Anti-proliferative potential of *erythrina indica* leaf aqueous extract against human breast cancer cells

Running title: Effect of *erythrina indica leaf aqueous extract* on breast cancer cells.

ABSTRACT

Introduction: Breast cancer is cancer that develops in breast cells. The cancer forms in either the lobules or the ducts of the breast. Cancer can also occur in the fatty tissue or the fibrous connective tissue within your breast.

Materials and methods: The effect of *Erythrina indica (E.indica)* on cell viability was measured by MTT assay. Briefly, the cells (1×10^5 cells/ml) were seeded in a 96 well microtiter plate with replications. Treatment was conducted for 24 with different concentrations (50-300 µg) of *E.indica*. The percentage of cell viability was calculated and plotted in graph. The cell morphological changes of *E. indica leaf aqueous extract* treated cells were observed under inverted phase contrast microscopy.

Results: The crude extract obtained from *E.indica* leaf greatly inhibits the cancer cell proliferation in dose dependent manner. We observed IC^{50} at 100 µg/ml of *E. indica leaf aqueous extract* treated for 24 hrs in breast cancer cells and also it induces apoptosis, which was confirmed by cell morphological changes evaluated using phase contrast microscope.

Conclusion: The results suggest that the *E. indica leaf aqueous extract* shows the potent anti-proliferative activity against breast cancer cells, and it might be a novel new anticancer drug for cancer therapy.

Key words: Anticancer, Sea grass, Breast cancer cell line, *Erythrina indica*, Cytotoxicity

1. INTRODUCTION:

E. indica is a medium-sized, spiny, deciduous tree usually developing to tall (1,2). Young stems and branches are thickly armed with stout conical spines up to 8 mm lengthy, which fall off after 2-four years; rarely, some spines persist and are retained with the corky bark (3, 4). Leaves

trifoliate, alternate, shiny emerald -inexperienced, on lengthy petioles 6-15 cm, rachis 5-30 cm lengthy, prickly; leaflets easy, shiny, broader than lengthy, eight-20 with the aid of using 5-15 cm, ovate to acuminate with an obtusely pointed end (5-6). Leaf petiole and rachis are spiny. Flowers in shiny red to scarlet erect terminal racemes 15-20 cm lengthy; stamens barely sticking out from the flower (7,8). Fruit a cylindrical torulose pod, inexperienced, turning black and wrinkly as they ripen, thin-walled and constricted across the seeds. There are 1-eight easy, oblong, darkish pink to nearly black seeds consistent with pod.

Breast cancer is one of the most common styles of cancers internationally and yet, its pathophysiology is poorly understood. Single-mobileular electrophysiological research has furnished proof that membrane depolarization is implicated with inside the proliferation and metastasis of breast most cancers (9). However, metastatic breast most cancers cells are exceedingly dynamic microscopic structures with complexities past a single-molecular level. There is a pressing need for electrophysiological research and technology able to decipher the intercellular signaling pathways and networks that manage proliferation and metastasis, especially at a populace level. Hence, we gift for the primary time non-invasive in vitro electric recordings of strongly metastatic MDA-MB-231 and weakly/non-metastatic MCF-7 breast most cancers lines (10). *E. indica* incorporates glycosides and phenol compounds which can be capable of behaving as antifungal and anticancer, and even incorporates steroid compounds which act as antibacterial and anticancer (11). It has been said that crude extract from *E. indica* had excessive phenolic content material. Moreover, suggested the cytotoxicity of crude extract from *E.indica*. The maximum phenolic content material is at the leaves part. One that may be located in tidal coastal regions in Indonesia is *E. indica*. Since different sorts had been suggested to include anticancer bioactive compounds, any other studies to decide the capability of *E. indica* as a supply of anticancer bioactive compounds ought to additionally be conducted (1). The purpose of these studies was to decide the capability of *E.indica* leaves extract as an anticancer agent.

2. MATERIALS AND METHODS

2.1. CHEMICALS:

DMEM medium, 0.25% Trypsin-EDTA solution, sodium bicarbonate solution, bovine serum albumin (BSA), low melting agarose, MTT from Sigma Chemicals Co., St. Louis, USA. fetal bovine serum (FBS) and antibiotic/antimycotic solution, DMSO were from Himedia, Sodium phosphate monobasic and dibasic, sodium chloride, sodium hydroxide, sodium carbonate, hydrochloric acid and methanol were purchased from Sisco Research Laboratories (SRL) India.

2.2. PREPARATION OF EXTRACT:

E. indica herbal powder commercially purchased IMPCOPS - Chennai (Indian Medical Practitioners Co-operative Pharmacy and Stores Limited). 200g of sample was soaked in double distilled water and kept for 3 days at 37°C temperature in continuous intervals of shaking the flask. Further, the solution was filtered and placed in a rotary vacuum evaporator to concentrate fine filtered samples and leftover solvent was evaporated to dryness in a hot air oven. 2 grammes of material was obtained and immediately sorted at 4°C, for further experiments.

