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Cytotoxic evaluation of curcumin and quercetin in MCF-7 cell lines

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Abstract

Cytotoxic evaluation of Curcumin and Quercetin in MCF-7 cell lines was performed to assess their potential anticancer activity. MCF-7 is a widely used breast cancer cell line, and evaluating the cytotoxic effects of the compounds on these cells can provide valuable information about their potential as an anticancer agent. Curcumin, a naturally occurring compound found in turmeric, has been extensively studied for its potential anticancer properties, including its effects on MCF-7 cell lines. MCF-7 cells are commonly used as a model for studying breast cancer. Quercetin, a flavonoid found in various fruits, vegetables, and plant-based foods, has also been studied for its potential anticancer effects, including its effects on MCF-7 cell lines. The combination of curcumin and quercetin has been investigated for its potential synergistic effects on MCF-7 cell lines, aiming to enhance the anticancer activity of both compounds. The synergistic effects observed in the combination of curcumin and quercetin on MCF-7 cells suggests that the compounds may act through complementary mechanisms, enhancing their individual anticancer activities.

Keywords: Curcumin; Quercetin; Cytotoxic effects; MCF-7 cells

1. Introduction

Breast cancer is a complex and prevalent disease characterized by the abnormal growth of cells in breast tissue. It is one of the most common cancers worldwide and affects both men and women, although it is far more common in women. Breast cancer can develop in various parts of the breast, such as the milk ducts, lobules, or in the fatty tissue surrounding the breast. Breast cancer is a global health concern, with millions of cases diagnosed annually. In many countries, it is the most frequently diagnosed cancer among women. The incidence of breast cancer varies by geographical location, age and gentic predisposition.

The several risk factors associated with an increased likelihood of developing breast cancer include gender, age, family history, genetic mutations such as BRCA1 and BRCA 2, hormone replacement therapy, radiation exposure, obesity and lack of physical activity, alcohol consumption and early onset of mensturation or late menopause [1,2].

1.1. Types of Breast Cancer [3]

- Ductal Carcinoma In Situ (DCIS): Early-stage cancer where abnormal cells are confined to the milk ducts and have not invaded nearby tissues.
- Invasive Ductal Carcinoma (IDC): The most common type of breast cancer, which starts in the milk ducts and then invades surrounding tissues.
- Invasive Lobular Carcinoma (ILC): Develops in the milk-producing glands and can also spread to other areas.

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- Triple-Negative Breast Cancer: A subtype that lacks estrogen, progesterone, and HER2 receptors, making it challenging to treat.
- HER2-Positive Breast Cancer: Involves the overexpression of HER2 protein, which can promote cancer cell growth.
- Inflammatory Breast Cancer: A rare and aggressive form characterized by redness and swelling of the breast.

1.2. Symptoms and Diagnosis: [4]

Early breast cancer may not exhibit symptoms. Common signs include a lump in the breast, changes in breast size or shape, nipple discharge, or skin changes like dimpling.

Diagnosis typically involves a combination of mammography, ultrasound, MRI, and biopsy to determine the presence and type of breast cancer.

1.3. Treatment Options: [5]

Treatment approaches for breast cancer depend on the type, stage, and individual patient factors. Common treatment includes surgery, radiation therapy, chemotherapy, hormone therapy and targeted therapy.

Breast cancer prognosis varies widely depending on factors like the stage at diagnosis, type of cancer, treatment efficacy, and individual patient characteristics. Early detection and advances in treatment have improved survival rates significantly. Regular breast cancer screening and early intervention are critical for better outcomes.

