Review Article

A Review on Clinical and Experimental Studies on Ayurveda and Leukemia

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Abstract

Blood cancers such as leukemia are a public health crisis globally. 2018 cancer statistics reveal 437,033 new cases with leukemia accounting for 2.6% of all cancers, worldwide. Conventional medical science manages the disease quite effectively by targeting the signaling pathways causing leukemogenesis, but with serious side effects as it also damages healthy cells. In this context, a systematic review was carried out to understand the role of *Ayurvedic* interventions for the management of *Rakta arbuda* in context to leukemia. Articles were searched using the keywords "only *Raktarbuda* or leukemia" and "Ayurveda" and "management" or "case report" or "case series" or "*in vivo*" or "*in vitro*" "research or review" or "leukemia and Ayurveda" and their different combinations and permutations. Articles from 2000 to 2018, published in only English language, and related to the topic were screened for their contents, and finally, 88 articles were included in this review, which was studies exclusively focused on leukemia done using an Ayurvedic intervention in the form of case reports or case series, *in vivo*, *in vitro* studies, or review article. Some case reports were found which documented the beneficial effect of Ayurvedic interventions in the management of leukemias. Scientific researches documented that drugs such as *Withania somnifera* (*Ashwagandha*), *Tinospora cordifolia* (*Guduchi*), *Curcuma longa* (*Haridra*), *Zingiber officinale* (*Adrak*), *Berberis aristata* (*Daruharidra*), and *Moringa oleifera* (*Sahijan*) are efficient inducers of apoptosis. Cell line studies have demonstrated the efficacy of *Andrographolide* and methanolic extracts of *Andrographis paniculata* (*Kalmegh*), *Semecarpus anacardium* (*Bhallataka*), and *Curculigo orchioides* (*Kali musli*) against leukemia cell lines.

Keywords: *Ayurveda, leukemia, management, Rakta arbuda, research*

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Introduction

Leukemia, ranked among the top ten cancer killers globally, is a type of cancer affecting the blood and bone marrow and causing uncontrolled growth of abnormal white blood cells. Leukemia clinically presents in two forms – (i) acute (rapidly progressing) disease characterized as acute lymphocytic leukemia and acute myelogenous leukemia and (ii) chronic (slowly progressing) forms as chronic lymphocytic leukemia (CLL) and chronic myelogenous leukemia (CML). Acute Lymphocytic Leukemia (ALL) is the most common of pediatric malignancies accounting for one-fourth of all childhood cancers and three-fourth of all freshly diagnosed leukemia cases.[1] The incidence of childhood ALL is nearly 3–4 cases per 100,000 children under the age of 15 years.[2] In India, nearly 25,000 children per annum are diagnosed with this cancer.[2] AML accounts for approximately 20% of acute leukemia in children and 80% of acute leukemia in adults.[3] According to the most recent data, leukemia

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accounted for 2.5% of all cancers and 3.2% of all deaths, while other forms of blood cancer such as Hodgkin's lymphoma represented 0.5% of all cancers and 0.5% of cancer deaths.[4] 2018 cancer statistics reveal 437,033 new cases with leukemia accounting for 2.6% of all cancers globally.[5]

Management in contemporary medicine includes chemotherapy (the use of anticancer drugs), radiation therapy (in which the high-energy radiation is used to kill cancer cells), and bone marrow transplant (in which transplantation of blood-forming stem cells is done after high doses of chemotherapy and radiation therapy as required) along with other supportive treatment as platelet transfusion to control bleeding. Conventional medical science manages the disease quite effectively by targeting the signaling pathways causing leukemogenesis, but with serious side effects as it also damages healthy cells,[6] leading to low survival rate and rate of cure.[7]

Ayurveda may offer some solutions for the above as there are so many herbal, polyherbal, mineral, and herbomineral drugs, which may play a major role in the treatment of leukemia and many other blood cancers, with significant cure rate and fewer side effects than conventional therapies. Studies document the beneficial effect of *Ayurvedic* interventions in the management of different kinds of blood cancers. In this context, a qualitative review was carried out to understand the role of *Ayurvedic* interventions for the management of *Rakta arbuda* w.s.r. to leukemia.

Methodology

A review of the literature was carried out in two phases using Google, Google Scholar, PubMed, and hand search. Here, the term hand search refers to searching the articles from cross-references of the articles selected for review. It is a process of selection of articles based on their rationality, undertaken at the stage of eligibility and inclusion, which did not characteristically undergo the process of identification and screening.

Articles were searched using the keywords "only *Raktarbuda* or leukemia" and "*Ayurveda* and management or case report or case series or *in vivo* or *in vitro* research or review" or "leukemia and Ayurveda" or their different combinations and permutations. Articles from 2000 to 2018, published in only English language, and related to the topic were screened for their contents, and 88 articles were finally included in this review, which was studies exclusively focused on leukemia done using an Ayurvedic intervention in the form case reports or case series, *in vivo*, *in vitro* studies, or review article. This study adopted a narrative review approach instead of a quantitative approach as used in meta-analysis. Hence, no statistical analysis was carried out in this review. The studies that did not fall in these categories were excluded from the review.

Data extraction and analysis

In the initial part, the articles were recognized based on the objectives of the study. In the second phase, the articles identified based on the study objectives were pooled together for screening by reading the titles and thereafter the abstracts. Articles not satisfying the inclusion criteria were excluded at this stage. The eligible articles were further screened by reading the full texts, and those not meeting the inclusion criteria were excluded. By the end of this process, the eligible articles meeting the inclusion criteria were taken for the review.

Eighty-seven studies done on leukemia using Ayurvedic intervention were finally included for the review [Table 1].

Observation

Management of blood cancers through Ayurveda: Human studies

Some case reports documented the effectiveness of different *Ayurvedic* drugs for their clinical efficacy in leukemia. A case report by Rathi and Rathi documented the beneficial effect of a multimineral preparation, accentuated with the juices of *Shyama Tulsi* (*Ocimum sanctum*), *Bilva* leaves (*Aegle marmelos*), *Sadaphuli* (*Catharanthus roseus*), other *Tikta Rasatmaka Aushadhies* (bitter taste compound formulation medicines – *Rohitakarishta*, *Kumaryasava*, and *Lohasava*) given through oral route coupled with the per rectal administration of *Majjabasti* (medicinal preparation of animal bone marrow) with *Panchtikta Ghrita* (*Ghrita* cooked with several bitter taste medicines), to demonstrate a great role in the management of a case of acute lymphoid leukemia (ALL). The same report also documented the benefit of the above-mentioned regimen in the other two cases of ALL in the first and third stages (in conjunction with conventional treatment). No major side effects were noticed in the treatment duration (even in the case with

Table 1: The details of the kind and number of studies included in the review

Serial number	Study type	Total
2	Case studies	4
3	I*n vivo* studies	8
4	*In vitro* studies	69
5	Review articles	6
	All included studies	87

adjuvant chemotherapy), and liver and kidney function tests were normal.[8]

Prakash studied the effect of some herbomineral medications consisting of *Navjeevan*, *Valipani*, *Kamdhuda Rasa*, and *Prak*-20 in a relapsing case of Acute Myeloid Leukemia (AML). The report documents the therapy to be effective with the patient completing 12 years of disease-free survival till then.[9] Another case study by Prakash *et al*. in acute promyelocytic leukemia (APL) reported the efficacy of the treatment with complete disease remission and has completed 13 years of disease-free healthy life with the alternative treatment without any adverse side effect.[10] Both the above case reports documented the use of antibiotics and blood transfusions being provided to the patient, under the supervision of experts of modern medicine in the initial treatment period as and when required.