The required quantity of the herbal extract was weighed and dissolved in DMSO with concentration of 1mg/ml as a stock solution. This solution was subsequently diluted to a series of concentrations ranging from 50 to 300 µg/ml for cell viability assay.

2.3. CYTOTOXIC ASSAY:

The cytotoxic effect of *E. indica leaf aqueous extract* on MCF-7, were measured with MTT (3-(4, 5-dimethyl thiazol-2 yl)-2, 5-diphenyl tetrazolium bromide) assay by Alam (12) Cells were seeded in 96-well plates at the density of $5x10^3$/100µl and treated with different concentrations (50, 100, 150, 200, 250 and 300 µg) of *E. indica leaf aqueous extract* for 24hrs. After 24hrs incubation, 20 µl of 5 mg/ml MTT stock solution was added to each well and incubated for 4hrs at 37 °C. The obtained formazan crystals were solubilized with DMSO and the absorbance was measured at 570 nm using a microplate reader (SpectraMax M5, Molecular Devices, USA). Cell viability (%) has been shown as a ratio of absorbance (A570) in treated cells to absorbance (A570) in control cells (0.1 % DMSO). The IC_{50} was calculated as the concentration of sample

needed to reduce 50 % of the absorbance in comparison to the DMSO-treated control. Percent cell viability was calculated following the equation:

$$\text{Cell viability (\%)} = \frac{\text{Absorbance of sample}}{\text{Absorbance of control}} \times 100$$

2.4. STATISTICAL ANALYSIS:

All data obtained were analyzed and computed statistically (SPSS/10 Software Package; SPSS Inc., Chicago, IL, USA) using one-way ANOVA. Post-hoc testing was performed for inter comparisons using the LSD. In all tests, the level of statistical significance was set at $p<0.05$

3. RESULT AND DISCUSSION:

During the recent decades, a number of anticancer compounds derived from natural sources, such as vincristine, vinblastine, taxol, and bleomycin, have been identified and are now extensively utilized to treat various kinds of cancer. Many researchers report, phenolic compounds have anti-carcinogenic action and alter the bioenergetic processes of MCF-7 breast cancer cells. Edible plant material includes a large number of micro-constituents, all of which are active in biological systems (13-33). The present study aims to identify the anti-proliferative effect of *E. indica leaf aqueous extract* for breast cancer therapy. The results showed potential cytotoxic effects by MTT assay and morphometric analysis using phase contrast microscopy in Breast cancer cell lines are presented in figure 1 & 2, demonstrating the bioactivity of *E. indica leaf aqueous extract* in MCF-7 cells. *E. indica leaf aqueous extract* at a concentration of 250 µg ml−1 hindered the growth of MCF-7 cells.

MCF-7

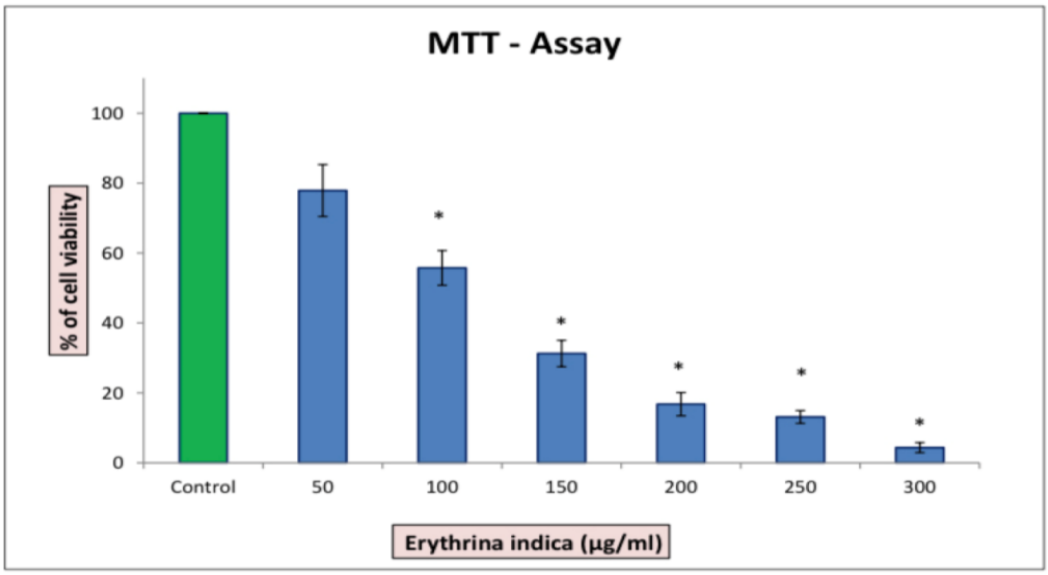

Fig.1 Represent the cytotoxic effect of *E. indica leaf aqueous extract* against breast cancer cells for 24hrs. The X axis represents different concentrations of *E. indica leaf aqueous extract* and Y-axis represents the percentage of cell viability. Green colour denotes control and blue colour represents the different concentration of *E. indica leaf aqueous extract* 50-300 µg/ml. Data are shown as means ± SD (n = 3) compared with the control-blank group, $p < 0.001$. At 100 µg/ml of *E. indica leaf aqueous extract* only 50% of the cells were viable, which shows the good cytotoxic activity of the herb.

