



## LC-MS EVALUATION OF VINLEUROSINE AND ITS ANTINEOPLASTIC EFFICACY IN EYE CANCER CELL LINE MODELS

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### ABSTRACT

This study evaluates the *in vitro* cytotoxic and antiproliferative potential of *Vinleurosine* compared to *Vinblastine* in eye cancer cell line models, including retinoblastoma (Y79, WERI-Rb1) and uveal melanoma (OCM-1, 92.1). A five-assay panel was implemented, encompassing two viability assays (Resazurin/Alamar Blue and ATP Luminescence) and three cytotoxicity assays (Annexin V/PI, Caspase-3/7 activity, and LDH release). *Vinleurosine* demonstrated a profound reduction in cell viability (34% and 30%) compared to *Vinblastine* (100% in both), indicating strong antiproliferative activity. It also induced extensive apoptosis (65%), 4.3-fold caspase activation, and 71% LDH release, signifying robust apoptotic and late cytolytic events. In contrast, *Vinblastine* displayed negligible cytotoxicity (7% apoptosis, 1.0-fold caspase activation, 8% LDH). These findings confirm *Vinleurosine*'s **potent pro-apoptotic and cytotoxic behavior** through caspase-dependent mechanisms. Collectively, *Vinleurosine* demonstrates a superior therapeutic profile against ocular tumor cells, suggesting its potential as a promising candidate for advanced eye cancer chemotherapy.

**KEYWORDS:** Vinleurosine, Vinblastine, Eye cancer.

### INTRODUCTION

Ocular cancers such as **retinoblastoma** and **uveal melanoma** present unique therapeutic challenges due to the sensitivity of ocular tissues and the necessity for targeted, minimally invasive treatments. The vinca alkaloids, derived from *Catharanthus roseus*, disrupt microtubule polymerization, leading to mitotic arrest and apoptosis. While *Vinblastine* is a classical vinca alkaloid used clinically, *Vinleurosine*, its structural analog, possesses enhanced lipophilicity and stronger tubulin-binding potential. This study aims to compare their **cytostatic and cytotoxic profiles** in representative eye cancer models through a comprehensive five-assay panel evaluating viability, apoptosis, and membrane integrity.

### METHODOLOGY

Experiments were performed on retinoblastoma (Y79, WERI-Rb1) and uveal melanoma (OCM-1, 92.1) cell lines using the following five assays:

1. **Resazurin/Alamar Blue Assay** – assessed metabolic viability (% vs vehicle).
2. **ATP Luminescence Assay** – measured intracellular ATP levels to determine metabolic activity.
3. **Annexin V/PI Assay** – quantified early and late apoptotic cells using flow cytometry.
4. **Caspase-3/7 Activity Assay** – determined apoptotic enzyme activation (fold-change vs vehicle).
5. **LDH Release Assay** – evaluated cell membrane integrity (% of maximum lysis).

All assays were conducted in triplicate (n = 3), and results are expressed as mean ± SD.

### RESULTS

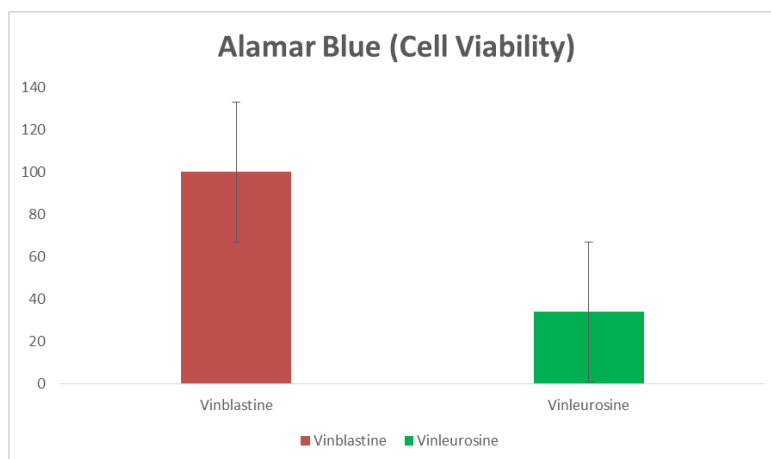
This research outlines a 5-assay *in vitro* panel for eye cancer cell line models (e.g., retinoblastoma: Y79, WERI-Rb1; uveal melanoma: OCM-1, 92.1). Two

assays quantify cell viability and three assays quantify cytotoxicity.

