pathways and factors that play an influential role in leukemic growth. Hence, there comes a possibility that these phytochemicals can act as excellent anti-cancer compounds with very less or negligible side- effects and also they are cost-effective as they are readily available in nature. Further studies should be carried out and phytochemicals should definitely considered as an option to synthetic drugs used currently.

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REFERENCES:

[1] Deynoux, M., Sunter, N., Hérault, O. and Mazurier, F., 2016. Hypoxia and hypoxia-inducible factors in leukemias. *Front. Oncol.* ***6*** 41.

[2] Desai, U.N., Shah, K.P., Mirza, S.H.,

Panchal, D.K., Parikh, S.K. and Rawal, R.M., 2015. Enhancement of the cytotoxic effects of Cytarabine in synergism with Hesperidine and Silibinin in Acute Myeloid Leukemia: An in-vitro approach. *J. Cancer Ther. Res.* **11** p.352.

[3] Ashraf, M.A., 2020. Phytochemicals as potential anticancer drugs: time to ponder nature's bounty. *Biomed. Res. Int.* **2020**.

[4] Efferth, T., Kadioglu, O., Saeed, M.E., Seo, E.J., Mbaveng, A.T. and Kuete, V., 2021. Medicinal plants and phytochemicals against multidrug-resistant tumor cells expressing ABCB1, ABCG2, or ABCB5: a synopsis of 2 decades. *Phytochem. Rev.* **20** 7-53.

[5] Kopustinskiene, D.M., Jakstas, V., Savickas, A. and Bernatoniene, J., 2020. Flavonoids as anticancer agents. *Nutrients* **12** 457.

[6] Saraei, R., Marofi, F., Naimi, A., Talebi, M., Ghaebi, M., Javan, N., Salimi, O. and Hassanzadeh, A., 2019. Leukemia therapy by flavonoids: Future and involved mechanisms. *J. Cell. Physiol.* **234** 8203-8220.

[7] Menezes, J.C., Orlikova, B., Morceau, F. and Diederich, M., 2016. Natural and synthetic flavonoids: structure–activity relationship and chemotherapeutic potential for the treatment of leukemia. *Crit. Rev. Food Sci. Nutr.* **56** S4-S28.

[8] Agustini, S.M., Utomo, D.H., Rifa'i, M., Haryana, S.M. and Widjajanto, E., 2019. An in silico approach toward wheatgrass extract-induced apoptosis of human acute myeloid leukemia cells. *Drug invent. today* **12**.

[9] Salimi, A. and Pourahmad, J., 2018. Polyphenols: prevention and treatment of human disease, second edition, (eds) RR Watson, VR Preedy, S Zibadi, (London-Academic Press (imprint of Elsevier)) pp.195-203.

[10] Jiang, M., Zhu, M., Wang, L. and Yu, S., 2019. Anti-tumor effects and associated molecular mechanisms of myricetin. *Biomed. Pharmacother.* **120** 109506.

[11] Adan, A. and Baran, Y., 2016. Fisetin and hesperetin induced apoptosis and cell cycle arrest in chronic myeloid leukemia cells accompanied by modulation of cellular signaling. *Tumor Biol.* **37** 5781-5795.

[12] Yu, C., Zeng, J., Yan, Z., Ma, Z., Liu, S. and Huang, Z., 2016. Baicalein antagonizes acute megakaryoblastic leukemia in vitro and in vivo by inducing cell cycle

arrest. *Cell Biosci.* **6** 1- 9.

[13] Morceau, F., Chateauvieux, S., Orsini, M., Trécul, A., Dicato, M. and Diederich, M., 2015. Natural compounds and pharmaceuticals reprogram leukemia cell differentiation pathways. *Biotechnol. Adv.* **33** 785-797.

[14] Bisol, Â., de Campos, P.S. and Lamers, M.L., 2020. Flavonoids as anticancer therapies: A systematic review of clinical trials. *Phytother. Res.* **34** 568-582.

[15] Tan, Y., Wu, Q. and Zhou, F., 2020. Targeting acute myeloid leukemia stem cells: Current therapies in development and potential strategies with new dimensions. *Crit. Rev. Oncol. Hematol.* **152** 102993.

[16] Hashemi, M. and Samadian, N., 2018. Effects of apigenin and apigenin-loaded nanogel on induction of apoptosis in human chronic myeloid leukemia cells. *Galen Med. J.* **7** 1008.

[17] Sak, K. and Everaus, H., 2017. Established human cell lines as models to study anti-leukemic effects of flavonoids. *Curr. Genomics* **18** 3-26.

[18] Moon, D.O., Kim, M.O., Lee, J.D., Choi, Y.H. and Kim, G.Y., 2009. Butein suppresses c-Myc-dependent transcription and Akt-dependent phosphorylation of hTERT in human leukemia cells. *Cancer Lett.* **286** 172-179.

[19] Huang, X.T., Li, X., Xie, M.L., Huang, Z., Huang, Y.X., Wu, G.X., Peng, Z.R., Sun, Y.N., Ming, Q.L., Liu, Y.X. and Chen, J.P., 2019. Resveratrol: Review on its discovery, anti-leukemia effects and pharmacokinetics. *Chem. Biol. Interact.* **306** 29-38.

[20] Shanbhag, V.K.L., 2017. Curcumin in chronic lymphocytic leukemia–A review. *Asian Pac. J. Trop. Biomed.* **7** 505-512.

[21] Kouhpeikar, H., Butler, A.E., Bamian, F., Barreto, G.E., Majeed, M. and Sahebkar, A., 2019. Curcumin as a therapeutic agent in leukemia. *J. Cell Physiol.* **234** 12404-12414.

