Curcumin [Diferuloylmethane] is a major component of turmeric [Curcuma longa], which is used as a spice to give a specific flavor and yellow color in Asian food. The application of curcumin as a radiation sensitizer on PC-3 prostate cancer cells was investigated. Curcumin at 2 μM and 4 μM concentrations in combination with radiation showed significant enhancement of the clonogenic inhibition and apoptosis induced by radiation. The clonogenic enhancement of the radiation was found to be a factor of 2.6 and 7 for addition of 2 μM and 4 μM of curcumin, respectively. The enhancement of the radiation effect by curcumin can be partially attributed to the reduction or reversal of pro-survival factors (e.g. TNF-α, NFκB, Bcl-2) within PC-3 cells, which occur when they are treated with radiation alone. In addition, the down regulation of Bcl-2 and no changes in Bax protein levels in curcumin plus radiation treated PC-3 cells, altered the Bcl2:Bax ratio which caused the enhanced radiosensitization. In addition, significant activation of cytochrome c, caspase-3, and caspase-9 were observed in curcumin plus radiation treatments. Together, these mechanisms strongly suggest that the natural compound curcumin is a potent radiosensitizer acting through deteriorating the mitochondria of PC-3 prostate cancer cells.