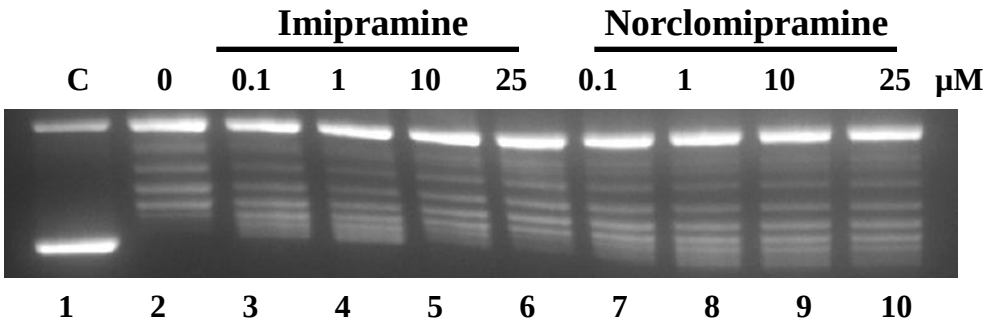
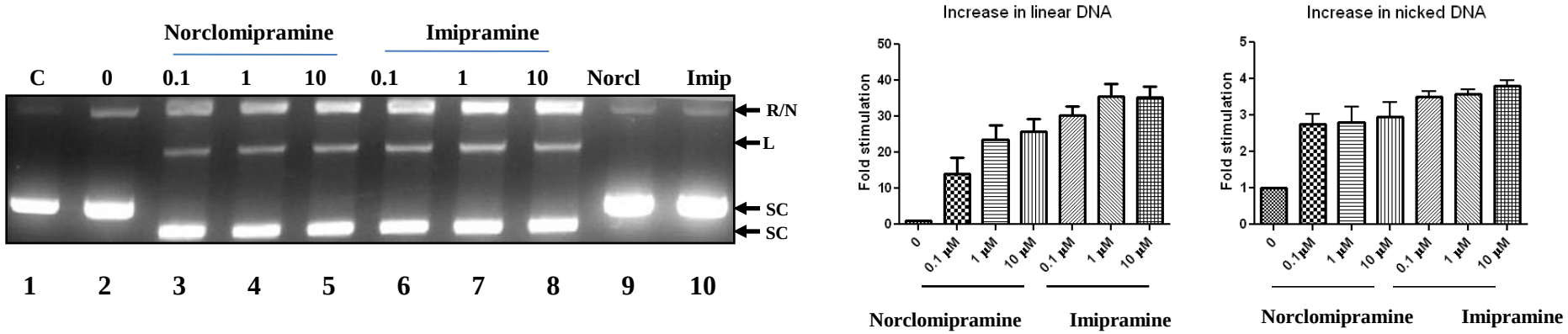
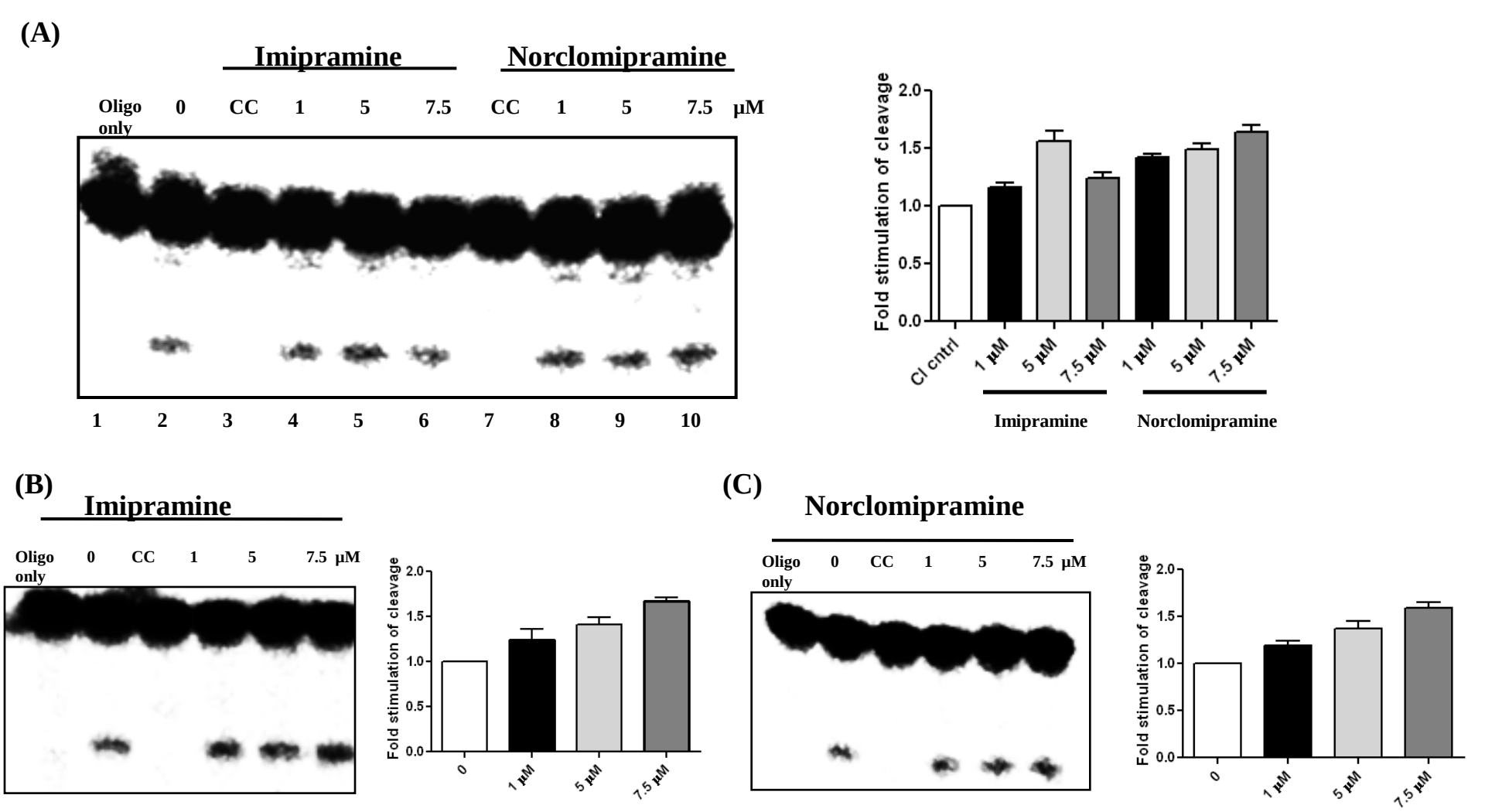


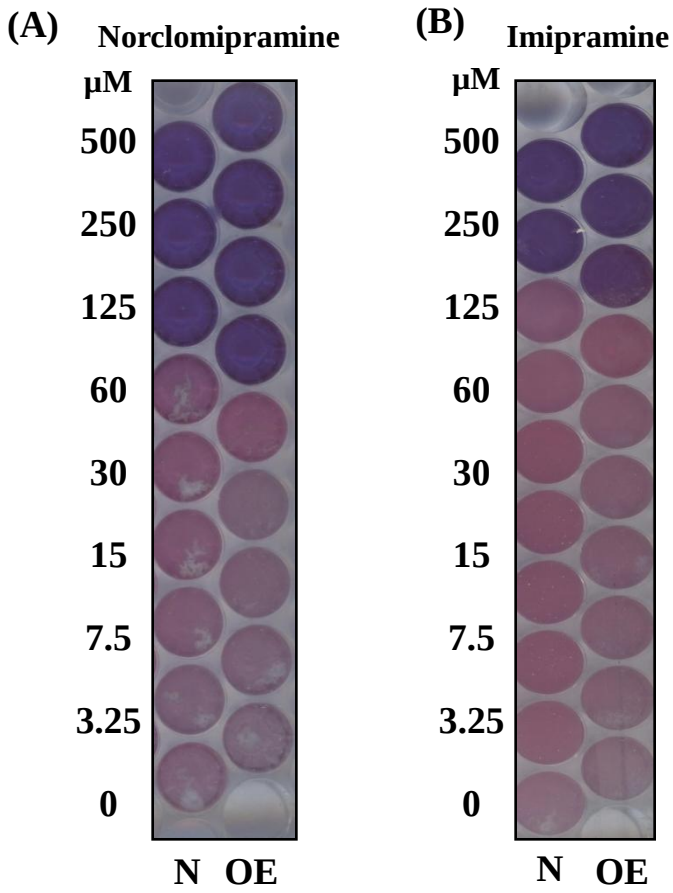
Supplementary Fig.1: DNA relaxation activity of EctopoI is not affected by imipramine or norclomipramine: 1 unit of EctopoI was incubated with various concentrations of the molecules at 37^{o}C for 15 min following which, 500 ng of supercoiled pUC18 was added. The incubation was further continued at 37^{o}C for 30 min and the reactions were terminated by addition of 0.6% SDS-agarose dye. The reaction products were resolved on a 1.2 % agarose gel followed by staining with EtBr. Lane 1, supercoiled pUC18 ; lane 2, relaxation reaction in the absence of compound; lanes 3-6, various concentrations of imipramine; lanes 7-10 , various concentrations of norclomipramine.



