Demethoxycurcumin (DMC) , a phenolic compound obtained from rhizome of *Curcuma longa*, is known to have antiproliferative and antitumor properties. Nucleotide excision repair (NER) is the primary DNA repair mechanism that removes platinum-DNA adducts from DNA. Excision repair cross-complementing 1 (ERCC1) is a critical protein in the NER mechanism. The aim of this study is to investigate whether DMC could potentiate Cisplatin–induced apoptosis through down regulation of ERCC1-related pathways in the NSCLC. First, the cell viability was determined by MTT assay. The data showed that DMC has cytotoxicity to A549 cells, but did not affect MRC-5 cell viability. Furthermore, to identify DMC-induced apoptotic pathway on A549, apoptotic protein levels were measured by western blotting. DMC treatment markedly increased Bax/Bcl-2 ratio, and Cytochrome *c* expression that were correlated with post-target Cisplatin resistance pathway. In addition, it was found that DMC also significantly inhibited on target protein, ERCC1, expression via PI3K- Akt- Snail pathway. Moreover, we also revealed that DMC alleviated ERCC1 protein through reducing TP expression. And, we created a model of short-term exposure to Cisplatin up-regulated ERCC1-related protein in A549 cells that we could continue the combination of DMC and Cisplatin. Importantly, it was found that, followed by CDDP treatment, DMC could inhibit ERCC1–related signalling pathways, which have been validated to reduce ERCC1 protein expression and which significantly increased apoptosis induced by the combination of CDDP and DMC. In conclusion, our results revealed that DMC can reduce both the on-target and post-target related proteins induced Cisplatin resistance.