Study on finding the role of Peroxisome Proliferator – Activated Receptor -g (PPAR-gamma) agonist Pioglitazone in A549 Lung Adenocarcinoma Cell line

Purushoth E[1], Daphne Bernice V[2], Shila S[2]

[1]SRM Medical College Hospital and Research Centre, SRM University, [2]Udaya School of Engineering, Udaya Nagar, Vellamodi, [3]VRR Institute of Biomedical Science, kattupakkam, Chennai - 56

Background: Pioglitazone is a synthetic ligand of nuclear receptor peroxisome proliferator-activated receptor PPAR-gamma that is approved for the treatment of type2 diabetes mellitus. PPAR-gamma has been associated with anticancer activities in a variety of cancer cell lines through inhibition of proliferation and promotion of apoptosis. The exact mechanism of PPAR-gamma to cancer growth inhibition remains unclear.

Aim: The present study is aimed to find the anti-proliferative and apoptotic effect of pioglitazone on lung adenocarcinoma cell lines (A549.).

Materials and Methods: A549 Lung adeno carcinoma cell line was used for the study. Cells were treated with different concentrations of pioglitazone (5, 25, 50,100 μM). The cytotoxic effect was assessed by Tryphan blue assay and apoptosis by DNA fragmentation assay and protein expression of PPAR-gamma and MMP 9 by western blot technique.

Results: On treatment with pioglitazone, the morphology of A549 cells was changed in a time and dose dependant manner. At 100μM concentration, the change in cell morphology was observed immediately. The percentage of viability showed significant ($p<0.05$) reduction of viable cells at 100 μM concentration at 24h and 48h and more significant ($p<0.01$) at 72h. At 25 and 50 μM concentration the significance ($p<0.05$) was observed from 48hrs. Treated cells showed significant increase in PPAR-gamma expression with respect to the increasing dose, but MMP 9 expression was decreased with respect to higher dose. The DNA fragmentation results showed multiples of 180 bp, and produced band width of 1440 and 720 bp at the concentration 100 μM.

Conclusion: It is concluded that pioglitazone causes change in cell morphology, reduction in cell viability, DNA fragmentation and inhibition of MMP 9 expression by activation of PPAR-gamma expression.