The Burden of Cancer
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Synthesis and evaluation of anticancer activity of pyrrolo[3,4-d]isoxazoles against tumor cell lines

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INTRODUCTION & AIM

The Burden of Cancer

Oncological diseases are a leading global health problem and the second leading cause of death worldwide.

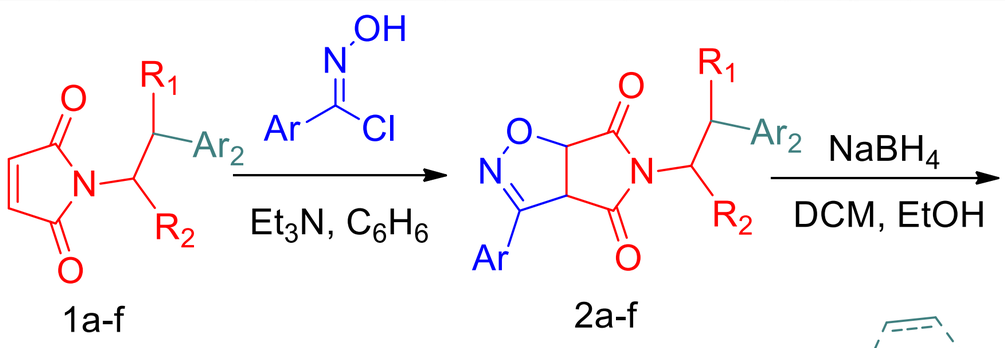
Natural Products in Drug Discovery

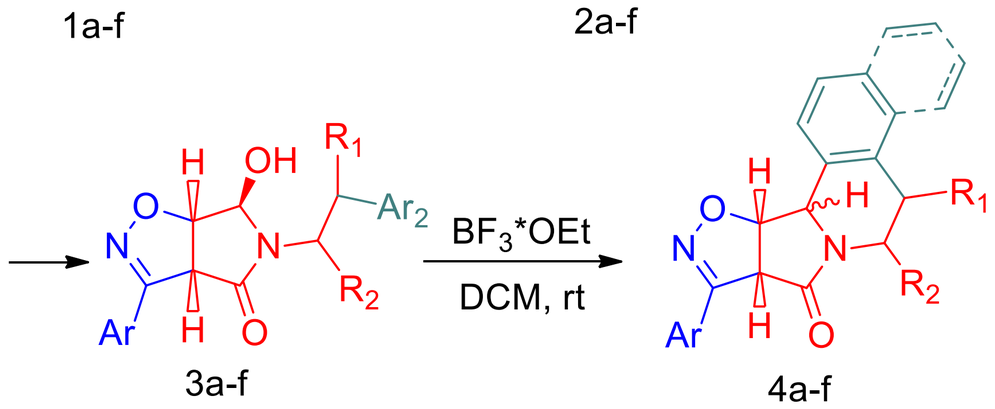
Natural products and synthetic compounds inspired by them are invaluable sources for new drug candidates.
A "privileged scaffold" in drug discovery. Binds to diverse biological targets and exhibits broad biological activities.

Research Aim

1. Synthesize novel pyrrolo[3,4-d]isoxazole derivatives.
2. Evaluate their anticancer activity.
3. Investigate their mechanism.

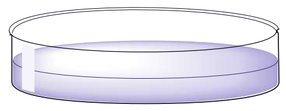
METHOD



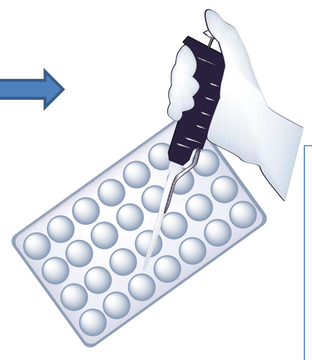


Ar	R_1	R_2	Ar_2	№, Yeild (%)					
p-ClC_6H_4	H	H	Naphtyl	2a	31	3a	54	4a	54
p-ClC_6H_4	H	H	Naphtyl	2b	46	3b	66	4b	54
p-ClC_6H_4	H	Ph	Ph	2c	100	3c	59	4c	21
p-ClC_6H_4	Me	Ph	Ph	2d	98	3d	40	4d	63
p-$CH_3C_6H_4$	Ph	H	Ph	2e	64	3e	42	4e	68
p-ClC_6H_4	Ph	H	Ph	2f	64	3f	92	4f	48