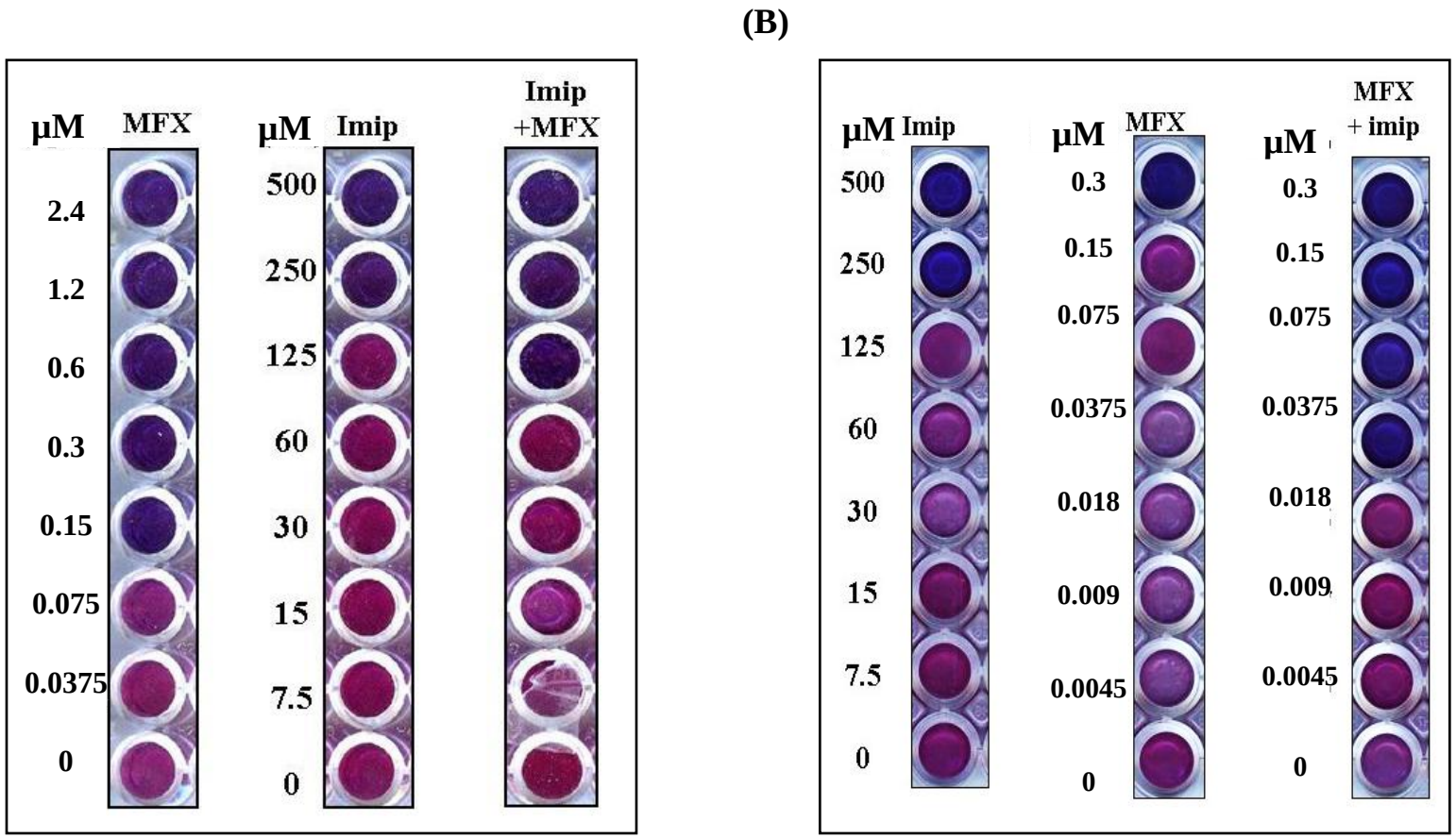
Supplementary Fig.2:Plasmid cleavage assay: Increasing concentrations of the compounds were incubated with 2 units of MttopoI at 37^{o}C for 15 min following which 500 ng of supercoiled pUC18 was added and the reactions were allowed to proceed at 37^{o}C for 30 min. The reactions were terminated by addition of 0.6% SDS-agarose dye. The reaction products were resolved on a 1.2 % agarose gel and visualized by a gel documentation system. . Lane 1, supercoiled pUC18 ; lane 2, cleavage reaction in the absence of compound; lanes 3-5, various concentrations of norclomipramine; lanes 6-8 , various concentrations of imipramine. Lanes 9 and 10 pUC18 incubated with only compound in absence of MttopoI. . Error bars in the graphs represent the standard deviation obtained in three experiments. R/N indicates relaxed or nicked DNA; L indicates linear DNA; SC indicates negatively supercoiled DNA



Supplementary Fig.3:Oligonucleotide cleavage assay: (A) Increasing concentrations of imipramine (lanes 4-6) or norclomipramine (lanes 8-10) were incubated with 5'end labeled specific 32-mer annealed to a complimentary sequence at 37^{o}C for 15 min followed by the addition of MttopoI and the reactions were allowed to continue at 37^{o}C for 30 min. **(B,C)** Alternatively, increasing concentrations of imipramine or norclomipramine were incubated with MttopoI at 37^{o}C for 15 min followed by addition of double stranded 32-mer DNA and the reactions were allowed to continue at 37^{o}C for 30 min. The reactions were terminated by the addition of 45% formamide and heating at 95^{0}C for 2 min. The products were resolved on a 12% denaturing PAGE and analyzed by phosphorimager. CC indicates compound control in all panels. Graphs indicate quantification of cleavage product. . Error bars represent the standard deviation obtained in three experiments.