A case study by Sharma on AML using several *Ayurvedic* drugs documents significant changes in signs and symptoms of the patient with simultaneous improvement in their blood investigations after 2 months of therapy.[11] The details of these studies are summarized in Table 2.

Ayurveda drugs and their efficacy in leukemias: *In vitro* and *in vivo* studies

Besides the above case reports, several other *in vivo*, *in vitro* researches, and review articles documented the efficacy of various herbal and herbomineral formulations studied for their efficacy in different types of leukemias. Satadru *et al*. reviewed the role of arsenic-based *Ayurvedic* compounds in the management of leukemia, and through the study of ancient classics and pieces of evidence from the contemporary researches, they found that *Bhasmikarana* process (the classical process of preparation of metal powders which converts them into nanoparticles) may enhance the bioavailability of the

Table 2: Case reports on the role of Ayurvedic interventions in different types of Leukaemia

Author and type of leukemia	Ayurvedic intervention used and Dosage	Major outcomes/Result
Renu Rathi, Bharat Rathi Acute lymphoid leukaemia (ALL)	Multi mineral formulation - 8 mg QID with 5 ml each of *Shyama Tulsi (Oscimum sanctum)* juice, *Juice of Bilva* leaves (*Aegle marmelos*), *Sadaphuli* (*Catharanthus roseus*) juice, *Rohitakarishta, Kumariasava, Lohasava*, 1 hour after meal. *Majja Basti* was given for 30 days daily	Haemoglobin increased Leucocyte count reduced to 32,600/cu.mm with no change in thrombocytopenia Bone marrow studies revealed Normal picture
Balendu Prakash on Acute myeloid leukemia (AML-M0)	Oral AYT comprising of *Navjeevan* - 250 mg BD *Valapani* - 1 gm BD *Kamdhuda* - 250 mg TDS *Prak*-20-500 mg BD	Good response and tolerance to therapy. Bone marrow Cytopathology showed 1% blast cells after 6 months of AYT.
Balendu Prakash on Acute promyelocytic leukemia (AML-M3)	N*avjeevan* tablet - 250mg TDS x three months followed by 125 mg TDS x nine months *Kamdudha Rasa* (250mg) + *Kehruba Pishti* (125mg) - QDS with honey x three months followed by *Kamdudha Rasa* 250 mg TDS x nine months.	Complete remission of disease with no relapse after AYT
Ved Bhushan Sharma on Acute Myeloid Leukemia (AML)	*Phaltrikadi Kwath* (a polyhebal formulation) along with *Mulethi kwath* (Glycyrrhiza glabra) and *Giloy Kwath* (*Tinospora cordifolia*) - 50 ml twice a day empty stomach *Swarna Basant Malti* - 3 gm} Mixed and divided in total 60 doses, taken TDS with honey *Amrita Satva* - 20 gm *Praval Panchamrit*- 10 gm *Mukta Pishti*- 6 gm *Mukta Shukti* - 10 gm *Kahrava Pishti* - 20 gm *Heerak Bhasma* - 300 mg *Mulethi Churn* -50 gm *Godanti* - 20 gm *Kashore Guggulu* - 2 TDS+*Arogya Vardhini Vati* - 1TDS, after meal with luke warm water	Significant changes in signs and symptoms Simultaneous improvement in blood investigations

drug and hence potentiate its action. They also reported that there is a huge scope of the cellular apoptosis property of arsenic-containing drugs in combating leukemia.[12] The same study has also quoted the work of Prakash and Prakash for documenting several success stories of APL in a pilot study.[10]

Withania somnifera root aqueous extract (WRE) was proved to effectively modulate antioxidant activity, inflammatory cytokines, and cell death in human leukemia monocytic cell line (THP-1 cells). WRE was also found to decrease proinflammatory cytokine levels which may relieve cachexia due to cancer and excessive leukemic cell growth.[13,14]

Curcumin from the herb *Curcuma longa* (*Haridra*) has been discovered to modulate several regulatory proteins and inhibits carcinogenicity through the modulation of the cell cycle by binding to molecular targets directly and indirectly, including transcription factors (NF-kB, STAT3, β-catenin, and AP-1), growth factors (EGF, PDGF, and VEGF), enzymes (COX-2, iNOS, and MMPs), kinases (cyclin D1, CDKs, Akt, PKC, and AMPK), inflammatory cytokines (TNF, IL-1, and IL-6, MCP), upregulation of proapoptotic proteins (Bax, Bad, and Bak), and downregulation of antiapoptotic proteins (Bcl (2) and Bcl-xL). A variety of animal models and human studies have proven that curcumin is safe and well tolerated even at very high doses.[15] A study of curcumin on acute and chronic myeloid leukemia cell lines, i.e., HL-60 and K562 cells, reveals different cellular mechanisms in chronic or acute myeloid leukemia cells and more potent antitumoral effect in K562 as compared with HL-60 cells.[16]

Andrographolide, the major diterpene lactone extracted from *Bhunimba* (*Andrographis paniculata*), in the cell line studies is found to be cytotoxic toward several cancer cells, including lymphocytic leukemia[17] and APL cells.[18,19] They exhibit anticancer activities on cancer cells directly by arresting cell cycle at the G0/G1 phase through induction of cell cycle inhibitory protein and decreased expression of cyclin-dependent kinase.[17,20]

Gingerol from *Zingiber officinale* (*Ardraka-Shunthi*) has been demonstrated to induce apoptosis (programmed cell death) by a mitochondrial pathway in the leukemia cells K-562 along with exhibiting antioxidant, anti-inflammatory, and antitumor properties.[21] Galanals from ginger on exposure to leukemia cells cause apoptosis, due to caspase-3 activation and induced DNA fragmentation.[22]

Berberine, a natural isoquinoline alkaloid isolated from *Berberis* (*Daruharidra*), has been shown to induce apoptosis by topoisomerase II inhibition,[23] stimulate caspase activation, and also exhibit antiproliferative, cytotoxic, and proapoptotic activities in leukemia, which lack p53 expression.[24] Studies have also proved berberine to demonstrate anticancer activities against leukemic cells – HL-60 and WEHI-3.[25,26]

