Phytochemical, antioxidant, anticancer, cell migration inhibitory potentials of *Erythrina caffra* Thunb. leaf extracts and pharmacoinformatic analysis of its constituents

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INTRODUCTION

With an estimated 19.3 million morbidities and 10 million mortalities in the year 2020, cancer currently stands as one of the leading cause of death globally and a major barrier to prolonged life expectancy. While the mortality ratio appears to have witnessed a steady decline in most countries, the rate of cancer mortality has continued to grow in Asia and Africa [1]. The current surge in cancer mortality is indicative of the failed therapeutic modalities in these regions, which could be attributed to lack of access to adequate medical facilities [2]. As a means of combating cancer, most developing nations in Africa still rely on medicinal plants. Keeping in mind the significant multiphasic pharmacological prospects of medicinal plants, the current study aims to explore the chemopreventive and anticancer potential of *Erythina caffra* and possibly identify lead compounds against cancer.

Methods

Solvent extraction of *E. caffra* in n-hexane, dichloromethane (DCM), ethylacetate and methanol → Antioxidant activity analysis using DPPH radical scavenging assay and ferric ion scavenging activity

Cell migration inhibition studies using wound healing assay and Anticancer activity analysis using MTT assay and apoptosis studies. → Phytochemical analysis of compounds present in extracts by GCMS and pharmacoinformatic studies of constituents against cancer targets using molecular docking analysis, AutoQSAR studies and pharmacokinetics profiling

RESULTS AND DISCUSSION

Table 1. IC50 values for antioxidant and cytotoxicity studies on HEK293, MCF-7 and Hela following treatment with *E. caffra* leaf extracts

Extracts/Standard	DPPH (µg/mL)	FRAP (µg/mL)	HEK293 (µg/mL)	MCF-7 (µg/mL)	Hela (µg/mL)
Hexane	4099.718	171932.6	336.0442	433.8068	15861.16
DCM	839.499	103.0904	56436.95	318.8498	490.9694
Ethylacetate	181.124	184.6623	307.1478	235.0802	768.0499
Methanol	8807.154	86.43519	192.3223	459.1824	165.5622
Ascorbic acid	85.75925	59.30982	-	-	-
5-Fluorouracil (5FU)	-	-	54.50498	147.9033	510.3547

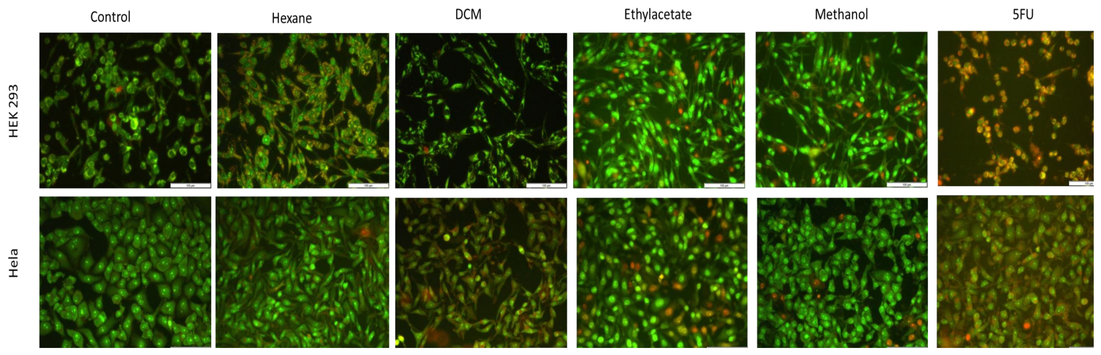

Figure 1. Fluorescent images of acridine orange/ ethidium bromide dual stained HEK293 and Hela cells treated with 100µg/ml extracts of *E. caffra*. Viable cells show green fluorescence, necrotic cells are dark red, cells in late apoptosis have yellow to orange coloration and early apoptotic cells have yellow-green nuclei

