Abstract

Cancer possesses a big challenge in the developing world. The available therapeutics fails to fully cure cancer because cancer cells use the DDR pathway to tackle the DNA damage induced by the genotoxic therapeutics. It is proven that inhibition of the kinases involved in the DDR pathway in the presence of genotoxic therapeutics can force cancer cells to undergo apoptosis. Hence, our focus was on ATM kinase, the key mediator of the DDR pathway. The X-ray crystal structure of the active monomeric ATM kinase is unresolved till date, and it possesses a huge challenge in designing inhibitors for ATM kinase. Here in this study, the expression of ATM kinase in soluble form was successfully performed using *E. coli BL21(DE3)* bacterial expression host and purification of expressed ATM kinase was carried out. Results showed that further optimization of the buffer compositions and purification is needed. Cell biological studies with designed inhibitors were also carried out using HCT116 cell line. Inhibitors of ATM kinase were synthesized and tested against HCT116 cells pre-treated with quercetin, which induces DNA damage. We report that the synthesized inhibitors showed promising cytotoxicity towards HCT116 cells, and Western-Blot analysis confirmed the down-regulation of ATM kinase after induction of DNA damage by quercetin.