8. Summary & Conclusion

Cervical cancer is the serious issue in the developing countries though the vaccinations and the regular screening programs are available. The present study was on the \textit{in silico} and \textit{in vitro} inhibition of viral oncoproteins using idaein chloride.

1. The clinical analysis of 50 FFPE tissues showed the occurrence of high risk human papilloma virus (HPV) of both 16 and 18 types in 35 samples. PCR amplification on E6 & E7 regions integration was confirmed in HPV positive samples and E2 regulatory region disruption was also observed in the clinical samples.

2. During \textit{in silico} docking analysis on 5 different anthocyanidins, only idaein chloride showed good solubility with lesser log p value (1.018) and docking score (-23.3). Further, 15 hydrogen bond and 17 aminoacids had actively participated in the docking/ inhibition of viral oncoproteins. Idaein chloride exhibited radical scavenging activity on DPPH and ABTS at the inhibitory concentration values (μg/ml) of 12 & 23.66 respectively.

3. Idaein chloride showed potential anticancer effect on human papillomavirus (16 & 18) positive HeLa and CaSki cell lines with the IC$_{50}$ values (μg/ml) of 2.579 and 31.64 respectively. Apoptotic hallmarks of Sub G1 phase induction indicated the fragmented DNA, significantly reduced expression of oncoproteins (p < 0.05), the restoration of p53, downregulated cell cyclins, cyclin dependent kinases, cleaved caspases in both cell lines and thus confirming the cytotoxic activity of idaein chloride.

4. The idaein chloride had the potent anticancer effect on the different grades of cervical cancers with the IC$_{50}$ values (μg/ml) of 37.14 for SiHa, 1.885 for C-33A, 8.107 for C-4 I and 20.11 for C-4 II. The expressed levels of cyclin proteins and their kinases induced the cell cycle arrest, oncoproteins (E6 & E7) inhibition and tumor suppressor proteins (p53, p21, p16 & Rb) restoration and thus confirming the occurrence of apoptosis in a sequential manner.
5. It is proposed that the possible inhibitory mechanism of Idaein chloride on human papilloma virus could have been p53 dependent apoptosis as depicted here:

The presently generated data on the action of idaein chloride cytotoxic potential and hpv oncoproteins down regulation in cervical cancer form important baseline information and further studies are warranted in transfected animals, for the validation of the present findings.