Cell lines' study with oil of *Semecarpus anacardium* (*Punarnava*), *Convolvulus pluricaulis* (*Shankhpushpi*), and *Curculigo orchioides* (*musli*)[28] in leukemia cell lines has documented very promising positive results. A study of *S. anacardium* nut milk extract in leukemic mice showed clearance of the leukemic cells from the bone marrow and internal organs, a significant increase in lipid peroxides and glycolytic enzymes, a decrease in gluconeogenic enzymes, and a significant decrease in the activities of Krebs cycle and respiratory chain enzymes as compared to control animals.[29]

A study on the proliferation and myeloid differentiation of the bone marrow hematopoietic precursor cells in mice-bearing transplantable T-cell lymphoma with the alcoholic extract of *Tinospora cordifolia* (*Guduchi*) whole plant indicates that *T. cordifolia* can influence the myeloid differentiation of bone marrow progenitor cells and the recruitment of macrophages in response to tumor growth *in situ*.[30]

The study of wheatgrass methanolic extract in Wistar rats with benzene-induced leukemia revealed the antileukemic effect of the extract.[31] Ethanolic extract of *Moringa oleifera* (*Sahjan* or *Shigru*) revealed antileukemic and antiproliferative effect on AML cell lines.[32] Study of grape seed extracts on leukemia cell lines (Jurkat cells, U937, and HL-60) revealed that it causes cell death and induces apoptosis in leukemia cell lines through the activation of JNK pathway.[33] Pomegranate (*Punica granatum*) juice extracts have been found to induce apoptosis in different leukemia cell lines (lymphoblastic cell lines – Jurkat, SUP-B15, MOLT-3, and CCRF-CEM and myeloblastic cell lines – HL-60, THP-1, K562, and KG1a).[34] Carrot juice extract exposure to leukemia cell lines induced apoptosis and inhibited progression through the cell cycle. Lymphoid cell lines were affected to a greater extent than myeloid cell lines, and normal hematopoietic stem cells were less sensitive than most cell lines.[35] Methanolic extract of *Vacha* (*Acorus calamus*) exhibits antineoplastic activity against P388 lymphocytic leukemia cell line due to epieudesmin.[36] Active principles of *Aloe vera* (*Aloe barbadensis*) exhibit significant concentration-dependent cytotoxicity against acute myeloid leukemia (AML) and acute lymphocytes leukemia (ALL) cancerous cells.[37] Saponoins from *Asparagus* shoot (*Asparagus officinalis* L)

demonstrated antitumor activity inhibiting the growth of human leukemia HL-60 cells.[38,39] Plumbagin from *Chitraka* (*Plumbago zeylanica*) is reported with anticancer activity against THP-1 cell line.[40]

Laser-activated calendula extract of Marigold (Genda, *Calendula officinalis*) exhibited significant tumor cell proliferation inhibition through caspase-3-induced apoptosis and arrest of cell division at G0/G1 phase.[41] Leukemic cell apoptosis is also exhibited by *Senna* (*Senna alexandrina*) plant extract.[42] *Amalaki* (*Emblica officinalis*) was also found to be effective against leukemia cells *in vivo*.[43] Potent antiproliferative and cytotoxic activity is shown against Jurkat cells (human leukemia cell line) by *Kasani* (*Cichorium intybus*) n-hexane extract.[44] *Karela* (*Momordica charantia*) extract showed anticancer activity against lymphoid leukemia.[45-47] Amooranin, a plant terpenoid from *Rohitaka* (*Amoora rohituka*) stem bark, exhibited significant cytotoxicity in multidrug-resistant human leukemia cell line with cell cycle perturbation in G2 + M phase.[48] Mangiferin from mango (*Mangifera indica*) is also found to exhibit significant cytotoxic activity against K562 leukemia cell lines.[49] *Neem (Azadirachta indica)* compounds liminoids and nimbolide are found to be effective against leukemic cell lines.[50] Anti-inflammatory and proapoptotic effects have been reported via the modulation of the nuclear factor-kappa B pathway for methanolic *neem* (*A. indica*) leaf extract.[51] β-sitosterol-3-O-β-D-glucoside isolated from ethanolic extract of dried *neem* leaves effectively reduced the proliferation of acute lymphoblastic leukemia (ALL) MOLT-4 cell lines in a dose- and time-dependent manner, with a check at G1 phase of cell cycle progression.[52,53] Thymoquinone, an active component isolated from the seed extract of *Kalaunji* (*Nigella sativa*), exhibits antiproliferative effect, induces apoptosis, disrupts mitochondrial membrane potential, and triggers the activation of caspases 8, 9, and 3 in the myeloblastic leukemia HL-60 cells.[54,55] Eugenol, a derivative of *Tulasi* (*O. sanctum*), exhibits mechanism of induced apoptosis in leukemia cell lines.[56] Methanol extract of *Mesua ferrea* Linn. is found to be cytotoxic to T-lymphocyte leukemia cells.[57] Ethanolic extract of *Shallaki* (*Boswellia serrata*) gum resin containing defined amount of boswellic acid-induced dose-dependent antiproliferative effects on all five leukemia (HL-60, K562, U937, MOLT-4, and THP-1) cell lines, with GI50 values (extract concentration producing 50% cell growth inhibition) between 57.0 and 124.1 μg/ml. The effect of total extract expressed in GI50 was 2.8, 3.3, and 2.3 times more potent ($P < 0.05$) than pure 3-O-acetyl-11-keto-beta-boswellic acid in three of the hematological cell lines (K562, U937, and MOLT-4).[58] Zerumbone, a cyclic sesquiterpenoid of essential oil obtained from *Kebuk* (*Costus speciosus*), is a potential anticancer natural compound that shows activity on rat bone marrow cells, T-acute lymphoblastic leukemia cells.[59] Methanol extract of flowers of *Dhatura* (*Datura metel*) has exhibited promising effects against K562 leukemia cell lines.[60] Methanolic and hexane fractions of *Sihora* (*Streblus asper*) demonstrate highly cytotoxic potency against K-562 leukemia cell lines.[61] *Ananthamoola* (*Hemidesmus indicus*) is found to induce cytotoxicity and alter cell cycle progression in human promyelocytic leukemia cell line (HL-60).[62-64] Dimethyl-crocetin, crocetin, and crocin, the derivatives of *Kesar* (*Crocus sativus*), inhibit human CML K562 and promyelocytic leukemia HL-60 cells.[65]

Rudanti (*Astragalus* species, *Astragalus candolleanus* and *Astragalus malacophyllous*)[66-68] extracts exhibit antitumor effects, specifically against melanoma and leukemia cell lines. *Triphala* (a combination of *E. officinalis*, *Terminalia chebula*, and *Terminalia belerica*) is a rich source of gallic acid which is reported to possess anticancer properties against leukemia cell lines.[69] Exosome-like nanovesicles present in the juice of *Nimbuka* (*Citrus limon*) affect cell growth of leukemia cells, through activation of TRAIL-mediated apoptosis and also through angiogenesis inhibition.[70] Guggulsterone from *Guggulu* (*Commiphora mukul*) inhibited the proliferation of drug-resistant leukemia cells.[71]