HELA
K-562
SK-MEL-2

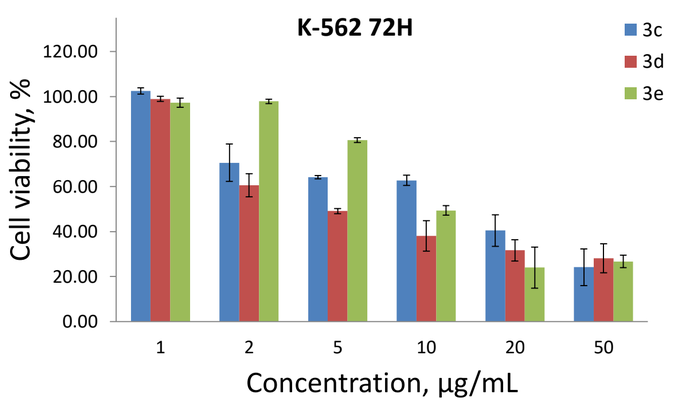


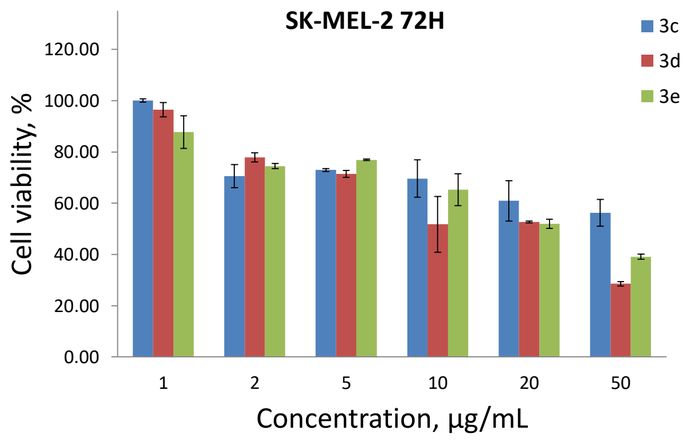
Antiproliferative activity was evaluated against three human cancer cell lines using **MTS assay**.

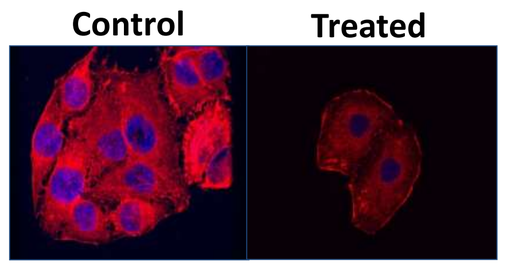


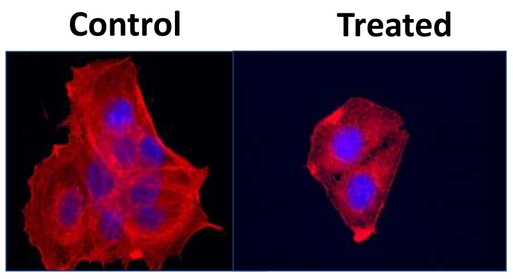
Cells were treated with compounds, stained with rhodamine-phalloidin (red) for actin and DAPI (blue) for nuclei, and visualized by **confocal microscopy**.

RESULTS & DISCUSSION





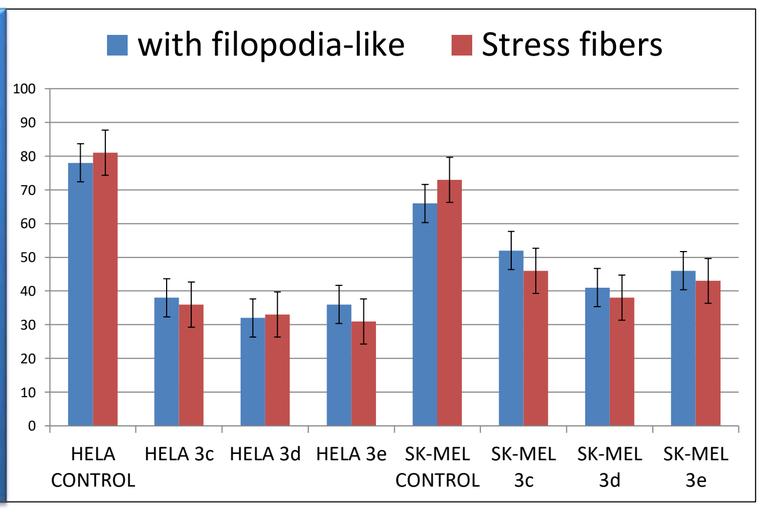




Potent Antiproliferative Activity

Cell Line	Most Potent Compound	IC_{50} (µg/mL)
HeLa	**3e**	**12.2 ± 0.7**
K-562	**3d**	**16.2 ± 0.8**
Sk-Mel-2	**3d**	**26.8 ± 1.3**

Confocal microscopy revealed that the compounds act through a dual mechanism: disrupting the actin cytoskeleton into a granular form and significantly reducing filopodia, thereby inhibiting both cell proliferation and invasion.



CONCLUSION

Novel pyrrolo[3,4-d]isoxazoles were synthesized.

Showed potent anticancer activity

Mechanism involves disruption of the actin cytoskeleton. Reduced filopodia formation, inhibiting invasion.

This scaffold is a **promising candidate** for further development.

FUTURE WORK / REFERENCES

Broader Screening vs. resistant cell lines.

Target Identification of the primary molecular target.