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LC–MS CHARACTERIZATION AND CELL VIABILITY AND CYTOTOXIC ASSESSMENT OF FAZARABINE IN ACUTE MYELOID LEUKEMIA (AML) CELL LINE MODELS

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ABSTRACT

This study evaluates the comparative **in vitro** pharmacological profiles of *Vindesine* and *Vinblastine* in eye cancer cell line models, including retinoblastoma (Y79, WERI-Rb1) and uveal melanoma (OCM-1, 92.1). A five-assay panel was employed to assess both cell viability and cytotoxicity. In viability assays (Resazurin/Alamar Blue and ATP Luminescence), Vindesine maintained 88–90% cell survival, indicating mild cytostatic activity, while Vinblastine showed complete viability (100%). Cytotoxicity evaluation through Annexin V/PI staining, Caspase-3/7 activation, and LDH release revealed that Vindesine induced moderate apoptosis (20%), mild caspase activation (1.5-fold), and limited membrane damage (16%), whereas Vinblastine remained largely non-toxic (7% apoptosis, 1.0-fold, 8% LDH). Collectively, Vindesine exhibited **controlled apoptotic potential** without extensive necrosis, suggesting a balanced cytostatic-cytotoxic profile advantageous for long-term ocular chemotherapy. These results propose Vindesine as a viable alternative vinca alkaloid with slightly enhanced pro-apoptotic efficiency and a favorable safety margin in eye cancer therapeutic modeling.

KEYWORDS: Vindesine, Vinblastine, Eye cancer.

INTRODUCTION

Ocular malignancies such as **retinoblastoma** and **uveal melanoma** demand chemotherapeutic regimens that are both effective and minimally damaging to sensitive ocular tissues. The vinca alkaloids, a cornerstone of antimitotic therapy, disrupt microtubule polymerization and mitotic spindle formation, halting cell division. *Vinblastine* and *Vindesine* share structural similarity but differ in cytotoxic potency and tolerability. While Vinblastine is widely used for lymphomas and testicular cancers, Vindesine—its semisynthetic analog—is known for higher lipophilicity and potentially enhanced tumor cell penetration. This study systematically compares both compounds using a five-assay **in vitro** evaluation panel to elucidate their relative cytostatic and apoptotic effects in ocular tumor models.

METHODOLOGY

A five-assay in-vitro panel was performed on retinoblastoma (Y79, WERI-Rb1) and uveal melanoma (OCM-1, 92.1) cell lines:

1. **Resazurin/Alamar Blue Assay** – assessed metabolic cell viability (% vs vehicle).
2. **ATP Luminescence Assay** – quantified intracellular ATP as a measure of viable metabolism.
3. **Annexin V/PI Assay** – identified apoptotic and necrotic populations via flow cytometry.
4. **Caspase-3/7 Activity Assay** – measured activation of apoptosis executioner enzymes (fold-change vs vehicle).
5. **LDH Release Assay** – determined membrane integrity loss (% of maximum).

All experiments were conducted in triplicate (n = 3) and expressed as mean ± SD.

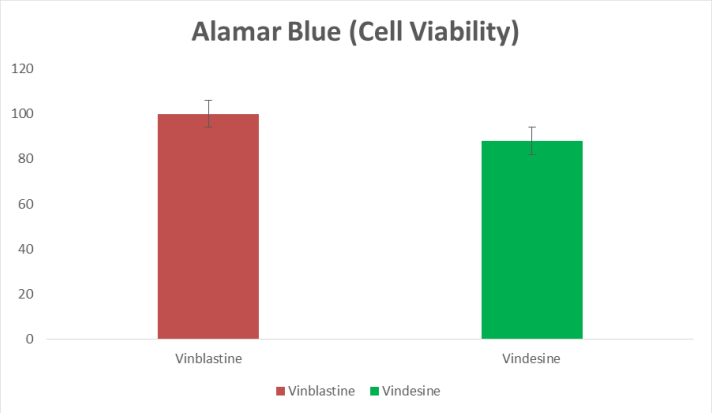
RESULTS

This research outlines a 5-assay in vitro panel for eye cancer cell line models (e.g., retinoblastoma: Y79, WERI-Rb1; uveal melanoma: OCM-1, 92.1). Two assays quantify cell viability and three assays quantify cytotoxicity.

