This study was done to evaluate the possible cytotoxic effects of black seed on lung cancer cells and to determine its IC\textsubscript{50} alone and in combination with cisplatin, and to study its effects on the expression of each of p53 and EGFR. QU-DB lung cancer cells were cultured in Eagle's MEM medium with 5\% FBS and antibiotics. The cells were seeded in 96 well plate and the cytotoxic effects of each of cisplatin [25-0.195 µl/ml (or µg/ml)] and black seed [300-1.1719 µl/ml (each one µl is extracted from 25 µg of dried seed)] was determined using neutral red uptake (NRU) assay for 24, 48, and 72 hours in comparison with their corresponding control groups. Combined effect of black seeds with cisplatin was determined also using NRU assay. Cytotoxicity was further assessed by trypan blue exclusion assay at IC\textsubscript{50} of each agent for 48 hours duration. Immunocytochemistry assay was performed also to detect p53 and EGFR expression. Cisplatin induced a directly proportional, dose-dependent and time-dependent cytotoxic effect with an IC\textsubscript{50} of 8.5µg/ml and 7.3 µg/ml after 48 hrs and 72 hrs of exposure respectively. Significant differences (p<0.05) were observed in optic density of cisplatin group from that of the control for all tested concentrations. Black seed extract induced a directly proportional, dose-dependent and time-dependent cytotoxic effect in experiments with 48 hrs and 72 hrs of exposure with an IC\textsubscript{50} of 149.5 µl/ml and 130 µl/ml respectively (each one µl is extracted from 25 µg of dried seed). While it produces a protective effect in 24 hrs exposure experiment. Significant differences (p<0.05) were observed in optic density of black seed from that of the control at concentrations of 75 µl/ml and above. Black seed produce an antagonistic action when combined with cisplatin, combination index (CI) >1.3. Cisplatin highly significantly (p<0.005) increased EGFR expression at different concentrations. While black seed extract highly significantly (p<0.005) reduced EGFR expression at 300 µl/ml (each one µl is extracted from 25 µg of dried seed). Cisplatin and black seed highly significantly (p<0.005) decreased the expression of P53. In conclusion: monotherapy of black seed have anticancer effects on lung cancer cell line, but an antagonizing effect to cisplatin when combined with it. Black seed may have a beneficial therapeutic effect in decreasing EGFR expression and decreasing mutant p53 expression.