International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE	STEROIDAL ALKALOIDS FROM SOLANACEAE SPECIES IN HEMATOLOGICAL MALIGNANCIES: MECHANISMS AND THERAPEUTIC POTENTIAL
DOI	https://doi.org/10.31435/ijitss.2(50).2026.5084
RECEIVED	02 February 2026
ACCEPTED	22 May 2026
PUBLISHED	30 May 2026
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

STEROIDAL ALKALOIDS FROM SOLANACEAE SPECIES IN HEMATOLOGICAL MALIGNANCIES: MECHANISMS AND THERAPEUTIC POTENTIAL

Alicja Szymczak *(Corresponding Author, Email: alicja.szymczak2.0@gmail.com)*
HCP Medical Center in Poznań, Poland
ORCID ID: 0009-0005-6640-1987

Anna Jaworowicz
MSWiA Hospital in Poznań, Poland
ORCID ID: 0009-0009-2915-5501

Joanna Piasecka
HCP Medical Center in Poznań, Poland
ORCID ID: 0009-0006-3042-6805

Bartosz Gołembiewski
MSWiA Hospital in Poznań, Poland
ORCID ID: 0009-0001-7008-2430

Grzegorz Mulski
University Hospital in Poznań, Poland
ORCID ID: 0009-0003-0026-0785

Martyna Manicka
HCP Medical Center in Poznań, Poland
ORCID ID: 0009-0000-6604-7926

Michał Baranowicz
Poznań University of Medical Sciences, Poland
ORCID ID: 0009-0008-6789-5917

Weronika Mazurkiewicz
MSWiA Hospital in Poznań, Poland
ORCID ID: 0009-0000-6241-993X

Zuzanna Borecka
Regional Hospital in Poznań, Poland
ORCID ID: 0009-0003-6846-1030

Agnieszka Marta Sobczak
University Hospital in Poznań, Poland
ORCID ID: 0009-0000-5159-6228

ABSTRACT

Background: Hematological malignancies remain a substantial contributor to global cancer morbidity and mortality, and as such – a major public health issue. Recent evidence has revealed that Solanaceae alkaloids (SAs) could contribute to developing new treatment strategies in hematological oncology.
Objective: To critically evaluate contemporary evidence on the anti-cancer effects of SAs, including alpha-solanine, solanidine, solasodine, solamargine, tomatine and tomatidine as well as their potential applicability as bioactive compounds in hematology-related research and therapy.
Methods: This narrative review was informed by studies retrieved from widely recognized search engines and databases, including PubMed/MedLine, Google Scholar, ScienceDirect, Wiley, Scopus and Springer Link. The search was conducted using the following MeSH terms: “Solanaceae Alkaloids”, “Solanine”, “Solanidine”, “Solasodine”, “Solamargine”, “Tomatine”, “Tomatidine”, “Leukemia”, “Lymphoma”, “Hematology” and "Blood cancer". Original English-language studies published between 2005 and 2025 were included. Case reports and non-primary data sources were excluded. No meta-analysis was performed.
Results: Steroidal alkaloids from Solanaceae species demonstrate significant cytotoxic and anti-proliferative effects against various leukemia and lymphoma cell lines. These compounds have the capacity to inhibit tumor growth and survival through multiple mechanisms, including the induction of apoptosis, oncosis, and cell cycle arrest.
Conclusions: Solanaceae-derived steroidal alkaloids exhibit promising antitumor activity in hematological malignancies by modulating apoptosis, survival signaling pathways, and mechanisms of drug resistance. Their ability to enhance chemosensitivity supports further investigation as potential therapeutic or adjuvant agents, pending validation in in vivo and clinical studies.

KEYWORDS

Glycoalkaloids (GAS), Steroidal Alkaloids, Solanine, Leukemia, Hematological Oncology, Multidrug Resistance (MDR)

CITATION

Alicja Szymczak, Anna Jaworowicz, Joanna Piasecka, Bartosz Gołembiewski, Grzegorz Mulski, Martyna Manicka, Michał Baranowicz, Weronika Mazurkiewicz, Zuzanna Borecka, Agnieszka Marta Sobczak. (2026) Steroidal Alkaloids from Solanaceae Species in Hematological Malignancies: Mechanisms and Therapeutic Potential. *International Journal of Innovative Technologies in Social Science*. 2(50). doi: 10.31435/ijitss.2(50).2026.5084

Introduction

Hematological malignancies encompass a broad and diverse group of neoplasms arising from the blood-forming and lymphoid tissues, including leukemias, lymphomas, and plasma cell dyscrasias. Incidence rates of these disorders vary greatly by age, gender, and geographical region. Nonetheless they represent a major global health burden, accounting for a substantial proportion of cancer-related morbidity and mortality amongst both children and adults (Pan et al, 2021; Zhang et al, 2023).

Despite significant advances in chemotherapy, targeted therapies and hematopoietic stem cell transplantation, many patients still face treatment failure. This being the case, we find ourselves in an ongoing pursuit of novel agents capable of selectively targeting malignant hematopoietic cells while sparing normal counterparts.

Tackling this conundrum, researchers have turned their interest towards traditional medicine, which has recognized the value of plants and their active agents for centuries. Several widely used compounds derived from plants – such as vinca alkaloids, taxanes, camptothecin derivatives and homoharringtonine – have established precedents for phytochemical-based therapies in hematology and oncology. Recent studies have explored the potential of underexamined bioactives, such as alkaloids, glycosides, and lignans, which serve as plant’s natural protection against animals, insects, bacteria and fungi (Friedman, 2006).

An abundant yet inconspicuous source of said phytoalexins are the members of the *Solanaceae* family, of which potatoes, tomatoes and eggplants are the most prominent and commonly known representatives. They have been a staple source of energy for people all over the world for centuries, however it is not their nutritional

value that has struck scholars' attention, but the biologically active secondary metabolites, especially steroidal alkaloids and glycoalkaloids. There has been a growing interest in their anti-inflammatory, antimicrobial, anti-pyretic, and antinociceptive effects (Zhao et al, 2018, 2021; Wang et al, 2023). Those qualities indicate potential applicability of *Solanaceae* steroidal alkaloids (SAs) in multiple diseases, like osteoarthritis (Zhou et al, 2024; Li et al, 2025), pulmonary hypertension (Nie et al, 2017; Cheng et al, 2017), COVID-19 (Teli, Shah & Chhabria, 2021) and malaria (Chen, 2010).

