Two New Orbitides, [1–10-NαC]-croheorbs A1 and A2, Isolated from the Latex of *Croton heliotropiifolius*

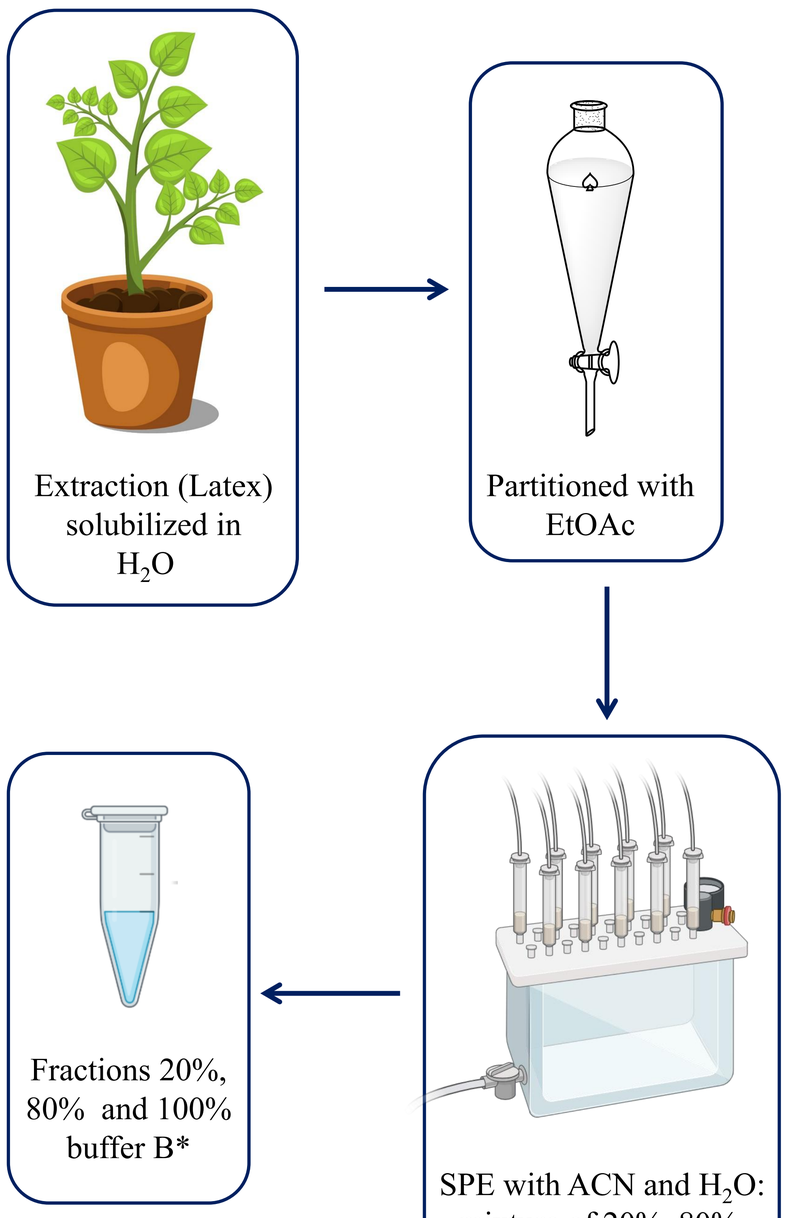
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INTRODUCTION

Peptides are an important class of natural products with significant therapeutic potential, due to their structural properties[1]. Among plants, there are three classes of ribosomal-synthesized cyclic peptides (RiPPs): cyclotides, PawS-derived peptides (PDPs), and orbitides. Among these, orbitides are ribosomally synthesized, head-to-tail cyclized plant peptides typically comprising 5 to 11 amino acid residues.[2] Although Brazil has the largest biodiversity in the world there are still few studies describing the isolation of orbitides from Brazilian plants.