A study of *Kajjali* (black sulfide mercury, HgS, a mineral compound purified and processed drug of Ayurveda) in chronic myeloid leukemic cells, K562 cell line with different concentrations revealed that increased concentrations of *Kajjali* significantly changed cell morphology and induced cell death by apoptosis.[72] Another scientific study documented the beneficial effect of *Abhraka Bhasma* (incinerated nanoparticle of mica) on leukemia U937 cell lines.[73]

Compounds of arsenic have demonstrated significant anticancer activity against leukemia cell lines, with arsenic trioxide (ATO, *Somal* or *Gauripashana*, As_2O_3) in acute megakaryocytic leukemia[74] and realgar (*Manhshila*, As_4S_4,) on K562 and fresh CML mononuclear cells.[75-79]

An *in vivo* study on albino mice with a herbomineral drug using purified arsenic (ATO), *Vinca rosea*, and *Urginia indica* and ATO as a control against myelocytic leukemia and lymphocytic leukemia was found to show good antileukemic activity and safety, though ATO produced better results.[80]

Discussion

Leukemia is among the top ten global killers. 2018 cancer statistics reveal 437,033 new cases with leukemia accounting for 2.6% of all cancers globally.[5] It is a type of cancer affecting the blood and bone marrow and causing uncontrolled growth of abnormal white blood cells. Leukemia is classified based on the onset and progression of the disease into acute or chronic. Based on the nature of cells involved in leukemia, it has been subdivided into further subtypes such as acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myelogenous leukemia (AML), CML, hairy cell leukemia (HCL), T-cell prolymphocytic leukemia (T-PLL), large granular lymphocytic leukemia, adult T-cell leukemia, juvenile myelomonocytic leukemia (JMML). Of these, ALL is the most common of pediatric malignancies accounting for one-fourth of all childhood cancer and three-fourth of all freshly diagnosed leukemia cases.[1] CLL, AML, and CML are common in adults, though AML and CML may also affect children. AML accounts for approximately 20% of acute leukemia in children and 80% of acute leukemia in adults.[3] HCL and T-PLL and large granular lymphocytic leukemia are relatively uncommon; however, while T-PLL is an aggressive form, large granular lymphocytic leukemia is nonaggressive. Human T-lymphotropic virus infection is associated with adult T-cell leukemia. JMML is a type of leukemia occurring in childhood with intermediate growth rate. The chief presenting features of leukemia in the patients are relatively unspecific and resemble the features of decreased immunity of the body. The patient suffers from fatigue, recurrent fevers and infections, loss of appetite, weight loss, swollen and palpable lymph nodes, bone and joint pains, bruising or bleeding, rashes, etc. Diagnostic tests include complete blood count, general blood picture, liver and kidney function tests, bone marrow aspiration and biopsy, lymph node biopsy, genetic studies, and spinal tap. The conventional medical system has developed a plethora of modalities for managing the disease with chemotherapy, radiation therapy, immunosuppression therapy, bone marrow transplants, splenectomy, and stem cell transplantation, and still, many more modalities are being researched to combat the disease. The treatment is aimed at improving the prognosis of the disease, as the treatment is associated with several dreaded side effects such as tumor lysis syndrome (with several metabolic abnormalities such as hyperkalemia, hyperuricemia, hyperphosphatemia, raised blood urea nitrogen, and hypocalcemia) and several features due to the damage of healthy cells, besides the neoplastic cells, resulting in bruising or bleeding, impaired immunity, alopecia, fatigue, anorexia, nausea, vomiting, nephropathy, acute kidney failure, cardiac arrhythmias, seizures, and even death. Due to the above-mentioned reasons, the search for better treatment interventions is the need of the hour with better efficacy and minimized side effects.

Ayurveda is being used for the management of many diseases in India since ages. Ayurveda has the description of many ailments specifically by name and describes the treatment principles for other ailments that may present in the patients based on *Dosha* (the particular physiological *Dosha*), *Dushya* (tissue involved), *Adhishthana* (the seat of the disease), and *Hetu* (etiological factor). Based on the above principles of *Ayurveda*, and based on knowledge about the drugs (herbs, minerals, herbomineral, and animal origin), any disease can be managed quite effectively. Acting on the body, these drugs also heal, potentiate, and regenerate the body to combat the disease itself besides directly targeting the abnormal cell growth. They also target and improve the digestive system and liver as proper digestion is the basis for health as per Ayurveda. Ayurveda recommends for the early diagnosis and management of diseases, as once a disease becomes deep-rooted in the body, it will be difficult to uproot it completely and it will cause significant damage to the body.

Leukemia as such is not described in *Ayurveda*; however, there are guidelines based on which any disease can be treated. These are based on the presentations of the patient. The presenting features of leukemia are summarized with their correlating diseases and features Table 3.

In the case reports documented above, it is very apparent that the treatment module adopted by the physicians in these patients was based on the concept of vitiation of blood (*Rakta Dushti*) and the pacification of *Pitta* (*Pitta Shaman*). The nature and properties of *Rakta* (blood) are similar to that of *Pitta Dosha* (one of the three physiological entities of the body responsible for all the functions of digestion, metabolism, inflammation, heat generation, etc.). Hence, formulations balancing *Pitta* will also bring *Rakta* in equilibrium, and vice versa. Further, all treatment principles adopted for purification of *Rakta*, also simultaneously address the organs liver (called as *Yakrita*) and spleen (called as *Pleeha*), which have been especially linked to blood as its root organs (*Moola*).

An observation of the drugs used above reveals that the majority of the drugs are mainly *Pitta Shamaka* (drugs pacifying *Pitta*), *Rakta Shodhaka* (purifying blood), *Agni Vardhaka* (correcting metabolism and acting on the liver) and having *Rasayana* (rejuvenating)