Moreover multiple *in vitro* and *in vivo* studies conducted over the past years showed promising results regarding their cytotoxic activity against many cancer cell lines, including but not limited to hepatocarcinoma (Meng et al, 2016; El-Daly, 2019), breast cancer (Mohsenikia et al, 2016; Li et al, 2021), prostate cancer (Pan et al, 2016; Yang et al, 2019), lung cancer (Zhang et al, 2016; Zou et al, 2022) and various tumors of gastrointestinal tract (Tang et al, 2023; Ma et al, 2024).

In this review, we focused primarily on synthesizing up-to-date knowledge about SAs' antitumor properties regarding hematological malignancies and collected data suggesting their usefulness as adjuvants or lead agents in hematologic cancer therapy. Additionally, we have delved into the mechanism of action of the six compounds with the most substantiated antitumor properties.

Materials and Methods

This narrative (non-meta-analytic) systematic review was conducted as a targeted literature search.

Search Strategy

This study was informed by original papers sourced from PubMed/MedLine, Google Scholar, ScienceDirect, Wiley, Scopus and Springer Link. MeSH terms included in a search query were: "Solanaceae Alkaloids", "Solanine", "Solanidine", "Solasodine", "Solamargine", "Tomatine", "Tomatidine", "Leukemia", "Lymphoma", "Hematology" and "Blood cancer". Boolean operators ("AND", "OR") were used to refine results. Considered were the articles published between the years 2005 and 2025, regarding the influence of SAs on human leukemia and lymphoma cells. Priority was given to peer-reviewed works. Filters were applied for English language. Case reports and secondary data sources, like reviews and meta-analyses, were excluded. The manuscript was prepared with language-editing assistance. As a narrative review, this study does not include formal quality or risk-of-bias scoring or meta-analysis.

Plant alkaloids – structure and biological activity

Plant alkaloids function primarily as phytoalexins, providing plants' natural protection against pathogens and herbivores. When ingested in adequate amounts, they can pose a threat to humans as well, causing excessive perspiration, diarrhea, vomiting, and bronchospasm. Severe poisoning can even lead to death (Singh, 2016).

Structurally, glycoalkaloids are nitrogenous steroidal glycosides, composed of a non-polar aglycone bound to a heterocyclic carbohydrate side chain and a polar water-soluble trisaccharide. Their steroidal nuclei are in fact cholesterol derivatives and confer both lipophilic and amphiphilic properties. This makes SAs capable of interacting with lipid membranes and intracellular signaling molecules, which underlies their diverse biological activities. Solanine and chaconine, which together comprise over 95% of potato glycoalkaloids, contain the same steroidal alkaloid – solanidine – bound to different trisaccharides. The same pattern is reproduced when it comes to eggplant metabolites, for its main active compounds – solasonine and solamargine – are built with solasodine as an aglycone. Tomatine's centerpiece tomatidine has the same skeletal type; both occur naturally in tomatoes (Osman, 1983; Heftmann, Lieber & Bennet, 1967; Mensinga et al, 2005; Milner et al, 2011; Nielsen et al, 2020).

Alkaloid concentrations in those commercially grown cultivars can differ depending on both growing and post-harvest conditions, temperature, sunlight, and other stressors. It also varies in different parts of a singular plant – generally the highest levels of SAs are found in blossoms, foliage and peels, whereas their accumulation in the flesh tends to be several-fold lower. This tendency makes *Solanaceae* family a potentially promising and cost-effective source of desirable phytochemicals, since they could be extracted from the non-edible agricultural residues and through processing by-products, without necessarily downsizing the number of crops collected (Percival, Dixon & Sword, 1994; Hlywka et al, 1994; Lafta & Lorenzen, 2000; Friedman, Roitman & Kozukue, 2003; Mensinga et al, 2005; Kasnak et al, 2018).

While historically SAs have been regarded as antinutritional or toxic compounds, recent studies have discovered their pleiotropic activity against multiple human diseases. Since cancer is still one of the leading

causes of death worldwide, an extensive amount of research has been dedicated specifically to their anti-tumor and cytotoxic properties in hopes of formulating novel approaches towards oncological treatment (WHO *(7 August 2024*); The top 10 causes of death. Retrieved from URL). We narrowed our search to papers regarding SAs' role in hematological malignancies, to find data proving that some of the aforementioned phytochemicals showed bioactivity against leukemia and lymphoma cell lines.

Solanine

Various molecular mechanisms have been described when it comes to solanine's activity against hematological malignancies. We have summarized studies describing those pathways below.

miR-16/Bcl-2 Axis

The miR-16/Bcl-2 axis plays a well-established and biologically significant role in the pathomechanism of several leukemias. miR-16 is a part of the microRNA cluster miR-15a/miR-16-1, which acts as a tumor suppressor crucial for promoting apoptosis and controlling cell-cycle progression. It inhibits various pro-survival genes, such as Bcl-2, Cyclin D1, Mcl-1, and others (Braga et al, 2017; Pekarsky, Balatti & Croce, 2018). The first one is a central anti-apoptotic regulator that prevents mitochondrial outer membrane permeabilization. Physiologically miR-16 binds directly to Bcl-2 mRNA, which reduces its translation, thus decreasing proliferation-promoting properties. Disbalance of those two molecules occurs primarily in chronic lymphocytic leukemia (CLL) and acute myeloblastic leukemia (AML), where gene mutations or epigenetic silencing reduce miR-16. This leads to inhibition of programmed cell death and extended survival of otherwise abnormal or damaged cells (Hanada et al, 1993). Targeted and selective Bcl-2 inhibitors developed recently, like venetoclax or sonrotoclax, have already proven their effectiveness in hematological treatments. For this reason, the pursuit of new agents with the same properties is so promising and desirable.

Zheng, Li, Gao, Niu & Wang (2020) demonstrated that normal NCI-H526 as well as leukemia AML-193 cells were exposed to different concentrations of solanine's solution and cultured for 24 hours. As a result, researchers observed a significant suppression of cell growth and augmented apoptosis in both NCI-H526 and AML-193. A molecular mechanism for that, further confirmed by western blotting and TargetScan analysis, was an increase of miR-16 expression followed by Bcl-2 downregulation. Those effects were dose-dependent and more prominent in leukemia cells, where half maximal inhibitory concentration (IC_{50}) of solanine was 10 μM, compared to 125 μM in normal cells.