EXPERIMENTAL PROCEDURES

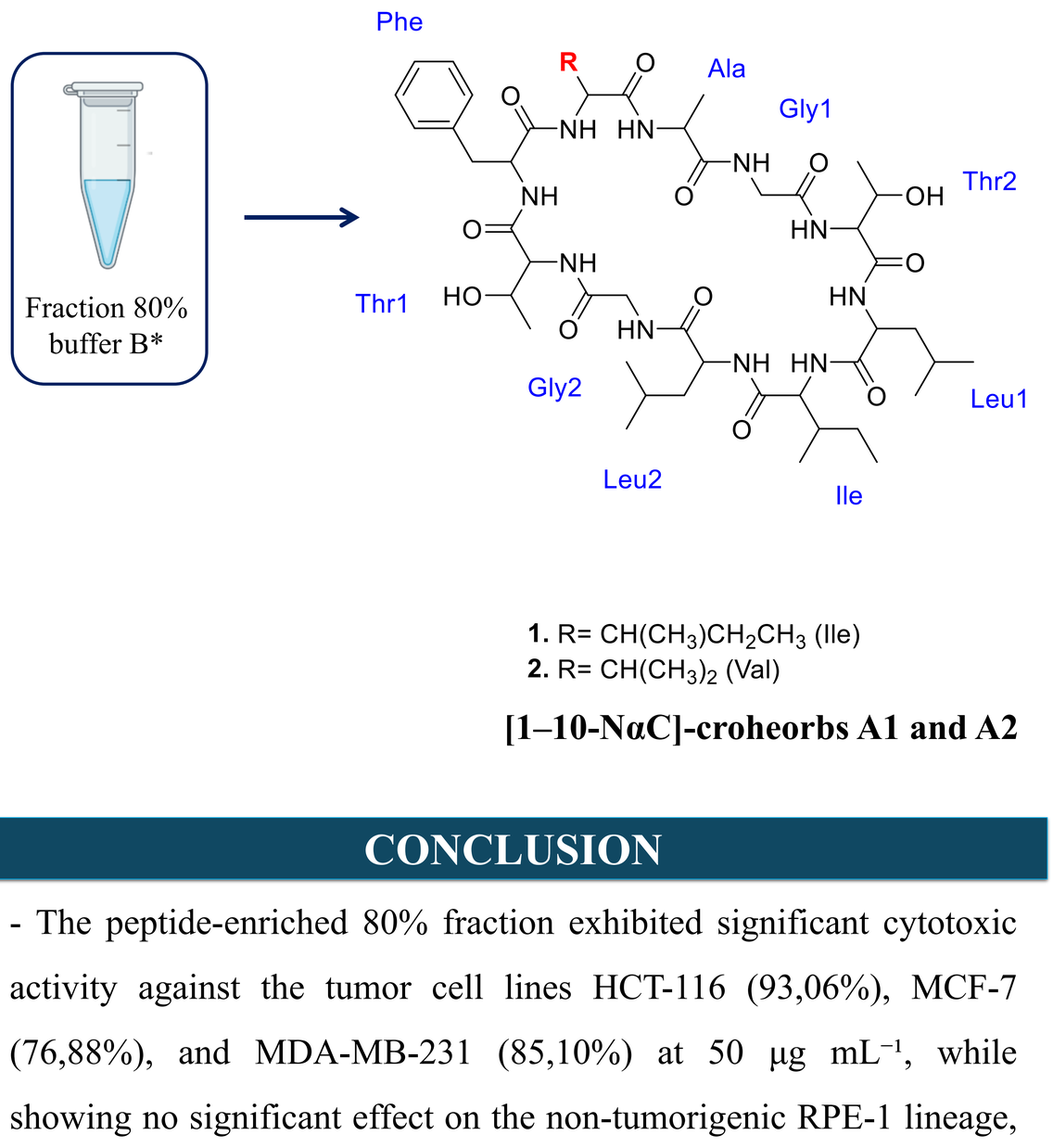


Solvent A: H_2O + 0.1% CF_3COOH
Solvent B: ACN + 0.1% CF_3COOH

RESULTS AND DISCUSSION

Table 1. Cytotoxic activity with fraction 80% from latex of *Croton heliotropiifolius*

Cell lines	Fraction 80%	
	50 µg mL^{-1}	**5 µg mL^{-1}**
HCT-116	93.06%	15.46%
MCF-7	76.88%	16.30%
MDAMB-231	85.10%	0%
RPE-1	4.67%	0%



1. R= $CH(CH_3)CH_2CH_3$ (Ile)
2. R= $CH(CH_3)_2$ (Val)

[1–10-NαC]-croheorbs A1 and A2

CONCLUSION

- The peptide-enriched 80% fraction exhibited significant cytotoxic activity against the tumor cell lines HCT-116 (93,06%), MCF-7 (76,88%), and MDA-MB-231 (85,10%) at 50 µg mL^{-1}, while showing no significant effect on the non-tumorigenic RPE-1 lineage, suggesting selective activity.

- This study expands the structural diversity known for orbitides and represents the first phytochemical investigation of *C. heliotropiifolius*

REFERENCES

1. Buchanan, D. et al. *Biomedicines*. **2025**,13, 240.
2. Shim, Y. Y., Young, L. W., et al. *J. Nat. Prod.* **2015**, 78, 645.
3. Icons were obtained from BioRender.com.

ACKNOWLEDGMENTS

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