Table 3: Ayurveda guidelines for deriving the treatment principle of leukemia

Symptoms of leukemia	The guiding disease of Ayurveda or correlating feature in Ayurveda	The treatment (*Chikitsa*) principle
Fever, weakness, fatigue, appetite loss, splenomegaly	*Jvara* (fever) - A disease characterized by increased temperature along with other associated features, such as body ache, loss of sweating, body pain, and ache[81]	*Ama Pachaka Chikitsa* - Improving the process of digestion and metabolism of the body, thus helping it to clear the toxins accumulated in the body
	Jeerna Jvara (fevers of long duration) - Fevers existing beyond 3 weeks duration which are associated with splenomegaly[82]	*Jvara*ghna *Chikitsa* - Ayurveda line of treatment of fevers which focuses on letting the body take rest and heal by itself, by decreasing the load on the digestive fire along with *Ama Pachaka Chikitsa* initially, followed by *Pitta* pacification drugs, diets, and measures[84]
	Pleehodara (splenomegaly) - a disease described in the chapter of *Udararoga* (abdominal growths) which occurs primarily due to vitiation of *Rakta* (blood)[83]	*Pleehodara Chikitsa* - The principle of management of splenomegaly in Ayurveda is the purification of *Rakta* (blood) along with specific drugs acting on the spleen
Hepatomegaly	*Yakriddalyodara* (hepatomegaly) - A disease described in the chapter of *Udararoga* (abdominal growths) which occurs primarily due to vitiation of *Rakta* (blood)[83]	*Yakriddalyodara Chikitsa* - The principle of management of splenomegaly in Ayurveda is the purification of *Rakta* (blood) along with specific drugs acting on the liver
Easy bleeding, bruising, reddish patches	*Pitta Vriddhi* (state of increased *Pitta* - one of the three biological humors responsible for the function of digestion, metabolism, catabolism, heat and energy production, and causing inflammation when deranged).[85] Vitiated *Pitta* deranges many biological processes going on in the body and vitiates *Rakta* (blood) primarily and essentially due to many similarities in their properties[86]	*Pitta Shamaka* (pacifying *Pitta* - One of the three biological humors which are responsible for performing digestion, metabolism, energy, and heat production, also causing inflammation in the deranged state).[87] - Done either through *Shodhana* (purificatory) process, i.e., *Virechana* (medicated purgation which cleanses the body of vitiated *Pitta Dosha* and brings it to normalcy) or *Shamana* (pacification) with drugs which are *Kashaya* (astringent), *Tikta* (bitter), *Madhura* (sweet) in taste and cold in potency (*Sheeta Veerya*)[88]
	Rakta Pitta (bleeding disorders) - Ayurveda considers the bleeding disorders to result due to vitiation of *Pitta* which then vitiates *Rakta* (blood) and its root organs, i.e., *Yakrit* (liver) and *Pleeha* (spleen)[86]	*Rakta Shodhaka or Rakta Prasadaka Chikitsa* (treatment for purification of blood) - the vitiated three *Doshas*, especially *Pitta* vitiates *Rakta* (blood), which manifests with several clinical presentations, such as inflammation, swelling, pain, bleeding diathesis, skin disorders, and enlargement of liver and spleen.[89] Hence, when such symptoms are observed in the patient, the treatment module consists of blood purification wherein mostly bitter taste and cold potency medicines are used. Other measures for the purification of blood are similar to those mentioned under *Pitta* pacification since they have many similar properties
		Rakta-Pitta Chikitsa (management of bleeding diathesis) - This encompasses *Shodhana* (purification of the body) done either through *Vamana* (medicated controlled emesis administered to cleanse the body of vitiated *Kapha Dosha* and restore its normalcy) or *Virechana* (medicated purgation for cleansing vitiated *Pitta*) or *Shamana* (pacification) therapies based on the strength of the patients. *Shamana Chikitsa* is done with drugs, diet, and behaviors which are opposite in properties to *Pitta* and also act on *Rakta* (blood), *Yakrit* (liver), and *Pleeha* (spleen) and restore their normalcy states[90]
Lymph node swelling	*Granthi* (growths or swellings)[91] *Arbuda* (tumors)[92]	*Granthi*[93] - *Arbuda Chikitsa*[94] - The treatment principles of these diseases include the management of *Shotha* (inflammation and edema) as well as specific procedures such as *Shastra Karma* (surgical intervention), *Kshara Karma* (application of Ayurvedic-medicated alakalies), and *Agni Karma* (cauterization) followed by various internal medications and external applications based on Doshika predominance[95]

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Table 3: Contd...

Symptoms of leukemia	The guiding disease of Ayurveda or correlating feature in Ayurveda	The treatment (*Chikitsa*) principle
Increased proliferation of cells and tissue destruction going on in a body	*Vata Vriddhi* - Increased *Vata* (one of three biological humors responsible for all sorts of movement, sensing, regulation, cell division, etc.).[96] It is very important as it also regulates *Pitta* (biological humor-regulating digestion, metabolism, catabolism, etc.) and *Kapha* (the biological humor responsible for growth, anabolism, lubrication, providing protective lining to the body surfaces, protection against damage from outside agents as well as negating the effects of *Vata* and *Pitta Doshas*)[97]	*Vata Shaamak Chikitsa* - Therapies pacifying *Vata* with *Shodhana* (purificatory) measures such as *Vasti* (medicated enema prepared from decoction of drugs with added oils customized to the condition of the patient) or with *Shamana Chikitsa* (pacification therapy) with drugs which are *Madhura* (sweet), *Amla* (sour), and *Lavana* (salt) in taste and *Ushna Veerya* (hot in potency)[88] *Rasayana Chikitsa* - This treatment modality of Ayurveda refers to replenishing and regenerating the body tissues and cells of the body, depleted either due to aging or as a consequence of certain diseases. It involves initial *Shodhana* (purificatory) measures followed by customized and specified drugs, dietary regimen, and activities. However, in patients suffering from ailments, *Shodhana* (purificatory procedures are not possible), hence, they are administered *Rasayana* drugs suitable as per their disease condition after stimulating the digestive fire

properties as per the Ayurvedic concept. *Heeraka bhasma* (processed and incinerated diamond ash)[98] and *Bhallataka* (*S. anacardium*)[99] are the drugs described for the management of tumors in Ayurveda. *Rajat bhasma* (purified, processed, and incinerated silver ash) as per the concept of *Samanya* (similarity) in Ayurveda is a component of bone tissue and is supposed to act on white blood cells also. Every processed and incinerated *Dhatu Bhasma*s (metal ash) in Ayurvedic preparations are also combined with purified and processed *Parad* (mercury) and *Gandhak* (sulfur), to potentiate their action within the human body. Based on these principles, the medicines, *Navjeevan* and *Valapani* were prepared and used in the therapy of leukemia patients.[100,101] The combination of *Parada* and *Gandhak* called as *Kajjali* in Ayurveda has also been proven to be an efficient inducer of apoptosis. The approach adopted by Prakash also points toward the integrated approach of Ayurveda and conventional experts in the management of leukemia with scientific documentation of data. That particular approach with adequate infrastructure within the same premises helps to save the leukemic patient during stages of crisis, with the help of scientific advancements, such as blood transfusions or any antibiotic course required, which may appear during treatment regimen.

A review of the drugs reported for their experimental efficacy against leukemia, as per the classical texts of Ayurveda, reveals the following properties, actions, and indications [Table 4].