Similar observations were made by both Yi et al (2018a) and Huang et al (2023) in models using Jurkat cells derived from T-cell acute lymphoblastic leukemia (ALL) and M2-like TAMs cells, respectively. To assess how various glycoalkaloid concentrations impacted both cell lines, researchers treated them in an analogical manner to that mentioned above. The presented outcome showed a subsided proliferation rate as well as promoted apoptosis. As a molecular mechanism behind that, authors pointed to modulation of mRNA of Bcl-2 and Bax. A decrease in the expression of Bcl-2 and a simultaneous increase in the expression of Bax was proportional to administered dose of solanine.

Solanine shows affinity to those biological pathways in other malignancies as well, for example hepatocarcinoma, where solanine targeted Bcl-2 concentrations (Shiyong, Yubin, Xiang & Chenfeng, 2007). Similarly, in esophageal cancer, it has induced expression of another tumor suppressor, microRNA-138 (Wang et al, 2016).

PI3K/AKT/mTOR Signaling Pathway

PI3K/AKT/mTOR is an indispensable intracellular signaling cascade that determines many vital functions including, but not limited to, growth and survival, cell cycle progression and apoptosis resistance. In malignant clones, PI3K/AKT/mTOR signaling pathway frequently becomes constitutively activated, even without growth factor stimulation. Those alterations entail potentiation of carcinogenesis, enhancing proliferation and prompting Warburg-like metabolic effect, which enables defective cells to endure a hypoxic environment.

The invention of selective PI3K/AKT/mTOR blockers has revolutionized an approach towards refractory and relapsed disease treatment. Pharmaceuticals like idelalisib, copanlisib, umbralisib or duvelisib, targeting multiple PI3K isoforms, are registered for the treatment of CLL, marginal zone lymphoma (MZL) and follicular lymphoma (FL). Ipatasertib, a recently developed experimental drug demonstrating anti-AKT activity, showed clinical efficacy against multiple myeloma (MM). Lastly, a specific inhibitor of mTOR, temsirolimus, is approved by the EU for the treatment of patients with mantle cell lymphoma (MCL). All of

those are highly effective, yet carry serious adverse effects, which is the rationale for the continuous strive for new active agents (Sandhöfer et al, 2015; Darici et al, 2020; Hus, Puła & Robak, 2022; Isa et al, 2022).

Asgaritarghi et al (2023) conducted research evaluating solanine's potency against K562 BCR-ABL1-positive human erythroleukemia cell line as well as the promyelocytic leukemia HL60 cell lines. Given the glycoalkaloids' lipophilic nature and poor water solubility, they implemented a nanocarrier, creating dendrosomal nano solanine (DNS) with enhanced ability to penetrate cell membranes. Additionally, they incorporated imatinib into some of the samples exposed to DNS to examine interaction between the two substances. Their conclusion was that solanine, especially in its encapsulated form, showcased the ability to attenuate the expression of PI3KCA and mTOR, as well as to inactivate AKT protein through dephosphorylation. This led to decreased proliferation and migration but promoted the apoptosis of leukemic cells. Said effects were potentiated by the DNS + imatinib combination, which implies solanine's applicability in approaching drug-resistant cases of chronic myelogenous leukemia (CML).

This molecular mechanism was described in Huang's study as well, where solanine directly modulated p-PI3K and p-AKT levels in exposed cells, thus diminishing their viability and the process of angiogenesis (Huang et al, 2023).

MRP1 and multidrug resistance

MRP1 plays a crucial role in the prevalence of multidrug resistance (MDR), particularly in chronic and acute myeloid leukemia (AML). Also known as ABCC1, it is a member of the ATP-binding cassette (ABC) transporter family and functions as a transmembrane efflux pump extruding chemotherapeutics from the inside of leukemic cells. Its overexpression grants the neoplasm chemoresistance, making it unsensitive to many front-line cytotoxic drugs. This situation is generally associated with a higher risk of primary treatment failure, relapse, and an overall poor prognosis (van der Kolk, Vellenga, Müller & de Vries, 1999; Kunadt et al, 2020).

To address this matter, a few groups of researchers investigated solanine's influence on K562/ADR cells, a CML-derived subline resistant to Adriamycin (ADR; doxorubicin), in an *in vitro* model. Their attempt to re-sensitize leukemic cells to ADR by glycoalkaloid exposure proved its ability to reverse multidrug resistance in a dose-dependent manner. Further evaluation of an underlying mechanism revealed increased intracellular accumulation of doxorubicin in a solanine-augmented environment, which led to boosted cytotoxicity. On a molecular level, researchers discovered a decrease in MRP1 and p-JNK expression, resulting in attenuated expelling abilities of treated cells (Zhu, Jia, Yi, & Li, 2017; Yi et al, 2018b).

Consistent conclusions were drawn concerning Jurkat cells cultivated in a combination of aforementioned substances. Likewise, enhanced chemosensitivity to ADR was observed due to solanine addition, although the mechanism behind that was not specifically analyzed. Either way, the foregoing results present solanine as a potential supplement, synergistic to standard chemotherapy (Yi et al, 2018a).

Solanidine

Next molecule worth mentioning is the aglycone portion of solanine, solanidine, also derived from potatoes. Even more so than the native steroid, solanidine's synthetic analogs have been investigated as potential anticancer drugs. We have found two papers relevant to their applicability in hematological oncology.

MDR-reversal

The objective of a study designed by Minorics et al (2014) was to delve into the intrinsic activities of solanidine's analogs with the focus on their ability to attenuate drug resistance in neoplasm cells. It was performed with the use of T-cell lymphoma line obtained from mice and transfected by a human MDR1 gene. Similarly to the ABCC1 mentioned above, the MDR1 or ABCB1 gene encodes another member of ABC transporters, known as P-glycoprotein 1 (P-gp). This protein is associated with reduced drug accumulation inside targeted cells and has a well-established role in limiting treatment options for multiple malignancies (van der Kolk et al, 1999). Some of the solanidine-derivates developed by the scientists have displayed the ability to reverse MDR through the downregulating the expression of said genes, thus decreasing the amount of active transmembrane efflux pumps. Additionally, one of the agents potentiated the antiproliferative properties of ADR despite the lack of its own cytostatic function.

