Abstract

Combinatorial therapy might be the solution for the rising incidence of CRC around the world. By combining multiple anti-cancer drug, a more effective cancer killing ability might be produced at lower dosage and toxicities. As a potential anti-cancer sources, ethyl acetate extract of soursop leaves (EEAM) has been reported to work against HT-29 CRC cell line. The mechanism in which it may works remains unknown. Another possible anti-cancer drug sources are repurposed drug, with simvastatin being one of them. In this experiment we tried to elucidate the effect of combining both EEAM and simvastatin against HT-29 CRC cell line, through cell viability and cell death assessment. In addition, we also perform molecular docking study of one of the active compounds in the extract, annomurcin E, to explore potential mechanism in which the extract might works. Combination of both compounds resulted in antagonistic interaction, with worse anti-cancer effect compared to both individual drugs. The EEAM does not induce cell death despite able to cause lower cell viability compared to simvastatin. The docking analysis showed the ability of annomuricin E to inhibit Complex I and Complex III (BC1) of mitochondria, all of which has potential to induce cell cycle arrest and eventual cell death. It is also revealed that simvastatin also able to bind to those complexes, without inducing inhibition. The complex III in particular, had the same binding location for both simvastatin and annomuricin E. Thus, it is possible that simvastatin acting as a competitive inhibitor, lowering the efficacy of EEAM to induce cellular senescence. Regardless, the combination of both EEAM and simvastatin produce an unfavored anti-cancer activity and should not be pursued as cancer treatment.