The exact methodology of action of these drugs as per the Ayurveda principle in cell line studies cannot be explained; however, it is observed that majority of herbal drugs studied experimentally were having *Katu* (pungent) and *Tikta* (bitter) tastes with hot potency and were mostly having properties of *Kapha-Vata* pacification, blood purification, digestive stimulant, nourishing, rejuvenate, etc. They could be acting on cell lines due to the above-mentioned properties. Reference of their classically being used in *Arbuda* (cancer) treatment is not available, except for *Draksha* (*Vitis vinifera*)[135] and *Haridra* (*C. longa*).[136]

Regarding the mineral preparations, Ayurveda describes that the drugs should be prepared only after proper purificatory measures and following proper methodology to attain the following properties in the final *bhasma* (incinerated ash) preparation – *Nirmalatva* (bitter less taste), *Niscandratva* (absence of any metallic luster), *Rekha purnatva* (penetrating in the finger ridges when held in between the thumb and index finger), *Varitaratva* (floating on the surface of water when a pinch of *Kajjali* or *bhasma* is dropped over it), *Apunarbhava* (the *bhasma* should not regain the elemental metal form on strong heating with *jaggerry*), *Gunja* (*Abrus precatorius*, honey and ghee), and *Niruttha* (*Bhasma* should not regain its metallic nature after strong heating with silver). The metal preparations studied experimentally, i.e., *Kajjali* (mercuric sulfide)[137] as well as *Abhraka bhasma* (mica)[138] as per the Ayurveda, are described to have the property of *Rasayana* (nourishing the body tissues). In addition, *Kajjali* has been described to be useful in curing abscesses (*Vidradhi*), cervical lymphadenopathy (*Gandamala*), warts (*Charmadala*), eryseplas (*Visarpa*), etc., while *Abhraka bhasma* (mica) is described to be useful in nonhealing wounds and abscesses (*Dushta Vrana*), bleeding diathesis (*Rakta-pitta*), tuberculosis (*Rajayakshma*), etc.

Regarding *Somal* (*Gauripashana*, ATO), it is mentioned in *Rasatarangini* that it stimulates the digestive fire and

Table 4: The properties and actions of drugs (as per Ayurveda) studied experimentally in leukemia

Name of drug with Latin name	Properties as per Ayurveda				Pacification action on *Doshas*	Mode of action and indications
	***Rasa* (taste)**	***Guna* (properties)**	***Virya* (potency)**	***Vipaka* (properties after digestion in the body)**		
Ashwagandha (*Withania somnifera*)[102]	*Katu* (pungent) *Tikta* (bitter) *Madhura* (sweet)	*Snigdha* (oily) *Laghu* (light to digest)	*Ushna* (hot)	*Katu* (pungent)	*Vata-Kapha Dosha*	*Balya* (improves strength) *Rasayana* (rejuvenates body) *Shophahara* (mitigates inflammation) *Kshayahara* (treats emaciation)
Haridra (*Curcumin longa*)[103]	*Tikta* (bitter) *Katu* (pungent)	*Ruksha* (dry) *Laghu* (light to digest)	*Ushna* (hot)	*Katu* (pungent)	All three *Doshas*	*Vranahara* (quick wound healing), Vishodhini (natural detoxifier), Panduhara (useful in anemia), *Pitta Rechaka* (expels *Pitta* out of the body utilizing purgation)
Bhunimba (*Andrographis paniculata*)[104]	*Tikta* (bitter)	*Laghu* (light to digest) *Ruksha* (dry)	*Ushna* (hot)	*Katu* (pungent)	*Kapha Pitta Dosha*	*Yakrita Uttejaka* (stimulates liver), *Pitta* Saraka (expels vitiated *Pitta*), *Katu Paushtika* (bitter pungent, yet nourishing)
Shunthi (*Zingiber officinale*)[105]	*Katu* (pungent)	*Guru* (heavy) *Ruksha* (dry) *Teekshana* (penetrating)	*Ushna* (hot)	*Katu* (pungent)	*Kapha* and *Vata Dosha*	*Rochana* (improves anorexia) *Shophahara* (anti-inflammatory) *Deepana* (improves digestion)
Daruharidra (*Berberis aristata*)[106]	*Tikta* (bitter) *Kashaya* (pungent)	*Laghu* (light to digest) *Ruksha* (dry)	*Ushna* (hot)	*Katu* (pungent)	*Kapha-Pitta Dosha*	*Vishahara* (antitoxic) *Shophahara* (anti-inflammatory) *Vranajit* (quick wound healing)
Bhallataka (*Semecarpus anacardium*)[107] fruit	*Katu* (pungent) *Tikta* (bitter) *Kashaya* (astringent)	*Laghu* (light) *Teekshana* (piercing) *Snigdha* (unctuous)	*Ushna* (hot)	*Madhura* (sweet)	*Kapha-Vata Dosha*	*Medhya* (improves intelligence), *Agni Vardhaka* (promotes digestion), *Shophahara* (relieves inflammation)
Giloy (*Tinospora cordifolia*)[108]	*Kashaya* (astringent) *Tikta* (bitter)	*Guru* (heavy to digest) *Snigdha* (oily)	*Ushna* (hot)	*Madhura* (sweet)	All three *Doshas*	*Rasayana* (rejuvenates the body tissues), *Balya* (provides strength), *Agni Deepana* (improves digestion), *Panduhara* (cures anemia), *Vrishya* (aphrodisiac)
Sahijan (*Moringa oleifera*)[109]	*Katu* (pungent) *Tikta* (bitter)	*Laghu* (light) *Ruksha* (dry) *Teekshana* (penetrating)	*Ushna* (hot)	*Katu* (pungent)	*Vata* and *Kapha Dosha*	*Shothahara* (anti-inflammatory), *Pleehaghna* (useful in spleen disorders)
Draksha (*Vitis vinifera*)[110]	*Madhura* (sweet)	*Snigdha* (oily) *Guru* (heavy)	*Sheeta* (cold)	*Madhura* (sweet)	*Vata* and *Pitta Dosha*	*Jvara* (fever) *RaktaPitta* (bleeding disorders) *Kashata* (injury) *Kashaya* (weight loss) *Kamala* (jaundice)

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Table 4: Contd...