Antiproliferative and antioxidative action

In the same study, researchers have discovered that some of the investigated analogs exert the capability to inhibit cells' proliferation. DNA transcription and replication were suppressed by virtue of interference with topoisomerase I, a key enzyme in cell cycle progression. Furthermore, one compound modulated the expression of tumor necrosis factor alpha (TNF-α), growth arrest and DNA-damage-inducible protein 45 alpha (GADD45α), and S-phase kinase-associated protein 2 (SKP2) genes. As a result of those interactions, a decline in cells' growth and viability were observed.

A few years later another paper was published by a group of scholars from rom University of Szeged and its results confirmed the earlier conclusions. This time, however, HL60 human promyelocytic leukemia cells were subjected to the study. The most potent amongst all analyzed solanidine analogs, 4-methoxyphenylepyrazoline, exhibited the inhibitory effect on ribonucleotide reductase, thus restricting DNA synthesis inside the cells. Following necrosis and apoptosis occurred in a manner that was a function of administered dose. It was also effective in eliminating free radicals, which cause significant damage to the genetic material of the cell and can even trigger the process of carcinogenesis. This duality of cytotoxic and antioxidative features makes solanidine derivatives worthy of further investigation (Zupkó et al, 2014).

Solamargine

Moving forward to phytochemicals obtained from eggplants, solamargine is noteworthy for its multimodal antitumor properties. Hereinafter, we present a concise report on up-to-date scientific findings relevant to the topic of this review.

Oncosis

The objective of two assays performed by Sun et al was to determine the mechanisms and media behind solamargine's cytotoxic activity. K62 cells as well as their MDR-expressing subline (K562/A02) were subjected to the first study. Their exposition to the investigated constituent prompted an abrupt death of both types of cells. The expression of the P-gp in the drug-resistant K562/A02 lines did not seem to alter this outcome significantly, meaning that efflux pumps were inefficient in granting cells protection against solamargine. Researchers described a drastic ATP depletion, together with disruption in plasma membrane and organelles' swelling as main killing mechanisms, which lead to a conclusion that this cytotoxic effect is mediated through oncosis rather than cell-cycle arrest (Sun et al 2011).

Apoptosis

The array of the second study was slightly altered, and this time a different mechanism was recognized to take place – the lysosomal membrane permeabilization caused a release of cathepsin B to cytosol, thus initiating apoptosis. Disruption of mitochondria followed by a spike in intracellular Ca^{2+} levels was also reported. Those events were accompanied by an increase in caspase-3 and caspase-9 activity and previously mentioned down-regulation of Bcl-2 and up-regulation of Bax proteins (Sun et al 2010).

Presumably, whether cell death occurs via orderly or uncontrolled manner depends on the concentration of solamargine used, with apoptosis predominating at lower, and oncosis – at higher doses. Their simultaneous co-occurrence emerged at intermediate levels, indicating that those pathways are not necessarily mutually exclusive. Undoubtedly more research is needed to elucidate this conundrum.

Solasonine

Another active ingredient sourced from *Solanaceae* species, found in abundance in eggplants, is solasonine. There have been reports of its substantial antitumor activity against multiple cancers, although the evidence regarding hematological neoplasms has been scarce. Zhang et al (2021) tackled this topic and discovered a fascinating mechanism through which this molecule impacts AML cell lines, especially AML-M5, THP-1, and MV4-11 subtypes. The hallmark of this interaction is the activation of the AMPK/FOXO3A pathway. The specific role of this axis in pathogenesis of leukemia is yet to be determined. Based on the analogy to other cell lines, it is speculated that AMPK (AMP-activated protein kinase) functions as a cellular energy sensor, which can subsequently induce FOXO3A (Forkhead box O3A). This can lead to declined cell growth and escalated autophagy and apoptosis rates (Chiacchiera & Simone, 2010). In the discussed study, an *in vitro* exposure to solasonine resulted in anti-proliferative, pro-apoptotic, and cell cycle arrest effects. To see if corresponding results would be yielded *in vivo*, scientists duplicated their experiment using mouse and zebrafish xenograft models. Yet again, tumor suppression via the activation of the AMPK/FOXO3A axis was observed. Moreover, in this array, solasodine revealed its additional anti-metastatic properties, which makes it a promising antineoplastic agent.

Tomatine

With an objective to explore its antitumor properties, Huang et al (2015) exposed HL60 acute promyelocytic leukemia cells to different concentrations of tomatine, both *in vitro* and *in vivo*. Stimulated response was a time- and dose-dependent growth inhibition, resulting in a ~98% reduction in cell survival rate. Moreover, tomatine has been reported to encourage apoptosis. Those properties, however, were impaired by enriching the environment with free cholesterol, indicating that tomatine's activity may be modulated by interaction with the lipids comprising cell membrane. Additionally, said outcomes were juxtaposed with the efficacy of cytosine arabinoside (Ara-C), an essential chemotherapy medication in the treatment of AML, CML, and NHL. As it turned out, antiproliferative effects exerted by tomatine were more pronounced than those of Ara-C.

Another study performed by Chao et al (2012) on HL60 and K562 cells discovered that the discussed compound suppressed growth and promoted apoptosis in both exposed sublines. Caspase-3 was not activated in the process, suggesting that those changes were initiated through cell cycle- and caspase-independent manner. Instead, the group noticed an enhanced transcription of Bak and Mcl-1 short form (Mcl-1s) combined with a direct activation of permeability transition pore (PTP) complex, resulting in a loss of the mitochondrial membrane potential. Such perturbation triggered a translocation of the apoptosis-inducing factor (AIF) into cytoplasm and nucleus, leading to down-regulated expression of survivin, a protein associated with uncontrolled division of leukemic cells, and preventing apoptosis. Described findings were later confirmed in an *in vivo* experiment, where the reduction of HL60 xenograft tumor mass emerged in examined mice.

Conclusions from presented studies evince the complexity of tomatine's cytotoxic functions and emphasize the need for further research aimed at revealing its mechanisms of action.

Tomatidine

The last alkaloid we are going to discuss is tomatidine. Similarly to the rest of the molecules mentioned, it displays a range of desirable activities and has been evaluated as a potential plant-derived pharmaceutical.