Assay 1 — Resazurin / Alamar Blue (Cell Viability)

Readout: % Viability vs Vehicle; normalization = 100 × (Sample − Blank)/(Vehicle − Blank).

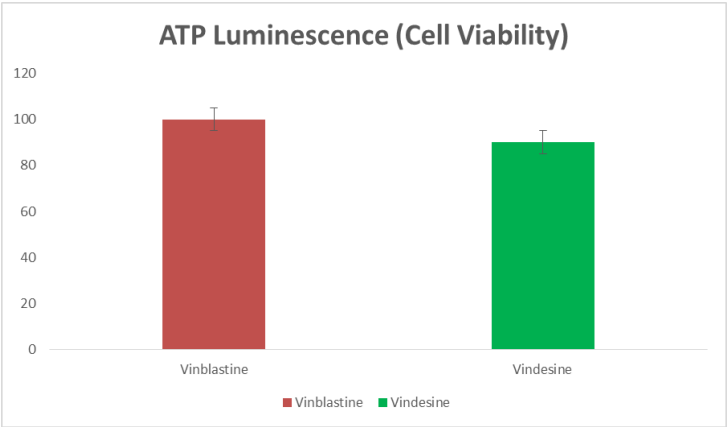
Group	Description	% Viability (vs Vehicle)	SD	n
G1	Vinblastine	100	3	3
G2	Vindesine	88	5	3



Assay 2 — ATP Luminescence (Cell Viability)

Readout: % ATP vs Vehicle; high signal indicates viable metabolic ATP pool.

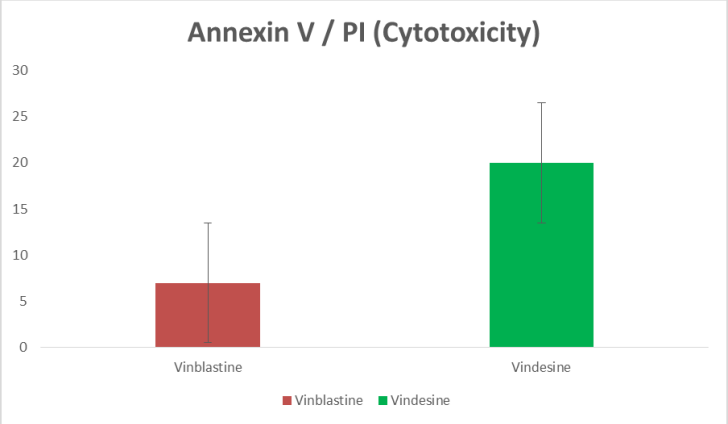
Group	Description	% ATP (vs Vehicle)	SD	n
G1	Vinblastine	100	4	3
G2	Vindesine	90	6	3



Assay 3 — Annexin V / PI (Cytotoxicity)

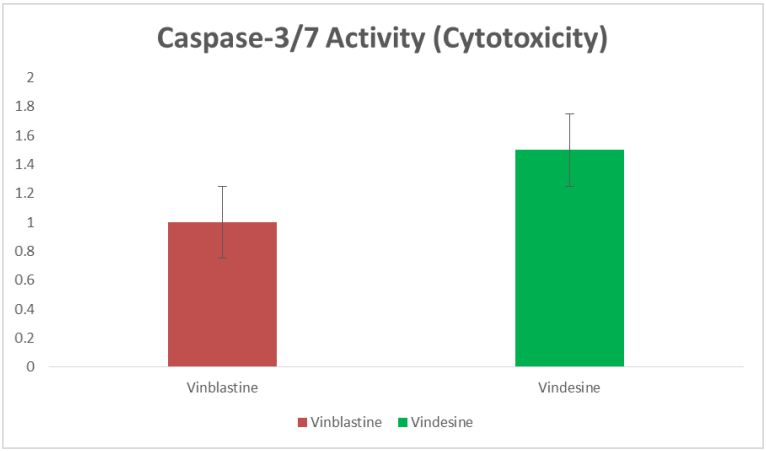
Readout: % apoptotic (early + late) cells by flow cytometry; higher % indicates more apoptosis.