Name of drug with Latin name	Properties as per Ayurveda				Pacification action on *Doshas*	Mode of action and indications
	***Rasa* (taste)**	***Guna* (properties)**	***Virya* (potency)**	***Vipaka* (properties after digestion in the body)**		
Shankhapushpi (*Convolvulus pluricaulis*)[111]	*Tikta* (bitter)	*Snigdha* (oily) *Picchila* (slimy)	*Sheeta* (cold)	*Madhura* (sweet)	Pacifies *Tridoshara*, especially *Vata* and *Pitta Dosha*	*Medhya* (promotes intelligence) *Rasayana* (rejuvenating) *Raktastam bhaka* (hemostatic)
Kali Musli (*Curculigo orchiodes*)[112]	*Madhura* (sweet) *Tikta* (bitter)	*Guru* (heavy) *Snigdha* (oily) *Picchila* (slimy)	*Ushna* (hot)	*Madhura* (sweet)	*Vata Pitta Shamaka* (pacifies *Vata* and *Pitta Dosha*)	Useful in *Daur Balya* (weakness), *Shukrakshaya* (oligospermia), *Mutrakriccha* (dysuria)
Dadim Pomogranate (*Punica granatum*)[113]	*Madhura* (sweet) *Amla* (sour) *Kashaya* (astringent)	*Laghu* (light), *Snigdha* (unctuous)	*AnUshna* (neither cold nor hot)	*Madhura* (sweet) and *Amla* (sour)	All three *Doshas*	*Medhakara* (improves intelligence), *Balya* (promotes immunity and body strength), *Hridya* (good for the heart)
Gajar *Carrot* (*Daucas carota*)[114]	*Madhura* (sweet), *Tikta* (bitter)	*Laghu* (light), *Teekshana* (penetrating)	*Ushna* (hot)	*Madhura* (sweet)	*Kapha Vata Dosha*	*Deepana* (induces appetite), *Rakta Pitta*ghna (bleeding disorders), *Arshoghna* (hemorrhoids), *Aruchi nashak* (anorexia)
Vacha (*Acorus calamus*[115]	*Katu* (pungent), *Tikta* (bitter)	*Laghu* (light), *Teekshana* (penetrating)	*Ushna* (hot)	*Katu* (pungent)	*Kapha Vata Dosha*	*Medhya* (improves intelligence), *Krimi* (worms), *Vibandha anaha* (abdominal distension), *Kanthya* (improves voice)
Kumari (*Aloe barbadensis*, *Aloe vera*)[116]	*Katu*, (pungent)	*Guru* (heavy), *Snigdha* (oily), *Picchila* (slimy)	*Sheeta* (cold)	*Katu* (pungent)	*Kapha Vata Dosha*	*Gulma* (abdominal lumps/tumors), *Pleeha-Yakridvridhi* (splenomegaly-hepatomegaly), *Kapha Jvara* (*Kapha Dosha* predominant fever)
Shatavari (*Asparagus racemosus*)[117]	*Madhura* (sweet), *Tikta* (bitter)	*Guru* (heavy), *Snigdha* (oily)	*Sheeta* (cold)	*Madhura* (sweet)	*Vata Pitta Shamaka*	*Medhya* (improves intelligence), *Gulma* (abdominal lumps/tumors), *Balya* (promotes immunity and body strength) *Shukra Stanyakar* (improves semen and breast milk production), *Atisara* (diarrhea),
Jhandu, Genda (*Tagetes erecta*)[118]	*Tikta* (bitter), *Kashaya* (astringent)	*Laghu* (light) *Ruksha* (dry)	*Sheeta* (cold)	*Katu* (pungent)	*Kapha Vata Dosha*	*Rakta Sangrahika* (stops bleeding), *Rakta Pitta Vikara* (cures bleeding disorders)
Amalaki (*Emblica officinalis*)[119]	Pancha rasa contains all tastes except *Amla* (sour)	*Guru* (heavy), *Ruksha* (dry), *Sheeta* (cold)	*Sheeta* (cold)	*Madhura* (sweet)	Pacifies all *Doshas* especially *Pitta*	*Rakta Pitta Pramehagna* (used in bleeding disorders, diabetes and urinary disorders), *Vrishya* (aphrodisiac), *Rasayana* (rejuvenative)

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Table 4: Contd...

Name of drug with Latin name	Properties as per Ayurveda				Pacification action on *Doshas*	Mode of action and indications
	Rasa (taste)	*Guna* (properties)	*Virya* (potency)	*Vipaka* (properties after digestion in the body)		
Kasani (*Cichorium intybus*)[120]	*Tikta* (bitter)	*Laghu* (light) *Ruksha* (dry)	*Ushna* (hot)	*Katu* (pungent)	*Kapha Pitta Dosha*	*Yakrit Vikara* (liver disorders), *Hridya roga* (cardiac disorders) and *Mutrakricha* (difficulty in micturition)
Kaarvellaka (*Karela*)/ (*Momordica charantia*)[121]	*Tikta* (bitter), *Katu* (pungent)	*Laghu* (light) *Ruksha* (dry)	*Ushna* (hot)	*Katu* (pungent)	*Kapha Pitta Dosha*	*Deepana* (improves digestion power), *Pandu* (anemia), *Shwasa Kasa* (respiratory disorders)
Rohitaka (*Tecoma undulata*)[122] (*Amoora Rohitaka*)	*Katu* (pungent), *Tikta* (bitter), *Kashaya* (astringent)	*Laghu* (light), *Ruksha* (dry)	*Sheeta* (cold)	*Katu* (pungent)	*Kapha Pitta Dosha*	*Plihaghati* (used in splenomegaly), *Rakta prasadana* (blood purifier)
Aamra (*MAgnifera indica Linn*., *Mango*)[123]	*Kashaya* (pungent)	*Laghu* (light), *Ruksha* (dry)	*Sheeta* (cold)	*Katu* (pungent)	*Kapha Pitta Shamaka*	*Aisaar* (diarrhea), *Asrikdara* (leucorhea)
Nimaba (*Azadirachta indica*)[124]	*Tikta* (bitter), *Kashaya* (astringent)	*Laghu* (light)	*Sheeta* (cold)	*Katu* (pungent)	*Kapha Pitta Shamaka*	*Kandu kotha Vrana* (skin diseases), *Krimighna* (destroys worms)
Kalajaaji (*Kalaunji*)/ (*Nigella sativa*)[125]	*Katu* (pungent), *Tikta* (bitter),	*Laghu* (light) *Ruksha* (dry), *Teekshana* (penetrating)	*Ushna* (hot)	*Katu* (pungent)	*Kapha Vata Shamaka*	*Deepana pachana* (improves digestion power), *Medhya* (improves intelligence), *Garbhashya Vishudhi Krita* (cleanses reproductive system of female)
Tulasi (*Ocimum sanctum*)[126]	*Katu* (pungent), *Tikta* (bitter)	*Laghu* (light) *Ruksha* (dry)	*Ushna* (hot)	*Katu* (pungent)	*Kapha Vata Shamaka*	*Krimighna* (worms), *Ruchikrada* (improves appetite)
Nagakesar (*Mesua Ferrea*)[127]	*Kashaya* astringent), *Tikta* (bitter)	*Laghu* (light) *Ruksha* (dry)	*Ishat Ushna* (slightly hot)	*Katu* (pungent)	*Kapha Pitta Shamaka*	*Aam pachana* (digest the toxicated indigested food)
Shallaki (*Boswellia serrata*)[128]	*Kashaya* (pungent), *Tikta* (bitter), *Madhura* (sweet)	*Laghu* (light) *Ruksha* (dry)	*Ushna* (hot)	*Katu* (pungent)	*Kapha Vata Shamaka*	*Atisara* (diarrhea), *Rakta Pitta* (bleeding disorders),
Dhatura (*Datura metel*)[129]	*Tikta* (bitter), *Katu* (pungent)	*Laghu* (light), *Ruksha* (dry), Vyavaayi (permeates in all over the body before getting digested) Vikaasi (decreases ojas and causes laxity of body tissues)	*Ushna* (hot)	*Katu* (pungent)	*Kapha Vata Shamaka*	*Vrana* (wound healing), *Twaka Dosha* (skin disorder) *Vishaghna* (clears toxins) Useful in Shwasa (dyspnea)
Anantamoola (*Hemidesmus indicus*)[130]	*Madhura* (sweet), *Tikta* (bitter)	*Guru* (heavy), *Snigdha* (oily)	*Sheeta* (cold)	*Madhura* (sweet)	All three *Dosha*	*Rasayana* (rejuvenates body tissues) *Vishaghna* (clears toxins) *Kushthaghna* (clears skin diseases)

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Table 4: Contd...