In a recently published paper, Ayvaz et al (2024) explored tomatidine's applicability as an addition to standard chemotherapy. AML cells were cultivated in low-dose cisplatin solution combined with different concentrations of tomatidine. As a result, they described synergistic anti-proliferative and pro-apoptotic effects of both agents. A slight decrease in the levels of caspase-3 was detected, yet the expression of cleaved PARP (Poly-ADP-ribose polymerase) was enhanced, which aligns with the observed outcomes and confirms execution of apoptosis. Those observations prove this kind of polytherapy to be potentially beneficial, lessening the toxicity of conventional cytostatic treatment.

Discussion

This review summarizes current evidence indicating that steroidal alkaloids derived from Solanaceae plants consistently exerted antiproliferative, pro-apoptotic, and cytotoxic activity against leukemia and lymphoma cells across multiple experimental models.

Notably, rather than acting through a single molecular target, Solanaceae alkaloids simultaneously modulate key mechanisms involved in hematologic oncogenesis, including apoptotic regulation (e.g., the miR-16/Bcl-2 axis), PI3K/AKT/mTOR signaling, mitochondrial and lysosomal integrity, cellular metabolism, and multidrug resistance mediated by ABC transporters. This multimodal activity is particularly relevant in hematological malignancies, where pathway redundancy and resistance to targeted therapies often limit long-term treatment success. Several compounds reviewed here also show potential clinical relevance as adjuncts to standard therapy.

Importantly, some studies reported preferential toxicity toward malignant cells compared with non-malignant counterparts, although this observation remains largely based on *in vitro* data. Significant challenges – including poor aqueous solubility, narrow therapeutic windows, observed systemic toxicity, and incomplete pharmacokinetic and pharmacodynamic characterization – must be addressed before clinical translation can be considered. Advances in drug delivery systems, such as nanoformulations, as well as rational structural modification of alkaloid scaffolds, may help mitigate these limitations and improve bioavailability and safety profiles.

Despite promising preclinical findings, the current evidence base is dominated by cell line and animal studies, with a lack of standardized toxicity assessments and no available clinical trial data in hematological malignancies. As such, conclusions regarding clinical efficacy must remain cautious.

Conclusions

Accumulating preclinical evidence indicates that steroidal alkaloids and glycoalkaloids derived from the Solanaceae family represent a diverse group of biologically active compounds with promising antitumor potential in hematological malignancies. As summarized in this review, alpha-solanine, solanidine and its synthetic derivatives, solamargine, solasonine, tomatine, and tomatidine exert cytotoxic, antiproliferative, and pro-apoptotic effects across a variety of leukemia and lymphoma models through multiple, often complementary, molecular pathways.

These phytochemicals have been shown to modulate key signaling axes implicated in hematologic oncogenesis and therapy resistance, including the miR-16/Bcl-2 axis, PI3K/AKT/mTOR signaling, AMPK/FOXO3A activation, mitochondrial dysfunction, lysosomal membrane permeabilization, and ABC transporter–mediated multidrug resistance. Moreover, several studies demonstrate preferential toxicity toward malignant cells, reversal of chemoresistance, and synergistic interactions with standard cytostatics such as doxorubicin, imatinib, and cisplatin. Such findings highlight the potential of Solanaceae alkaloids not only as direct antineoplastic agents but also as adjuvants capable of enhancing the efficacy of existing therapies and overcoming treatment resistance.

In conclusion, Solanaceae-derived steroidal alkaloids constitute a compelling and underexplored class of bioactive compounds in hematological oncology. Their applicability as therapeutic agents is even more compelling if we consider the fact that they could potentially be sourced from materials regarded as waste and by-products of food production, such as blossoms, foliage and peels of widely cultivated crops. Further well-designed *in vivo* studies, toxicological assessments, and ultimately clinical investigations are warranted to clarify their therapeutic potential and define their role in future treatment strategies for hematological malignancies.

Conflicts of Interest: No conflicts of interest to declare.

REFERENCES

1. Asgaritarghi, G., Farsani, S. S. M., Sadeghizadeh, D., Najafi, F., & Sadeghizadeh, M. (2023). Anti-cancer role of dendrosomal nano solanine in chronic myelogenous leukemia cell line through attenuation of PI3K/AKT/mTOR signaling pathway and inhibition of hTERT expression. *Current Molecular Pharmacology, 16*(5), 592–608. https://doi.org/10.2174/1874467215666220516143155
2. Ayvaz, H. B., Yenigül, M., & Gencer Akçok, E. B. (2024). Tomatidine, a steroidal alkaloid, synergizes with cisplatin to inhibit cell viability and induce cell death selectively on FLT3-ITD+ acute myeloid leukemia cells. *Cell Biochemistry and Biophysics, 82*(3), 2889–2900. https://doi.org/10.1007/s12013-024-01406-6
3. Braga, T. V., Evangelista, F. C. G., Gomes, L. C., Araújo, S. S. D. S., Carvalho, M. D. G., & Sabino, A. P. (2017). Evaluation of MiR-15a and MiR-16-1 as prognostic biomarkers in chronic lymphocytic leukemia. *Biomedicine & Pharmacotherapy, 92*, 864–869. https://doi.org/10.1016/j.biopha.2017.05.144
4. Chao, M. W., Chen, C. H., Chang, Y. L., Teng, C. M., & Pan, S. L. (2012). α-Tomatine-mediated anti-cancer activity in vitro and in vivo through cell cycle- and caspase-independent pathways. *PLOS ONE, 7*(9), e44093. https://doi.org/10.1371/journal.pone.0044093
5. Chen, Y., Li, S., Sun, F., Han, H., Zhang, X., Fan, Y., & Zhou, Y. (2010). In vivo antimalarial activities of glycoalkaloids isolated from Solanaceae plants. *Pharmaceutical Biology, 48*(9), 1018–1024. https://doi.org/10.3109/13880200903440211
6. Cheng, X., Narisawa, M., Jin, E., & Li, X. (2017). α-Solanine as potential therapeutic target in pulmonary artery hypertension. *Journal of Hypertension, 35*(12), 2377–2379. https://doi.org/10.1097/HJH.0000000000001483
7. Chiacchiera, F., & Simone, C. (2010). The AMPK-FoxO3A axis as a target for cancer treatment. *Cell Cycle, 9*(6), 1091–1096. https://doi.org/10.4161/cc.9.6.11035
8. Darici, S., Alkhaldi, H., Horne, G., Jørgensen, H. G., Marmiroli, S., & Huang, X. (2020). Targeting PI3K/Akt/mTOR in AML: Rationale and clinical evidence. *Journal of Clinical Medicine, 9*(9), 2934. https://doi.org/10.3390/jcm9092934
9. El-Daly, S. M., Gouhar, S. A., Gamal-Eldeen, A. M., Abdel Hamid, F. F., Ashour, M. N., & Hassan, N. S. (2019). Synergistic effect of α-solanine and cisplatin induces apoptosis and enhances cell cycle arrest in human hepatocellular carcinoma cells. *Anti-Cancer Agents in Medicinal Chemistry, 19*(18), 2197–2210. https://doi.org/10.2174/1871520619666190930123520
10. Friedman, M. (2006). Potato glycoalkaloids and metabolites: Roles in the plant and in the diet. *Journal of Agricultural and Food Chemistry, 54*(23), 8655–8681. https://doi.org/10.1021/jf061471t