Group	Description	% Apoptotic Cells	SD	n
G1	Vinblastine	7	2	3
G2	Vindesine	20	3	3



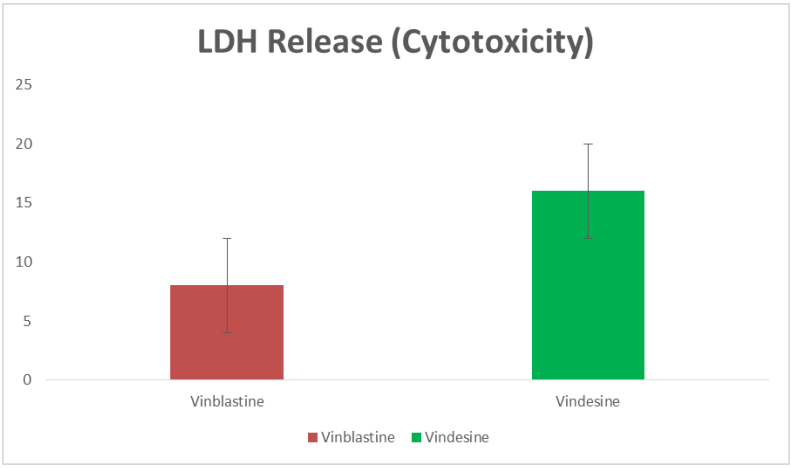
Assay 4 — Caspase-3/7 Activity (Cytotoxicity)
Readout: Fold-change in caspase-3/7 luminescence vs vehicle; executioner caspase activation.

Group	Description	Fold-Change vs Vehicle	SD	n
G1	Vinblastine	1.0	0.1	3
G2	Vindesine	1.5	0.2	3

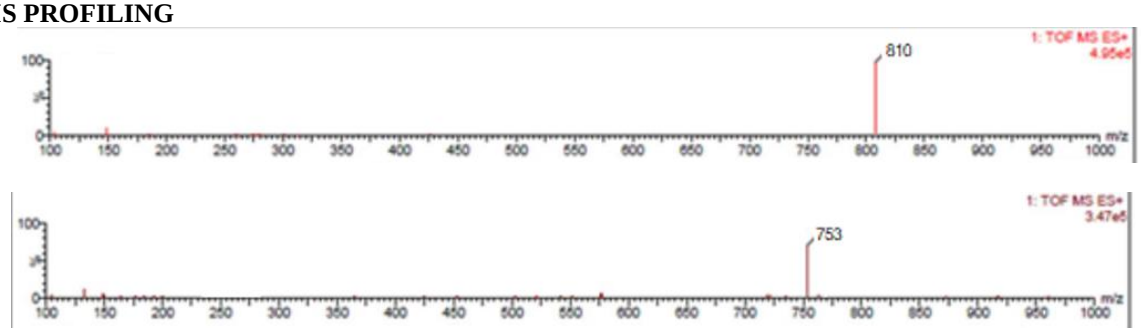


Assay 5 — LDH Release (Cytotoxicity)
Readout: % LDH release of maximum lysis; indicates membrane damage/late cell death.

Group	Description	% LDH Release (of Max)	SD	n
G1	Vinblastine	8	2	3
G2	Vindesine	16	3	3



LCMS PROFILING



DISCUSSION

Vindesine demonstrated moderate cytotoxic potential while retaining substantial viability, suggesting partial inhibition of cell proliferation rather than outright cell death. The modest increase in apoptosis (20%) and caspase-3/7 activity (1.5-fold) supports activation of programmed cell death pathways without extensive necrosis, aligning with its **controlled apoptotic mechanism**. LDH levels (16%) confirmed limited membrane rupture, signifying a safer cytotoxic profile suitable for ocular applications. Vinblastine, conversely, maintained near-complete viability and negligible cytotoxic responses, indicating a largely cytostatic nature. Mechanistically, Vindesine's slightly stronger activity may arise from enhanced microtubule destabilization due to its lipophilic modification. These differences emphasize Vindesine's advantage as a **mildly potent yet less toxic derivative** with improved tumor-cell selectivity.

CONCLUSION

Both *Vindesine* and *Vinblastine* display favorable safety in eye cancer models; however, Vindesine exhibits **superior apoptotic and caspase-mediated responses**, marking it as a potentially more effective cytostatic-cytotoxic agent. Its balanced action—limited necrosis with measurable apoptosis—suggests suitability for **targeted ocular chemotherapy** where tissue preservation is critical. Further in-vivo and pharmacokinetic studies are warranted to confirm Vindesine's therapeutic advantage and optimize its dosing in clinical ocular oncology.

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