Name of drug with Latin name	Properties as per Ayurveda				Pacification action on *Doshas*	Mode of action and indications
	Rasa (taste)	*Guna* (properties)	*Virya* (potency)	*Vipaka* (properties after digestion in the body)		
						Rakta Shodhaka (purifies blood)
						Mutra virajneeya (clears urine)
Rudanti (*Capparis moonii Wight*)[131,132]	*Kashaya* (pungent), *Tikta* (bitter)	*Laghu* (light), *Teekshana* (penetrating)	*Ushna* (hot)	*Katu* (pungent)	*Tridoshara* (pacifies all *Doshas*)	*Rasayana* (rejuvenates body)
						Shoshaghni (useful in emaciation), *Prameha* (diabetes),
						Rajyakshama (tuberculosis)
Jambira (*Citrus limon, Nimbu*)[133]	*Amla* (sour)	*Guru* (heavy), *Teekshana* (penetrating)	*Sheet* (cold)	*Amla* (sour)	Pacifies *Kapha Vata*, aggravates *Pitta*	*Hridya* (cardiac tonic), *Deepana - Pachana* (helps in digestion), *Pitta Vardhaka* and *Saraka* (increases *Pitta* and removes excess *Pitta*)
Guggulu (*Commiphora mukul*)[134]	*Tikta* (bitter), *Katu* (pungent)	*Laghu* (light), *Ruksha* (dry), *Teekshana* (penetrating), *Vishada* (clearness), *Sukshma* (fineness), *Sara* (mobility)	*Ushna* (hot)	*Katu* (pungent)	*Tridoshara* (pacifies all the *Doshas*)	*Shothahara* (removes edema and inflammation), useful in *Granthi* (cyst), *Jantughna* (kills microbes)
						Rakta Prasadaka (purifies blood)
						Vrishya (aphrodisiac), *Rasayana* (rejuvenates the body)

acts on fever, anemia,[139] dyspnea, spleenomegaly, skin diseases, body strengthening, *Rasayana* (rejuvenative), etc.[140] *Manhshila* (As_4S_4, realgar) is described as *lekhana* (scraping agent, removing excess tissues)[141] and *Rasayana* (rejuvenative), acting on cough, dyspnea, fevers, itching, anemia, and other such diseases.[142] These indications and properties make both these drugs a choice agent for leukemia management from Ayurveda perspective also, as it is resolving most of its symptom pathology. However, as per the Ayurveda, there are certain indications of diet and behavior which are to be followed while using these drugs.[139]

These two drugs, i.e., *Somal* (ATO) and *Manahshila* (As_4S_4, realgar), are now very widely being studied for their potent anticancerous effects in patients of APL, by the scientists of conventional medical science demonstrating their efficacy and safety.[143]

Many other compound drugs are described in Ayurveda texts for their potential usage in *Arbuda* (tumors) such as *Hargauri rasa*, *Nityanand rasa*, *Raudra rasa*, and *Vriddhadaru churna*,[144] but clinical studies are yet lacking for the same.

Hence, many drugs have been evaluated and documented to be effective in experimental studies, but their translation into a potential drug has been achieved only in a limited manner for some drugs as vincristine, vinblastine from *Sadanpushpa* (*Vinca rosea*), and arsenic compounds. It is also evident from the clinical and experimental studies documented above that both of the groups are reflecting very different approaches. Each drug in *Ayurveda* is described with a diverse number of properties, targets, and actions, which is very different from the conventional system approach where reductionist approach is applied with one molecule and one target. Since a drug has numerous phytoconstituent molecules in it, they demonstrate diversified action on several body systems and they also exhibit antagonistic properties to some of their own molecules, resulting in the reduction or nullification of side effects when used judiciously, with proper indications. In most of the experimental studies, the extracts of plants are taken and studied *in vivo* or *in vitro* to observe their results. However, the behavior observed experimentally at bench side will translate equivalently in to clinical results at bedside is not assured, though they definitely

form a first level of evidence for their efficacy against leukemia. The above-documented researches definitely present some evidence for the efficacy of Ayurveda drugs and treatment in leukemia, but the body of evidence is very small. Large sample size-based randomized controlled clinical trials are definitely, yet lacking for generating gold standard scientific evidence for the same. The authors propose to adopt the methodology adopted by Prakash *et al*. using integrated approach in conduction of future studies. This would help in effective management of all stages of patients under the domain experts and could hasten the recovery rates of the patients.

Besides being used as a main therapy for the management of leukemia cases, Ayurveda drugs can also be adopted as an adjuvant drug in the patients of leukemia placed on conventional treatment for chemotherapy or radiotherapy. Several studies have documented the beneficial effect of Ayurveda drugs in the reduction of side effects of radiotherapy, chemotherapy, and hastened recovery of the patients. Resveratrol (from grapes, *Draksha*) is reported as a potent chemoprotective and synergistic agent in cancer chemotherapy.[145] *Tulsi* (Holy basil) is proven through experimental, preclinical, and clinical studies as an effective radioprotective agent.[146] Similarly, *Triphala* (a combination of *E. officinalis*, *T. chebula*, and *T. belerica*),[147] Guduchi (*T. cordifolia*)[148,149] has been documented in studies to have radioprotective and/or chemoprotective effects. These drugs may also be assessed for their efficacy as a radio or chemopreventive agent in the treatment of leukemia patients placed on conventional therapy.

Conclusion and Way Forward

Significant numbers of leukemia patients in India try various systems of complementary and alternative medicine. The present study indicates that Ayurvedic medicines were effective in the treatment of major types of leukemia such as AML, APL, and CLL and did not produce any toxic side effects. An Ayurvedic approach like the one given here can be of some help to patients with relapses and nonresponsive to conventional leukemia treatment. The relapse observed in the patients even after undergoing the best of conventional therapy holds limited options for the patients. Integrated approach as documented by Prakash can be adopted to document the efficacy of Ayurveda drugs in these patients. The experimental studies conducted for leukemia will help in identifying and developing novel molecules against leukemia on the principles of conventional medical science, but that particular approach will be of any help to Ayurveda is questionable. However, randomized controlled trials with the Ayurveda approach in a larger sample size are needed to prove the safety and efficacy of Ayurveda drugs with more reliable evidence. Further, the efficacy of Ayurvedic drugs may also be assessed for their efficacy as a radio or chemopreventive agent in the treatment of leukemia patients placed on conventional therapy.

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Conflicts of interest

There are no conflicts of interest.

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