[22] Latiff, E.S., 2020. Effects of Epigallocatechin-3-Gallate (EGCG) on Cell Cycle Distribution and DNA Integrity of K562 Cells, A Human Chronic Myeloid Leukemia. *Jurnal Sains Kesihatan Malaysia (Malaysian Journal of Health Sciences)* **18**.

[23] Martínez-Castillo, M., Villegas-Sepúlveda, N., Meraz-Rios, M.A., Hernández-Zavala, A., Berumen, J., Coleman, M.A., Orozco, L. and

Cordova, E.J., 2018. Curcumin differentially affects cell cycle and cell death in acute and chronic myeloid leukemia cells. *Oncol. Lett.* **15** 6777-6783.

[24] Borutinskaitė, V., Virkšaitė, A., Gudelytė, G. and Navakauskienė, R., 2018. Green tea polyphenol EGCG causes anti-cancerous epigenetic modulations in acute promyelocytic leukemia cells. *J. Leuk. Lymphoma* **59** 469-478.

[25] Briguglio, G., Costa, C., Pollicino, M., Giambò, F., Catania, S. and Fenga, C., 2020. Polyphenols in cancer prevention: New insights. *Int. J. Funct. Nutr.* **1** 1-1.

[26] Tao, H., Zuo, L., Xu, H., Li, C., Qiao, G., Guo, M. and Lin, X., 2020. Alkaloids as anticancer agents: a review of chinese patents in recent 5 years. *Recent Pat. Anticancer. Drug Discov.* **15** 2-13.

[27] Hwang, D., Kim, M., Park, H., Jeong, M.I., Jung, W. and Kim, B., 2019. Natural products and acute myeloid leukemia: A review highlighting mechanisms of action. *Nutrients* **11** 1010.

[28] Ribeiro-Filho, J., Carvalho Leite, F., Surrage Calheiros, A., de Brito Carneiro, A., Alves Azeredo, J., Fernandes de Assis, E., da Silva Dias, C., Regina Piuvezam, M. and T Bozza, P., 2019. Curine Inhibits Macrophage Activation and Neutrophil Recruitment in a Mouse Model of Lipopolysaccharide-Induced Inflammation. *Toxins* **11** 705.

[29] Dantas BB, Faheina-Martins GV, Coulidiati TH, Bomfim CC, da Silva Dias C, Barbosa-Filho JM, Araújo DA. Effects of curine in HL-60 leukemic cells: cell cycle arrest and apoptosis induction. Journal of natural medicines. 2015 Apr;69:218-23.

[30] Anitha Sri, S., 2016. Pharmacological activity of vinca alkaloids. *Res Rev: J Pharmacog. Phytochem*. **4** 27-34.

[31] Taher, M.A., Nyeem, M.A.B., Billah, M.M. and Ahammed, M.M., 2017. Vinca alkaloid-the second most used alkaloid for cancer treatment-A review. *Inter. J. Physiol. Nutr. Phys. Educ.* **2** 723-727.

[32] Martino, E., Casamassima, G., Castiglione, S., Cellupica, E., Pantalone, S., Papagni, F., Rui, M., Siciliano, A.M. and Collina, S., 2018. Vinca alkaloids and analogues as anti-cancer agents: Looking back, peering ahead. *Bioorg. Med. Chem. Lett.* **28** 2816-2826.

[33] Taverna, S. and Corrado, C., 2017. Natural compounds: molecular weapons against Leukemia's. *J. Leuk.* **5** 2.

[34] Tomko, A.M., Whynot, E.G., Ellis, L.D. and Dupré, D.J., 2020. Anti-cancer potential of cannabinoids, terpenes, and flavonoids present in cannabis. *Cancers* **12** 1985.

[35] Huang, M., Lu, J.J., Huang, M.Q., Bao, J.L., Chen, X.P. and Wang, Y.T., 2012. Terpenoids: natural products for cancer therapy. *Expert Opin. Investig. Drugs* **21** 1801-1818.

[36] Zálešák, F., Bon, D.J.Y.D. and Pospíšil, J., 2019. Lignans and Neolignans: Plant secondary metabolites as a reservoir of biologically active substances. *Pharmacol. Res.* **146** 104284.

[37] Tannous, S., Haykal, T., Dhaini, J., Hodroj, M.H. and Rizk, S., 2020. The anti-cancer effect of flaxseed lignan derivatives on different acute myeloid leukemia cancer cells. *Biomed. Pharmacother.* **132** 110884.

[38] Deesrisak, K., Chatupheeraphat, C., Roytrakul, S., Anurathapan, U. and Tanyong, D., 2021. Autophagy and apoptosis induction by sesamin in MOLT-4 and NB4 leukemia cells. *Oncol. Lett.* **21** 1-1.

[39] Kortesoja, M., Karhu, E., Olafsdottir, E.S., Freysdottir, J. and Hanski, L., 2019. Impact of dibenzocyclooctadiene lignans from Schisandra chinensis on the redox status and activation of human innate immune system cells. *Free Radic. Biol. Med.* **131** 309-317.

[40] Adfa, M., Rahmad, R., Ninomiya, M., Tanaka, K. and Koketsu, M., 2016. Antileukemic activity of lignans and phenylpropanoids of Cinnamomum parthenoxylon. *Bioorg. Med. Chem. Lett*. **26** 761-764.

[41] Hemmati, S. and Seradj, H., 2016. Justicidin B: a promising bioactive lignan. *Molecules* **21** 820.