10.1 Conclusion:

The alkylation pathways of mitomycin drugs have been studied. The interaction ability of aziridine ring of mitomycin with \(-\text{NH}_2\) of guanine is not found promising. The influence of ions on aziridine ring is prominent for undergoing acid catalysed alkylation pathway. The formation of C1 carbocation for undergoing electrophilic pathway is essential for alkylation. Subsequently, the formation of monoadduct and biadduct as a result of alkylation with C1 and C10 carbocations of mitomycins has been studied. The alkylation abilities of these cationic centres are different. The bialkylated adducts are more stable than the monoalkylated adducts.

The model study on the change of acidic nature of hydrogen bond in GC due to alkylation has been analysed. The acidic behaviour of hydrogen bond in GC has been studied from the potential energy plots. Due to alkylation with \(-\text{NH}_2\) group of guanine the acidic behaviour within GC has been changed significantly. Hence, the alkylation of several mitomycins may produce significant effect on the proton transfer profile within GC.

Intercalation of daunomycin within DNA is an important feature that may be relevant to therapeutic value. The intercalating ability of daunomycin within base pairs are found quite different. Certain regions (aromatic rings) are found quite effective for intercalation whereas strong steric effects from certain groups are also found. The chromophore can stack more favourably with GC than AT. The interaction energies (MP2/6-31G*) of stacked chromophore with GC for the minor and major groove orientations are almost equal, and the respective values are -13.248 kcal/mol and -13.232 kcal/mol. The corresponding values for stacked chromophore with AT are -11.542 kcal/mol and -11.398 kcal/mol respectively.

The intercalations of daunomycin within certain oligonucleotide reported in crystal structures have been analysed. The base pair selectivity by chromophore can not be explained from the stacking and intercalation interactions. Here, the interaction energy of stacked chromophore with AT is found more negative than that of than stacked chromophore with GC, which is contradictory to the intercalation of this drug within CG/GC sequences rather than TA/GC sequences. It indicates that the side chain of drug might involve in DNA binding.
The intercalation of 9-aminoacridine and its analogues has been explored from the available crystal structure database. The stacking abilities of these chromophores with nucleobases obtained from MP2/6-31+G(d,p) range from -10.526 to -17.539 kcal/mol and the values for intercalation range from -29.419 to -32.977 kcal/mol respectively. The difference of stacking energies rather depend on the position of stacked 9-aminoacridine. The stacking energies have been used to explain the intercalation of this molecule within the oligonucleotide. The stacking interactions of 9-aminoacridine with nucleobases are more effective than that of stacked nucleobases.

The stacking interactions of nucleobases of few oligonucleotides have been calculated with various methods. The nucleobases present in the DNA sequences are not aligned in totally stacked positions and the calculated stacking energies [MP2/6-31++G(d,p)] for G$^{11}$/C$^{12}$ (-16.526 kcal/mol) sequence (PDB1LA1) is found stabilised better than the other sequences. Similarly, for PDB1K9L, the stacking of A$^{5}$/G$^{6}$ (-13.447 kcal/mol) sequence is found stabilised better than the other sequences.