11. Friedman, M., Roitman, J. N., & Kozukue, N. (2003). Glycoalkaloid and calystegine contents of eight potato cultivars. *Journal of Agricultural and Food Chemistry, 51*(10), 2964–2973. https://doi.org/10.1021/jf021146f
12. Hanada, M., Delia, D., Aiello, A., Stadtmauer, E., & Reed, J. C. (1993). bcl-2 gene hypomethylation and high-level expression in B-cell chronic lymphocytic leukemia. *Blood, 82*(6), 1820–1828.
13. Heftmann, E., Lieber, E. R., & Bennet, R. D. (1967). *Phytochemistry, 6*, 225.
14. Hlywka, J. J., Stephenson, G. R., Sears, M. K., & Yada, R. Y. (1994). Effects of insect damage on glycoalkaloid content in potatoes. *Journal of Agricultural and Food Chemistry, 42*, 2545–2550. https://doi.org/10.1021/jf00047a032
15. Huang, H., Chen, S., Van Doren, J., Li, D., Farichon, C., He, Y., Zhang, Q., Zhang, K., Conney, A. H., Goodin, S., Du, Z., & Zheng, X. (2015). α-Tomatine inhibits growth and induces apoptosis in HL-60 human myeloid leukemia cells. *Molecular Medicine Reports, 11*(6), 4573–4578. https://doi.org/10.3892/mmr.2015.3238
16. Huang, J., Wang, X., Pan, L., et al. (2023). α-Solanine affects the apoptosis and angiogenesis of M2-like TAMs cells by regulating the PI3K/AKT/mTOR signaling pathway under hypoxia. *Natural Product Communications, 18*(7). https://doi.org/10.1177/1934578X231186273
17. Hus, I., Puła, B., & Robak, T. (2022). PI3K inhibitors for the treatment of chronic lymphocytic leukemia: Current status and future perspectives. *Cancers, 14*(6), 1571. https://doi.org/10.3390/cancers14061571
18. Isa, R., Horinaka, M., Tsukamoto, T., Mizuhara, K., Fujibayashi, Y., Taminishi-Katsuragawa, Y., Okamoto, H., Yasuda, S., Kawaji-Kanayama, Y., Matsumura-Kimoto, Y., Mizutani, S., Shimura, Y., Taniwaki, M., Sakai, T., & Kuroda, J. (2022). The rationale for the dual-targeting therapy for RSK2 and AKT in multiple myeloma. *International Journal of Molecular Sciences, 23*(6), 2919. https://doi.org/10.3390/ijms23062919
19. Kasnak, C., & Artik, N. (2018). Change in some glycoalkaloids of potato under different storage regimes. *Potato Research, 61*, 183–193. https://doi.org/10.1007/s11540-018-9367-2
20. Kunadt, D., Dransfeld, C., Dill, C., Schmiedgen, M., Kramer, M., Altmann, H., Röllig, C., Bornhäuser, M., Mahlknecht, U., Schaich, M., & Stölzel, F. (2020). Multidrug-related protein 1 (MRP1) polymorphisms rs129081, rs212090, and rs212091 predict survival in normal karyotype acute myeloid leukemia. *Annals of Hematology, 99*(9), 2173–2180. https://doi.org/10.1007/s00277-020-04163-7
21. Lafta, A. M., & Lorenzen, J. H. (2000). Influence of high temperature and reduced irradiance on glycoalkaloid levels in potato leaves. *Journal of the American Society for Horticultural Science, 125*, 563–566. https://doi.org/10.21273/JASHS.125.5.563
22. Li, Q. W., Zhang, G. L., Hao, C. X., Ma, Y. F., Sun, X., Zhang, Y., Cao, K. X., Li, B. X., Yang, G. W., & Wang, X. M. (2021). SANT, a novel Chinese herbal monomer combination, decreasing tumor growth and angiogenesis via modulating autophagy in heparanase overexpressed triple-negative breast cancer. *Journal of Ethnopharmacology, 266*, 113430. https://doi.org/10.1016/j.jep.2020.113430
23. Li, W., Liu, Y., Wei, M., Yang, Z., Tang, H., & Huang, W. (2025). Chondrocyte-targeted α-solanine through HIF-1α regulating glycolysis to reduce the ferroptosis of chondrocyte in osteoarthritis. *International Immunopharmacology, 159*, 114841. https://doi.org/10.1016/j.intimp.2025.114841
24. Ma, X., Li, Y., Liang, D., Jiang, F., Zhang, L., Song, W., Wan, B., Xia, C., & Lu, Q. (2024). Solanine induces ferroptosis in colorectal cancer cells through ALOX12B/ADCY4 molecular axis. *Journal of Pharmacy and Pharmacology, 76*(3), 224–235. https://doi.org/10.1093/jpp/rgad122
25. Meng, X. Q., Zhang, W., Zhang, F., Yin, S. Y., Xie, H. Y., Zhou, L., & Zheng, S. S. (2016). Solanine-induced reactive oxygen species inhibit the growth of human hepatocellular carcinoma HepG2 cells. *Oncology Letters, 11*(3), 2145–2151. https://doi.org/10.3892/ol.2016.4167
26. Mensinga, T. T., Sips, A. J., Rompelberg, C. J., van Twillert, K., Meulenbelt, J., van den Top, H. J., & van Egmond, H. P. (2005). Potato glycoalkaloids and adverse effects in humans: An ascending dose study. *Regulatory Toxicology and Pharmacology, 41*(1), 66–72. https://doi.org/10.1016/j.yrtph.2004.09.004
27. Milner, S. E., Brunton, N. P., Jones, P. W., O'Brien, N. M., Collins, S. G., & Maguire, A. R. (2011). Bioactivities of glycoalkaloids and their aglycones from Solanum species. *Journal of Agricultural and Food Chemistry, 59*, 3454–3484. https://doi.org/10.1021/jf200439q
28. Minorics, R., Szekeres, T., Krupitza, G., Saiko, P., Giessrigl, B., Wölfling, J., Frank, E., & Zupkó, I. (2011). Antiproliferative effects of some novel synthetic solanidine analogs on HL-60 human leukemia cells in vitro. *Steroids, 76*(1–2), 156–162. https://doi.org/10.1016/j.steroids.2010.10.006
29. Mohsenikia, M., Farhangi, B., Alizadeh, A. M., Khodayari, H., Khodayari, S., Khori, V., Arjmand Abbassi, Y., Vesovic, M., Soleymani, A., & Najafi, F. (2016). Therapeutic effects of dendrosomal solanine on a metastatic breast tumor. *Life Sciences, 148*, 260–267. https://doi.org/10.1016/j.lfs.2016.02.008
30. Nie, X., Dai, Y., Tan, J., Chen, Y., Qin, G., Mao, W., Zou, J., Chang, Y., Wang, Q., & Chen, J. (2017). α-Solanine reverses pulmonary vascular remodeling and vascular angiogenesis in experimental pulmonary artery hypertension. *Journal of Hypertension, 35*(12), 2419–2435. https://doi.org/10.1097/HJH.0000000000001475
31. Nielsen, S. D., Schmidt, J. M., Kristiansen, G. H., Dalsgaard, T. K., & Larsen, L. B. (2020). Liquid chromatography mass spectrometry quantification of α-solanine, α-chaconine, and solanidine in potato protein isolates. *Foods, 9*(4), 416. https://doi.org/10.3390/foods9040416