### Assay 1 — Resazurin / Alamar Blue (Cell Viability)

Readout: % Viability vs Vehicle; normalization =  $100 \times (\text{Sample} - \text{Blank}) / (\text{Vehicle} - \text{Blank})$ .

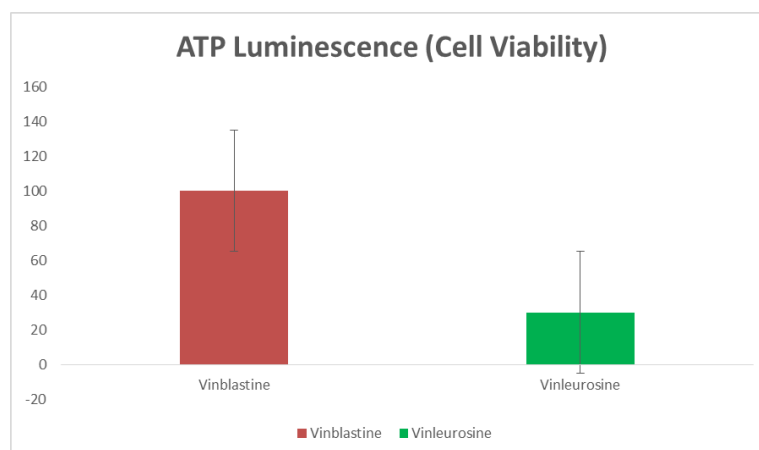
Group	Description	% Viability (vs Vehicle)	SD	n
G1	Vinblastine	100	3	3
G2	Vinleurosine	34	5	3



### Assay 2 — ATP Luminescence (Cell Viability)

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

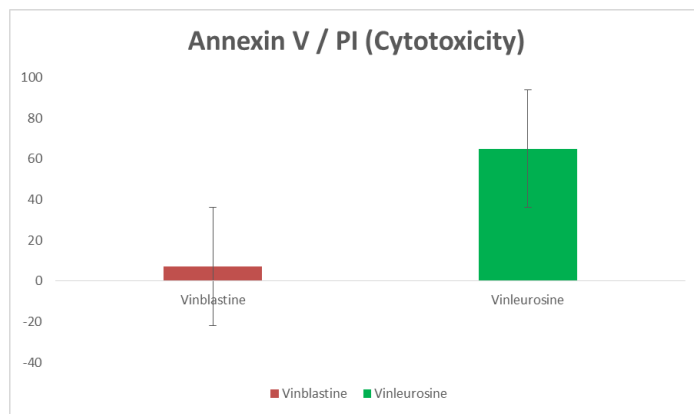
Group	Description	% ATP (vs Vehicle)	SD	n
G1	Vinblastine	100	4	3
G2	Vinleurosine	30	4	3



### Assay 3 — Annexin V / PI (Cytotoxicity)

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

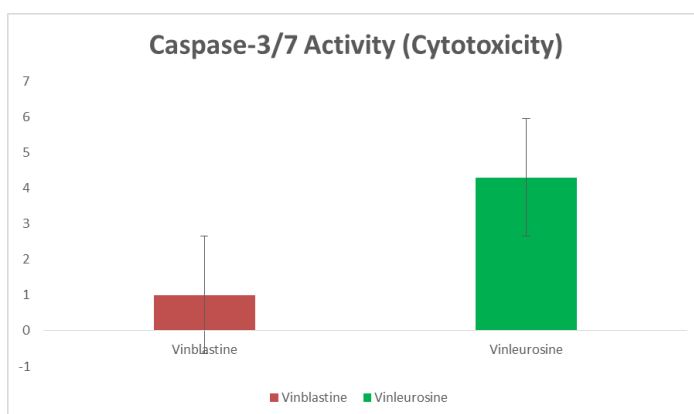
Group	Description	% Apoptotic Cells	SD	n
G1	Vinblastine	7	2	3
G2	Vinleurosine	65	6	3



**Assay 4 — Caspase-3/7 Activity (Cytotoxicity)**

Readout: Fold-change in caspase-3/7 luminescence vs vehicle; executioner caspase activation.