1.4. Curcumin and Quercetin

- Curcumin, a natural compound found in turmeric, has been the subject of extensive research due to its potential health benefits, including its potential cytotoxic effects on cancer cells. MCF-7 is a commonly used breast cancer cell line in scientific research [6,7]
- Quercetin is a flavonoid found in various fruits, vegetables, and plant-based foods. It has been studied for its potential health benefits, including its cytotoxic effects on cancer cells, including breast cancer cells like MCF-7 [8.9]
- Studies have investigated the cytotoxic effects of curcumin and Quercetin on MCF-7 cells, and here is a general overview of some findings:
- Apoptosis Induction: Curcumin and Quercetin has been shown to induce apoptosis (programmed cell death) in MCF-7 cells. This is a mechanism by which cancer cells can be killed off selectively without harming healthy cells [10].
- Inhibition of Cell Proliferation: They can inhibit the proliferation (growth and division) of MCF-7 cells. It does so by affecting various signaling pathways involved in cell cycle regulation [11].
- Anti-Inflammatory Effects: Both curcumin and quercetin possesses anti-inflammatory properties, and chronic inflammation is often associated with cancer development. By reducing inflammation, curcumin may indirectly contribute to the cytotoxic effect on cancer cells [12,13].
- Antioxidant Activity: They also acts as an antioxidant, which can protect cells from oxidative stress. While this may seem contradictory to its cytotoxic effects, the dual role of curcumin as both an antioxidant and pro-oxidant is context-dependent. In some cases, curcumin can induce oxidative stress specifically in cancer cells, leading to their demise [14].
- Disruption of Signaling Pathways: Both components can interfere with various signaling pathways that are dysregulated in cancer cells, such as the NF-κB pathway, which plays a role in cell survival and inflammation [15].
- Inhibition of Angiogenesis: These two compounds may inhibit angiogenesis, the formation of new blood vessels that supply tumors with nutrients and oxygen, which is essential for tumor growth [16].
- Sensitization to Chemotherapy: Curcumin and Quercetin has been investigated as a potential adjuvant in cancer therapy. It may sensitize MCF-7 cells to the effects of chemotherapy drugs, making the cancer cells more susceptible to treatment [17].

1.5. Materials Used

Cell line MCF-7 was obtained from National Centre for Cell Science, Pune, Dulbecco Minimum essential medium, Trypsin EDTA, Foetal calf serum, Phosphate buffer saline, Antimycotic solution, Dimethyl Sulfoxide, MTT-(3-(4, 5-dimethyl thiazol-2yl)-2, 5-diphenyl tetrazoliumbromide were procured from Himedia, Mumbai

2. Methodology - MTT Assay

The MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay [18] is a widely used colorimetric assay for evaluating the cytotoxic activity or cell viability in biological and pharmaceutical research. This assay measures the metabolic activity of cells, which is an indirect indicator of their viability. This assay was carried out to perform the comparative evaluation of curcumin, quercetin with its combination in the effect of MCF-7 cell line of breast cancer. This is a colometric assay that measures the reduction of yellow 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide by mitochondrial succinate dehydrogenase. The MTT gets reduced to an insoluble dark purple coloured formazan product. The cells are then solubilized with an organic solvent such as DMSO and the absorbance is measured spectrometrically. Since the reduction of MTT can only occur in metabolically active cells, the level of acitivity is a measure of the viability of the cells,. The MTT assay also measures the cell viability based on the generation of reducing equivalents in metabolic active cells. The higher the absorbance measured the higher is the cell viability.

Table 1 Cell viability of Curcumin at different concentrations

Concentration Curcumin µg/mL)	**% Cell Death**			**% Live Cells**			**IC50 (µg/mL)**
	Mean	SD	SEM	Mean	SD	SEM	
15.125	52.69	0.73	0.42	47.31	0.64	0.41	14.74
7.8	24.58	1.16	0.67	75.42	1.12	0.57	
3.125	16.37	2.83	1.63	83.63	2.44	1.47	

SD – Standard Deviation and SEM – Standard Error of Mean (Mean of three estimations)

Table 2 Cell viability of Quercetin at different concentrations

Concentration Quercetin (µg/mL)	**% Cell Death**			**% Live Cells**			**IC50 (µg/mL)**
	Mean	SD	SEM	Mean	SD	SEM	
15.125	58.99	3.67	2.12	41.01	2.54	2.14	10.52
7.8	46.04	3.28	1.89	53.96	1.65	1.78	
3.125	34.47	7.81	4.51	65.53	6.54	6.54	

SD – Standard Deviation and SEM – Standard Error of Mean (Mean of three estimations)

