Annexure II

Executive Summary of the work done in the UGC Major Research Project project entitled "
***In silico* design, synthesis and evaluation of newer azoles as HIV-1 RT inhibitors**

3D QSAR studies on a series of NAIMs analogues synthesized by Lagoja *et al* (Model 1) combined with the DAMNI series synthesized by Silvestri *et al* (Model 2)using Sybyl 7.1 was carried out by us. A 3D QSAR model was developed.

Based on the model developed various azo;les were designed viz., benzimidazoles, thizolidine diones, triazoles, pyrazoles and imidazoles.

Docking studies of these azioles was carried out in the active site of non nucleoside inhibitory binding pocket of enzyme reverse transcriptase(PDB ID 1 RT2).

Based on the docking studies a number of the azoles were synthesized and characterized by 1H NMR, Mass spectra and elemental analyses.

All the compounds were subjected to HIV-1-RT assays and the activities were ascertained.

It was found that the thjiazolidine diones and imidazoles had some significant activity against HIV-1-RT while benzimidazoles, traizoles and pyrazoles showed mild to moderate activities.

Based on the significant activities of thiszolidine diones and imidazoles bindinmg mode analyses was carried out of the most significant compounds fromeach series respectively in the non nucleoside inhibitory binding pocket of HIV-!-Reverse transcriptase.(PDB ID: 1 RT2)

Virtual ADME studies were carried out of all the compounds and it was found that all of them obeyed Lipinski's rule of five, thus all of the compounds were drug like or lead like.

Based on the observations, it was concluded that two hydrophobic groups suitable substituted by electron withdrawing hydrophobic groups with a hydrophilic linker in between attaching the two hydrophobic moieties are responsible for anti HIV activity.