32. Osman, S. F. (1983). Glycoalkaloids in potatoes. *Food Chemistry, 11*(4), 235–247. https://doi.org/10.1016/0308-8146(83)90073-0
33. Pan, B., Zhong, W., Deng, Z., Lai, C., Chu, J., Jiao, G., Liu, J., & Zhou, Q. (2016). Inhibition of prostate cancer growth by solanine requires the suppression of cell cycle proteins and the activation of ROS/P38 signaling pathway. *Cancer Medicine, 5*(11), 3214–3222. https://doi.org/10.1002/cam4.916
34. Pan, T., Zhang, J., Wang, X., et al. (2021). Global burden and trends of hematologic malignancies based on Global Cancer Observatory 2022 and Global Burden of Disease. *Experimental Hematology & Oncology, 14*, 98. https://doi.org/10.1186/s40164-025-00684-x
35. Pekarsky, Y., Balatti, V., & Croce, C. M. (2018). BCL2 and miR-15/16: From gene discovery to treatment. *Cell Death & Differentiation, 25*(1), 21–26. https://doi.org/10.1038/cdd.2017.159
36. Percival, G., Dixon, G., & Sword, A. (1994). Glycoalkaloid concentration of potato tubers following continuous illumination. *Journal of the Science of Food and Agriculture, 66*, 139–144. https://doi.org/10.1002/jsfa.2740660206
37. Sandhöfer, N., Metzeler, K. H., Rothenberg, M., Herold, T., Tiedt, S., Groiß, V., Carlet, M., Walter, G., Hinrichsen, T., Wachter, O., Grunert, M., Schneider, S., Subklewe, M., Dufour, A., Fröhling, S., Klein, H. G., Hiddemann, W., Jeremias, I., & Spiekermann, K. (2015). Dual PI3K/mTOR inhibition shows antileukemic activity in MLL-rearranged acute myeloid leukemia. *Leukemia, 29*(4), 828–838. https://doi.org/10.1038/leu.2014.305
38. Shiyong, G., Yubin, J., Xiang, Z., & Chenfeng, J. (2007). Effects of solanine on the contents of Caspase-3 and Bcl-2 protein in HepG2 cells. In *IEEE/ICME International Conference on Complex Medical Engineering* (pp. 1689–1693). IEEE. https://doi.org/10.1109/ICCME.2007.4382035
39. Singh, B. (2016). Glycoalkaloids in peels of Indian potatoes. *Potato Journal, 43*(1). https://epubs.icar.org.in/index.php/PotatoJ/article/view/48534
40. Sun, L., Zhao, Y., Li, X., Yuan, H., Cheng, A., & Lou, H. (2010). A lysosomal-mitochondrial death pathway is induced by solamargine in human K562 leukemia cells. *Toxicology in Vitro, 24*(6), 1504–1511. https://doi.org/10.1016/j.tiv.2010.07.013
41. Sun, L., Zhao, Y., Yuan, H., Li, X., Cheng, A., & Lou, H. (2011). Solamargine, a steroidal alkaloid glycoside, induces oncosis in human K562 leukemia and squamous cell carcinoma KB cells. *Cancer Chemotherapy and Pharmacology, 67*(4), 813–821. https://doi.org/10.1007/s00280-010-1387-9
42. Tang, X., Guo, Y., Zhang, S., Wang, X., Teng, Y., Jin, Q., Jin, Q., Shen, W., & Wang, R. (2023). Solanine represses gastric cancer growth by mediating autophagy through AAMDC/MYC/ATF4/Sesn2 signaling pathway. *Drug Design, Development and Therapy, 17*, 389–402. https://doi.org/10.2147/DDDT.S389764
43. Teli, D. M., Shah, M. B., & Chhabria, M. T. (2021). In silico screening of natural compounds as potential inhibitors of SARS-CoV-2 main protease and spike RBD: Targets for COVID-19. *Frontiers in Molecular Biosciences, 7*, 599079. https://doi.org/10.3389/fmolb.2020.599079
44. van der Kolk, D. M., Vellenga, E., Müller, M., & de Vries, E. G. (1999). Multidrug resistance protein MRP1, glutathione, and related enzymes: Their importance in acute myeloid leukemia. *Advances in Experimental Medicine and Biology, 457*, 187–198. https://doi.org/10.1007/978-1-4615-4811-9_20
45. Wang, Y., Wu, J., Guo, W., Sun, Q., Chen, X., Zang, W., Dong, Z., & Zhao, G. (2016). α-Solanine modulates the radiosensitivity of esophageal cancer cells by inducing microRNA 138 expression. *Cellular Physiology and Biochemistry, 39*(3), 996–1010. https://doi.org/10.1159/000447807
46. Wang, N., Jiang, D., Zhou, C., & Han, X. (2023). Alpha-solanine inhibits endothelial inflammation via nuclear factor kappa B signaling pathway. *Advances in Clinical and Experimental Medicine, 32*(8), 909–920. https://doi.org/10.17219/acem/158781
47. World Health Organization. (2024). *The top 10 causes of death*. https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death
48. Wu, J., Wang, L., Du, X., Sun, Q., Wang, Y., Li, M., Zang, W., Liu, K., & Zhao, G. (2018). α-Solanine enhances the chemosensitivity of esophageal cancer cells by inducing microRNA-138 expression. *Oncology Reports, 39*(3), 1163–1172. https://doi.org/10.3892/or.2018.6187
49. Yang, J., Hao, T., Sun, J., Wei, P., & Zhang, H. (2019). Long noncoding RNA GAS5 modulates α-solanine-induced radiosensitivity by negatively regulating miR-18a in human prostate cancer cells. *Biomedicine & Pharmacotherapy, 112*, 108656. https://doi.org/10.1016/j.biopha.2019.108656
50. Yi, Y. J., Jia, X. H., Wang, J. Y., Chen, J. R., Wang, H., & Li, Y. J. (2018). Solanine induced apoptosis and increased chemosensitivity to Adriamycin in T-cell acute lymphoblastic leukemia cells. *Oncology Letters, 15*(5), 7383–7388. https://doi.org/10.3892/ol.2018.8229
51. Yi, Y. J., Jia, X. H., Zhu, C., Wang, J. Y., Chen, J. R., Wang, H., & Li, Y. J. (2018). Solanine reverses multidrug resistance in human myelogenous leukemia K562/ADM cells by downregulating MRP1 expression. *Oncology Letters, 15*(6), 10070–10076. https://doi.org/10.3892/ol.2018.8563
52. Zhang, F., Yang, R., Zhang, G., Cheng, R., Bai, Y., Zhao, H., Lu, X., Li, H., Chen, S., Li, J., Wu, S., Li, P., Chen, X., Sun, Q., & Zhao, G. (2016). Anticancer function of α-solanine in lung adenocarcinoma cells by inducing microRNA-138 expression. *Tumour Biology, 37*(5), 6437–6446. https://doi.org/10.1007/s13277-015-4528-2