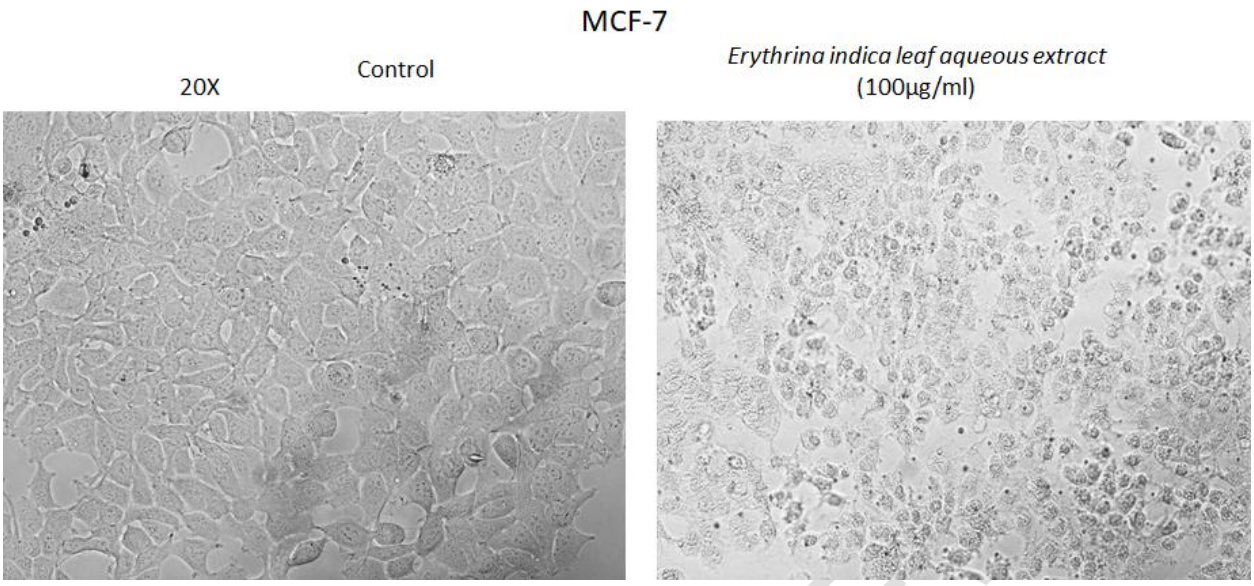

Fig.2. *E. indica leaf aqueous extract* anti-proliferative activity was evaluated by morphological changes with control and treated (100µg/ml) breast cancer cells. Cellular characteristics were disrupted upon herbal treated cells with membrane blebbing, nuclear condensation, fragmentation were observed under phase contrast microscopy 20x magnification,

Breast cell lethality level by semi polar extract was higher than polar extract, but not significantly different with cancer medicine doxorubicin. The extract of C. serrulata reveals the presence of phytocompounds that are biologically active. According to the chromatogram obtained by GCMS ethanol extract of *E. indica* consists of palmitic acid, myristic acid, and pentadecanoic acid as a major component. They may be produced by the plant defense itself from stress as secondary metabolites (34). These cytoprotectants proved to possess pharmacological activity in a similar way as synthetic drugs. The palmitic acid reported possessing anticancer activity, antimicrobial, and nematicide activity (35). The palmitic acid increases the number of probiotic bacteria in the gut; thus, they are involved in the development of the intestine. It is required in the biosynthesis of lung lecithin, which is related to fetal maturation as well as it has been reported that presence of palmitic acid in the Nigerian meal can partly be related to the low incidence of respiratory disease. Palmitic acid reported inhibiting human hepatoma cell growth in a dose dependent and time-dependent manner. Thus, they

possess anticancer. Since other types were reported to contain anticancer bioactive compounds, another research to determine the potential of *E. indica* as a source of anticancer bioactive compounds should also be conducted (36-53).

4. CONCLUSION:

This study aimed to reveal the anti-proliferative effect of *E. indica leaf aqueous extract* against breast cancer cells. The results show that the *E. indica leaf aqueous extract* has greatly inhibited cell proliferation at 100 µg/ml (IC^{50} value) concentrations for 24hrs. Further, morphological changes like membrane blebbing, nuclear condensation and fragmentation have been observed upon *E. indica leaf aqueous extract* treatment showing antitumor activity against cancer cells. These promising results suggest that *E. indica* as a promising source of natural ingredients, and pave the way to develop novel anticancer drugs for treating cancer, including breast cancer.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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