Table 3 Cell viability of Curcumin and Quercetin at different concentrations

Concentration of Curcumin and Quercetin (µg/mL)	**% Cell Death**			**% Live Cells**			**IC50 (µg/mL)**
	Mean	SD	SEM	Mean	SD	SEM	
15.125	83.63	1.18	0.68	16.37	0.57	0.57	<3.125
7.8	77.76	0.27	0.16	22.24	0.15	0.14	
3.125	73.50	0.37	0.22	26.50	0.23	0.35	

SD – Standard Deviation and SEM – Standard Error of Mean (Mean of three estimations)

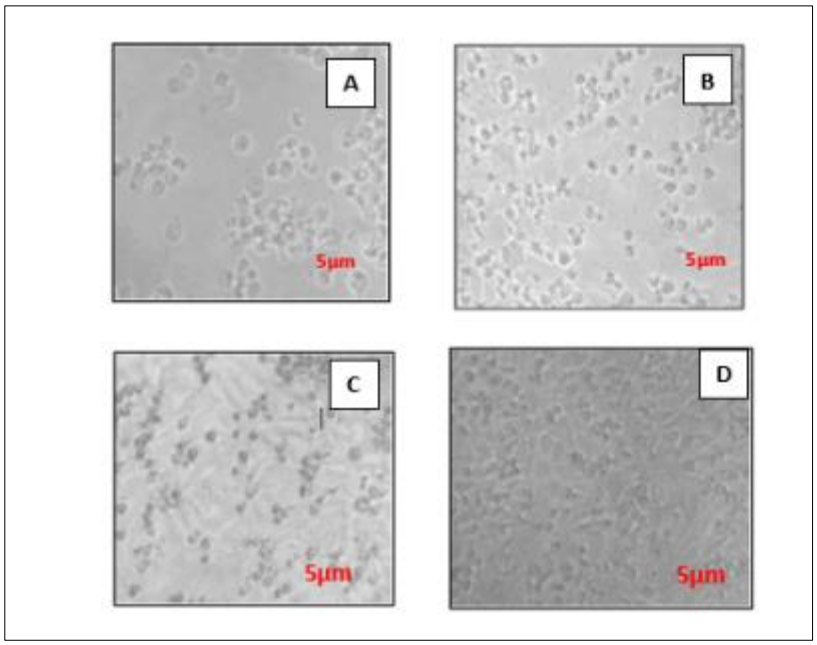

Figure 1 Photomicrographs showing the cytotoxicity of Curcumin at different concentration levels (A – 15.125 µg/mL ; B – 7.8 µg/mL; C – 15.125 µg/mL and D – Control)

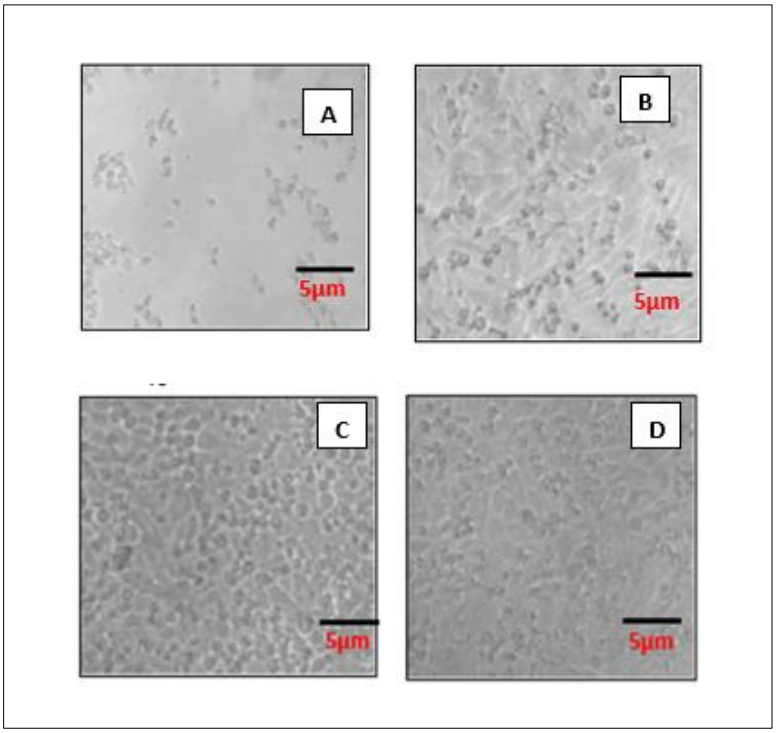

Figure 2 Photomicrographs showing the cytotoxicity of Quercetin at different concentration levels (A – 15.125 µg/mL ; B – 7.8 µg/mL; C – 15.125 µg/mL and D – Control)

