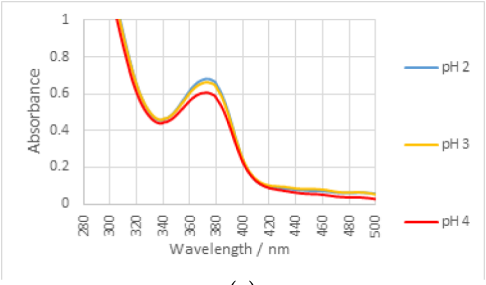
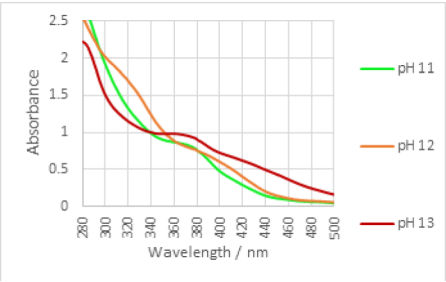


(a)



(b)

Figure 2: UV-Visible spectra of the red catappa leaf extract (a) pH 2 – 4, (b) pH 11 - 13

The methanolic extract of Terminalia catappa red leaves possesses pH sensitivity, and shows colour changes from red orange to yellow when the pH changes from 2 to 3, and from green yellow to purple when the pH changes from 12 to 13. It can be used to develop a natural pH indicator which is environment friendly and less toxic compared to synthetic indicators.

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Technical Sessions : A - 27

The inhibition of acetylcholinesterase *via* synthetically viable coumarin derivatives

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Acetylcholinesterase is a serine hydrolase responsible for the hydrolysis of acetylcholine. The reversible inhibition of acetylcholinesterase can be useful in combating Alzheimer's disease (AD). A computational study of the inhibition of acetylcholinesterase was conducted by performing Molecular Docking using a series of coumarin analogs generated by fragment based drug design methods.

The crystal structure with the PDB ID 1GQR was chosen as the receptor for docking studies. The synthetic coumarin analogs were each subjected to an energy minimization via the Spartan version 14 program, the level of theory being B3LYP /6-31G**. The drugs, rivastigmine and tacrine were used as reference molecules for identifying potential drug candidates by comparing the docking score and the interactions of the ligand with the active site. These two reference molecules were docked using Autodock Vina. The binding affinities are given in Table 1.

Table 1. Binding Affinities

Ligand	Binding Affinity(kJ/mol)
C_15	-11
C_06	-11
C_10	-10.5
C_05	-10
C_01	-9.9
C_13	-9.7
C_11	-9.6
C_14	-9.5
C_09	-9.4
C_07	-9.1
Tacrine	-8.9
C_02	-8.8
C_16	-8.7
C_12	-8.5
C_04	-8.4
C_08	-8.4
C_03	-8.2
Rivastigmine	-7.9
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The parent structure (Figure 1) was subjected to systematic changes by introducing different moieties at 'R', hence generating a series of coumarin analogues that were used in this study as shown in Figure 2. Note that an asterisk (*) is used to show where the moiety connects to the parent.

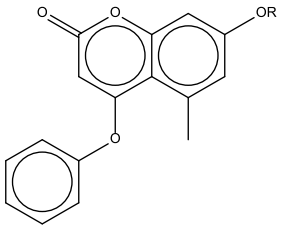

Figure 1: Parent Coumarin Structure

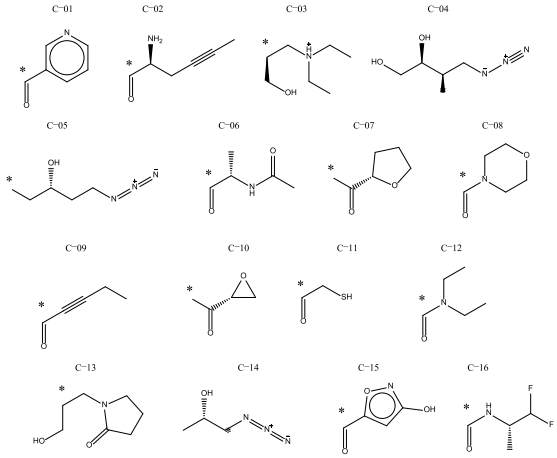

Figure 2: Structure of R side chains in the different coumarin analogues used in the study

This step was achieved by a programme called Autogrow 3.0. The set of ligands generated are synthetically viable to a significant extent. These ligands were screened through the following filters; Lipinski's Rule of Five, Criteria specified by Ghose et al. - calculated log P being between -0.4 and 5.6 with an average value of 2.52. For molecular weight, the qualifying range is between 160 and 480 with an average value of 357. For molar refractivity, the qualifying range is between 40 and 130 with an average value of 97. For the total number of atoms, the qualifying range is between 20 and 70 with an average value of 48.

The selected molecules were then docked into the prepared 1GQR structure using Autodock Vina and the binding affinities are reported in Table 1.

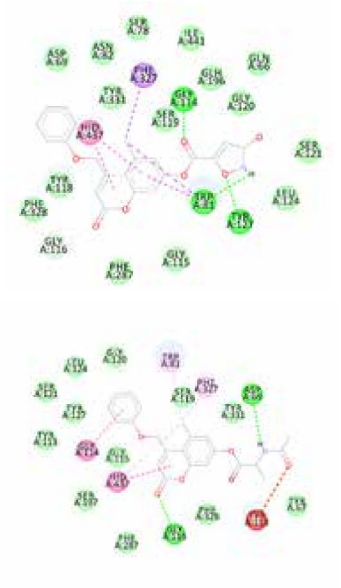

Figure 3: Interactions of C_15 and C_06

The 5 ligands showing the most favorable scores (highlighted) have electron withdrawing functional groups as the R side chain. The most favourable binding affinities are for ligands C_06 and C_15. Although both ligands have the same binding affinity, C_06 has an unfavourable interaction with Tyrosine 118. Ligands bearing side chains that formed pi-pi and pi-sigma interactions and hydrogen bonding with the residue Tryptophan 81 had a higher binding affinity. Due to this reason, ligands C_15, C_06, C_10, C_05 and C_01 appear to be accommodated in the binding pocket well.

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