53. Zhang, H., Tian, F., Jiang, P., Qian, S., Dai, X., Ma, B., Wang, M., Dai, H., Sha, X., Yang, Z., Zhu, X., & Sun, X. (2021). Solasonine suppresses the proliferation of acute monocytic leukemia through the activation of the AMPK/FOXO3A axis. *Frontiers in Oncology, 10*, 614067. https://doi.org/10.3389/fonc.2020.614067
54. Zhang, N., Wu, J., Wang, Q., et al. (2023). Global burden of hematologic malignancies and evolution patterns over the past 30 years. *Blood Cancer Journal, 13*, 82. https://doi.org/10.1038/s41408-023-00853-3
55. Zhao, D., Zhao, Y., Chen, S., & Kennelly, E. J. (2021). Solanum steroidal glycoalkaloids: Structural diversity, biological activities, and biosynthesis. *Natural Product Reports, 38*(8). https://doi.org/10.1039/d1np00001b
56. Zhao, L., Wang, L., Di, S. N., Xu, Q., Ren, Q. C., Chen, S. Z., Huang, N., Jia, D., & Shen, X. F. (2018). Steroidal alkaloid solanine A from *Solanum nigrum* Linn. exhibits anti-inflammatory activity in lipopolysaccharide/interferon γ-activated murine macrophages and animal models of inflammation. *Biomedicine & Pharmacotherapy, 105*, 606–615. https://doi.org/10.1016/j.biopha.2018.06.019
57. Zheng, Y., Li, L., Gao, Q., Niu, B., & Wang, H. (2020). Solanine inhibits proliferation and promotes apoptosis of the human leukemia cells by targeting the miR-16/Bcl-2 axis. *Journal of BUON, 25*(3), 1614–1618. PMID: 32862612
58. Zhou, J., Wu, J., Fu, F., Yao, S., Zheng, W., Du, W., Luo, H., Jin, H., Tong, P., Wu, C., & Ruan, H. (2024). α-Solanine attenuates chondrocyte pyroptosis to improve osteoarthritis via suppressing NF-κB pathway. *Journal of Cellular and Molecular Medicine, 28*(4), e18132. https://doi.org/10.1111/jcmm.18132
59. Zhu, C., Jia, X., Yi, Y., & Li, Y. (2017). Reversal effect of solanine on multidrug-resistance of leukemia K562/ADR cells and its mechanism. *Tumor, 37*, 1276–1281. https://doi.org/10.3781/j.issn.1000-7431.2017.11.604
60. Zou, T., Gu, L., Yang, L., Wei, J., Zhao, Y., Shen, J., Li, M., Wu, X., Du, F., Chen, Y., Ye, Y., Xiao, Z., & Wu, Z. (2022). Alpha-solanine anti-tumor effects in non-small cell lung cancer through regulating the energy metabolism pathway. *Recent Patents on Anti-Cancer Drug Discovery, 17*(4), 396–409. https://doi.org/10.2174/1574892817666220113144635
61. Zupkó, I., Molnár, J., Réthy, B., Minorics, R., Frank, E., Wölfling, J., Molnár, J., Ocsovszki, I., Topcu, Z., Bitó, T., & Puskás, L. G. (2014). Anticancer and multidrug resistance-reversal effects of solanidine analogs synthetized from pregnadienolone acetate. *Molecules, 19*(2), 2061–2076. https://doi.org/10.3390/molecules19022061