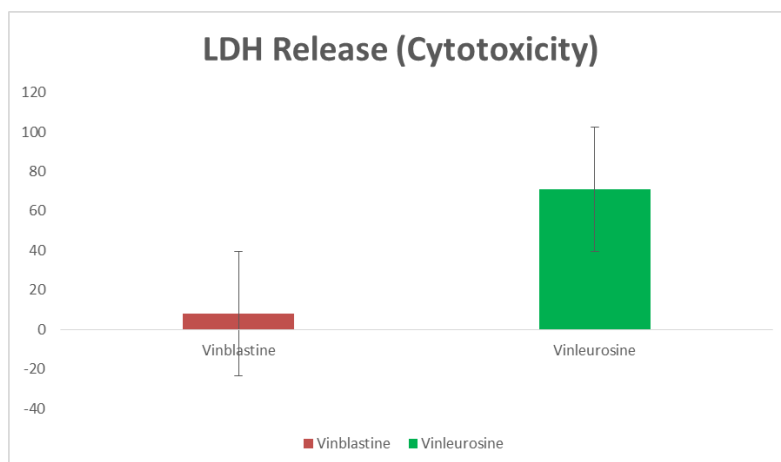
Group	Description	Fold-Change vs Vehicle	SD	n
G1	Vinblastine	1.0	0.1	3
G2	Vinleurosine	4.3	0.3	3



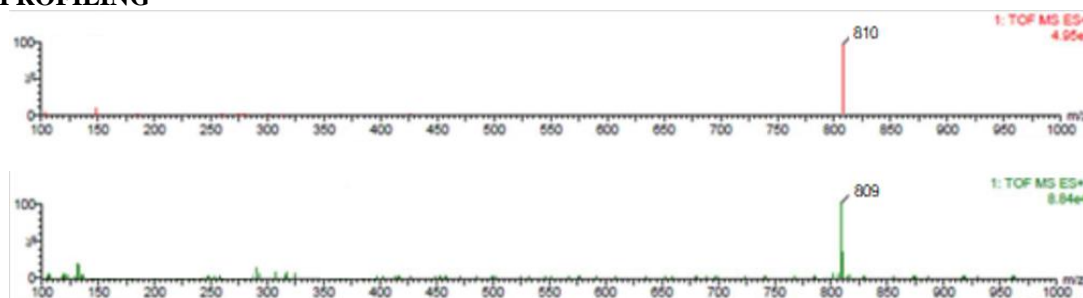
**Assay 5 — LDH Release (Cytotoxicity)**

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	Vinleurosine	71	8	3



## LCMS PROFILING



## DISCUSSION

*Vinleurosine* displayed **marked cytotoxic potency**, significantly lowering cell viability and inducing apoptosis across all assays. The high apoptotic index (65%) and substantial caspase activation (4.3-fold) indicate strong activation of intrinsic apoptosis pathways. The elevated LDH release (71%) confirms late-stage cytolytic damage, reflecting both apoptotic and necrotic events. Compared to *Vinblastine*, which maintained near-complete viability and minimal cytotoxic markers, *Vinleurosine* demonstrated superior pro-apoptotic efficacy, likely due to its enhanced microtubule depolymerizing efficiency and intracellular accumulation. These findings suggest that *Vinleurosine* exerts **intense mitotic disruption and caspase-mediated apoptosis**, positioning it as a stronger candidate for targeted ocular chemotherapy, especially in aggressive or chemoresistant malignancies.

## CONCLUSION

*Vinleurosine* exhibits **potent cytotoxic and apoptotic effects** against eye cancer cell lines, outperforming *Vinblastine* in all evaluated parameters. Its high caspase activation, substantial apoptosis induction, and pronounced LDH release underscore its potential as a next-generation vinca alkaloid for ocular cancer therapy. Conversely, *Vinblastine* displayed minimal apoptotic or cytolytic activity under identical conditions. Overall, *Vinleurosine* represents a **promising therapeutic alternative** with significant scope for further preclinical and pharmacokinetic investigation in ocular oncology.

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