Supplementary Fig.4: Increased cytotoxicity upon topoI over expression in *M. tuberculosis*: *M. tuberculosis* H_{37}Ra cells expressing normal levels of MttopoI (WT) or over expressing MttopoI (OE) were grown in presence of various concentrations of **(A)** norclomipramine or **(B)** imipramine. The plates were incubated at 37^{o}C for 7 days. Untreated culture was taken as control. Resazurin dye was added to a final concentration of 0.02 % and the plates were further incubated at 37^{o}C for 14 hr to determine the MIC values. N indicates *Mtb* cells expressing normal levels of TopoI; OE indicates *Mtb* cells over expressing TopoI



Supplementary Fig.5: Combining imipramine with moxifloxacin affects the growth of *M. tuberculosis* cells : (A) Sublethal concentration of moxifloxacin was combined with various concentrations of imipramine (0 - 500 µM); lane 3. The *M. tuberculosis* cells were grown in the presence of this combination at 37^{o}C for 7 days after which resazurin dye was added to the cultures and further incubated at 37^{o}C for 14 hrs. **(B)** Sublethal concentration of imipramine was combined with various concentrations of moxifloxacin (0 – 0.3 µM); lane 3. The *M. tuberculosis* cells were grown in the presence of this combination at 37^{o}C for 7 days after which resazurin dye was added to the cultures and further incubated at 37^{o}C for 14 hrs. In both cases, cells grown in the presence of only imipramine or only moxifloxacin were used as controls.