ABSTRACT

The thesis entitled “Design, synthesis and biological evaluation of acridine and quinazolinone based heterocycles” is divided into five chapters.

Chapter 1: It deals with the synthesis of 7-chloro-3,4-dihydro-9-phenylacridin-1(2H)-one, 1.33 and (E)-2-Benzylidene-7-chloro-9-phenyl-3,4-dihydroacridin-1(2H)-ones, 1.44a-f. All the synthesized compounds, 1.33 and 1.44a-f were confirmed by suitable experimental and spectroscopic techniques. All compounds were evaluated for antioxidant activity by DPPH free radical scavenging method. The results indicated that compounds, 1.44a and 1.44b have good antioxidant activity. Compound, 1.44b show moderate activity when compared with standard ascorbic acid. The antioxidant activities of these compounds were strongly associated with the type of substitution on the benzene ring. The results of this study provide useful information for further structural optimization of these compounds.

Chapter 2: It constitutes the synthesis of ethyl 10-chloro-4-(3,4-dimethoxyphenyl)-2-hydroxy-12-phenyl-1,4,5,6-tetrahydrobenzo[a]acridine-3-carboxylates, 2.39a-e and 1-(9-chloro-3,3a,4,5-tetrahydro-3-(3,4-dimethoxyphenyl)-11-phenyl pyrazolo[3,4-a]acridine-2-yl)ethanone isomers, 2.41a-e and 2.42a-e. Synthesized compounds, 2.39a-e, 2.41a-e and 2.42a-e were evaluated for larvicidal activity against Anopheles stephensi and C. Quinquefasciatus. The bioassay results indicated that acridine-3-carboxylate derivative, 2.39b and 2.39d and acridine pyrazole isomers, 2.41c and 2.42a exhibit higher larvicidal activities when compared with other derivatives. Further, the active compounds were tested against non-target aquatic species, like Sphaerodema annulatum Fabricius (Heteroptera: Belostomatidae) and Zyxomma petiolatum Rambur (Odonata: Libellulidae). The results showed low LC₅₀ values. From this, we have concluded that the synthetic compounds were non toxic to non-target organisms.

Chapter 3: In this chapter the synthesis of 10-chloro-4,12-diphenyl-5,6-dihydropyrimido[4,5-a]acridin-2-amines, 3.34a-f and 2-amino-10-chloro-1,4,5,6-tetrahydro-4-(3,4-dimethoxyphenyl)-12-phenylbenzo[j][1,7]phenanthroline-3-carbonitriles, 3.37a-f were performed. All the compounds were confirmed by suitable experimental and spectroscopic techniques. In this present study we have evaluated in
vitro α-amylase, α-glucosidase inhibitory activity and glucose diffusion tests of compounds, 3.34a-f. Compounds 3.34c and 3.34e showed significant inhibition activity. The predictive mode of highly active compounds to the α-amylase and α-glucosidase from point of protein-ligand interaction was studied. The docking calculations showed Van Der Waal’s electrostatic and desolvation energies play a key role in binding. These factors are considered for designing the inhibitors for α-amylase and α–glucosidase. Antioxidant activity results that compound, 2-amino-10-chloro-4-(2,5-dimethoxyphenyl)-12-phenyl-1,4,5,6-tetrahydrobenzo [j][1,7]phenanthroline-3-carbonitrile, 3.37b showed good antioxidant results when compared with all other derivatives.

Chapter 4: In this present chapter, we have synthesized novel 2-amino-10-chloro-4,12-diphenyl-5,6-dihydro-4H-pyran[2,3-a]acridine-3-carbonitrile derivatives, 4.43a-f. Further, compounds 11-chloro-5-(3,4-dimethoxyphenyl)-13-phenyl-6,7-dihydro-1H-pyrimido[5′,4′:5,6]pyrano[2,3-a]acridin-4(5H)-one, 4.44a, 11-chloro-5-(3,4-dimethoxyphenyl)-13-phenyl-6,7-dihydro-4Hpyrimido[5′,4′:5,6]pyrano[2,3-a] acridin-4-one, 4.44b and 10-chloro-4-(3,4-dimethoxyphenyl)-12-phenyl-3-(1H-tetrazol-5-yl)-5,6-dihydro-4H-pyran[2,3-a]acridin-2-amine, 4.44c ethyl 10-chloro-4-(4-chlorophenyl)-2-hydroxy-12-phenyl-1,4,5,6-tetrahydrobenzo[a]acridine-3-carboxylate, 4.44d 10-chloro-4-(3,4-dimethoxyphenyl)-2-oxo-12-phenyl-5,6-dihydro-2H-pyran[2,3-a]acridine-3-carbonitrile, 4.44e were synthesized using an intermediate 2-amino-10-chloro-4-(3,4-dimethoxyphenyl)-12-phenyl-5,6-dihydro-4H-pyran[2,3-a]acridine-3-carbonitrile, 4.43a. All the compounds were confirmed by suitable experimental and spectroscopic techniques. The synthesized derivatives were subsequently evaluated for its cytotoxicity by the MTT assay on human hepatocellular carcinoma (HepG2) cell line after and during a period of about 6 days. The cells were exposed to concentrations of 0 % (control), 5 %, 10 %, 15 %, 20 % and 25 %. Further, HDAC enzyme activity was performed. MTT assay revealed that all compounds when tested were found to cause DNA damage and cell death in a dose dependent manner. Using the MTT assay, we have demonstrate that, in general, the cytotoxic effects of fried meat extracts correlated with the extent of DNA damage observed in the HepG2 cells. Compound, 4.44b showed potent inhibitory activity in a histone deacetylase (HDAC) enzyme assay.
**Chapter 5:** This chapter deals with the synthesis of 10-chloro-2-ethoxy-4,12-diphenyl-5,6-dihydrobenzo[j][1,7]phenanthrolines, \(5.36a-h\) 10-chloro-4-(3,4-dimethoxyphenyl)-2-ethoxy-12-phenyl-5,6-dihydrobenzo[j][1,7]phenanthrine-3-carbonitrile, \(5.39a-d\) and 2,3-disubstituted 2,3-dihydroquinazolin-4(1H)-ones, \(5.42a-g\) via reusable catalyst. In this present study, we have developed the first example of regioselective 5,6-dihydrobenzo[1,7]phenanthrolines, \(5.36\) using NaH as base. The expected 5,6-dihydrobenzo[1,7]phenanthrene-3-carbonitriles, \(5.39\) was obtained by Montmorillonite KSF clay as catalyst. These data have lead to the development of an alternative and straight forward mechanistic pathway for Michael addition reaction. This report provides an easy method for direct access to regioselective expected and unexpected compounds. Further, we have successfully synthesized the TiO\(_2\) nanoparticles using aqueous A. squamosa peel extract. These synthesized TiO\(_2\) nanoparticles were characterized using UV, XRD and TEM. The synthesized TiO\(_2\) nanopowders were used as a catalyst for 2,3-dihydro-3-methyl-2-phenylquinazolin-4(1H)-one analogues, \(5.42a-g\) synthesis. All compounds were confirmed by suitable experimental and spectroscopic techniques.