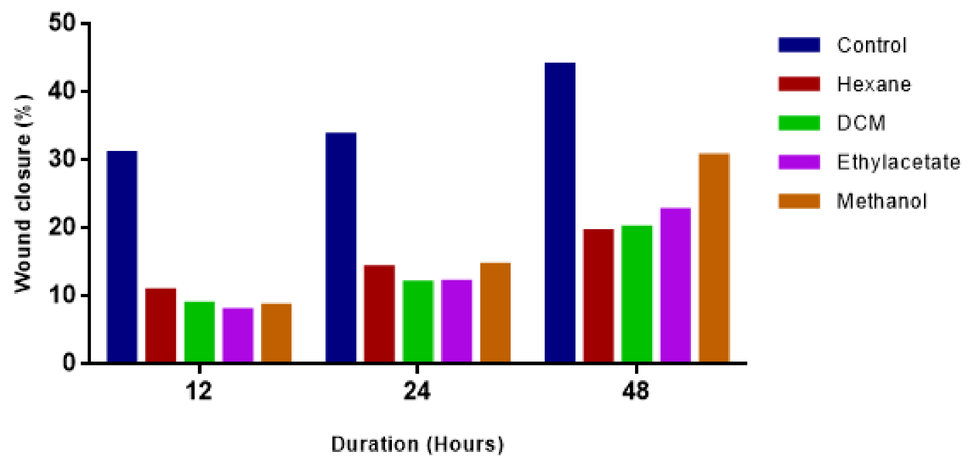

Figure 3. Percentage wound closure of Hela cells treated with 50 µg/ml *E. caffra* extracts

Table 2. Molecular docking score, MMGBSA post docking analysis and predicted logarithmic IC50 value of some identified compounds against MDM2, CDK2 and CDK6 protein

Entry Name	Solvent	MDM2			CDK2			CDK6		
		Docking score	MMGBSA dG Bind	Pred IC50	Docking score	MMGBSA dG Bind	Pred IC50	Docking score	MMGBSA dG Bind	Pred IC50
5-Bromovaleric acid	DCM	-6.142	-49.7005	5.53	-6.6	-36.4153	6.729	-	-	-
25,26-Dihydroxycholecalciferol	DCM	-6.125	-52.6448	6.997	-	-	-	-	-	-
Liquiritigenin	DCM	-	-	-	-9.232	-41.2029	6.881	-6.2	-38.5871	6.425
Lumazine, 8-ethyl-6,7-dimethyl	DCM	-	-	-	-7.525	-44.4946	7.022	-8.082	-42.3355	6.719

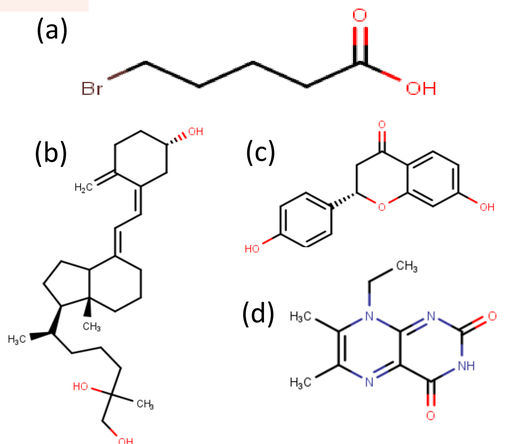

Figure 2. 2D structure of some compounds identified from *E. caffra* (a) 5-bromovaleric acid, (b) 25,26-dihydroxycholecalciferol, (c) liquiritigenin and (d) lumazine, 8-ethyl-6,7-dimethyl

Table 3. Predicted druglikeness and toxicity properties of identified lead compounds from *E. caffra*

Entry Name	Lipinski violation	PAINS alert	hERG blocker
5-Bromovaleric acid	No	No	No
25,26-Dihydroxycholecalciferol	No	No	No
Liquiritigenin	No	No	No
Lumazine, 8-ethyl-6,7-dimethyl	No	No	No

CONCLUSION

The study have thus far shown that solvent extracts of *E. caffra* (especially dichloromethane extract) possess significant chemopreventive and cytotoxic properties against the cancer cells tested. The anticancer activity could be linked to the presence of bioactive compounds such as 5-bromovaleric acid, 9,10-Secocholesta-5,7,10(19)-triene-3,25,26-triol, (3.beta., 5Z,7E) and liquiritigenin which were found to have significant potential to interact with cancer targets such as MDM2, CDK2 and CDK6. The compounds were also found to have favorable properties and can be explored further as drug candidates against cancer progression.

REFERENCES

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