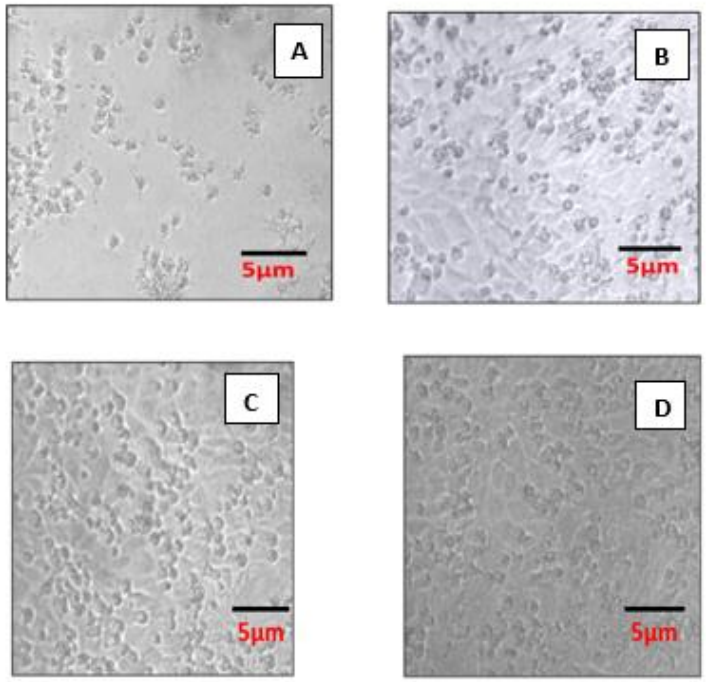

Figure 3 Photomicrographs showing the cytotoxicity of Curcumin and Quercetin combination at different concentration levels in 1:1 ratio (A – 15.125 µg/mL ; B – 7.8 µg/mL; C – 15.125 µg/mL and D – Control)

3. Results and Discussion

The MCF-7 cells were initially maintained in minimum essential media supplemented with 10% FBS, penicillin (100 µg/ml) and streptomycin (100 µg/ml)in a 5% CO2 at 370C. Cells were seeded at 5000 cells /wall in 96-well plates and were incubated for 48 hours. These cells were treated for a period of 24 hrs at the various doses such as 3.9 µg/ml, 7.8 µg/ml and 15.125 µg/ml and the cell viability or death was assessed visually after the treatment period. The viable cells were determined by the absorbance at 570 nm by micro plate reader. The IC 50 values were determined and found to be 14.74 µg/ml for curcumin, 10.52 µg/ml for quercetin and less than 3.125 µg/ml for the combination of curcumin and quercetin in 1:1 ratio. The results are shown in Table 1, 2 and 3. The 96-well plate was observed under an inverted microscope for evidence of cytotoxicity. The figures 1-3 are the representative photomicrographs showing dose dependent increase in the number of rounded cells indicative of apoptosis.

4. Conclusion

In this study, the cytotoxic potential of a curcumin was found to be greater than the cytotoxic potential of quercetin in the individual testing, however the phyto nutrient combination & natural extracts of both curcumin and quercetin shows the better cytotoxic potential in the MCF7 Breast cancer cell line. The combination of both the phytoconstituents shows an effective synergistic effect that can elicit a powerful cytotoxic response on the breast cancer cells. The synergistic effects observed in the combination of curcumin and quercetin on MCF-7 cells suggest that the compounds may act through complementary mechanisms, enhancing their individual anticancer activities. However, it's important to note that the specific synergistic effects and optimal combination ratios may vary depending on the concentrations used, treatment protocols and experimental conditions. Further research, including in vivo studies and clinical trials, is necessary to validate and optimize the potential synergistic effects of curcumin and quercetin in treating breast cancer, particularly in estrogen receptor-positive breast cancer like MCF-7 cells.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

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