ABSTRACT

Title: ***"Tuning of novel organic scaffolds for competent detection of bio-relevant, environmentally hazardous ions and chemical weapons"***

Submitted by

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The design and fabrication of fluorescence chemosensors is a highly interdisciplinary field of research today, owing to their significant importance and wide-ranging applications in chemistry, biology, medicine, environmental science, and beyond. My thesis work entitled, **"Tuning of novel organic scaffolds for competent detection of bio-relevant, environmentally hazardous ions and chemical weapons"** involves the design and synthesis of a range of fluorescent and non-fluorescent probes, supported by thorough binding studies aimed at the accurate detection of targeted ions and toxic analytes. The structures of the synthesized probes were validated using a combination of spectroscopic techniques, such as ^{1}H and ^{13}C NMR, mass spectrometry, IR spectroscopy, and single-crystal X-ray diffraction. The binding interactions of the host-guest system and the resulting complex or adduct formation were comprehensively analyzed using UV-Vis spectroscopy, fluorescence, Job's plot, $^{1}H/^{13}C$ NMR, and HRMS. The biological relevance of the designed probes was investigated through their application as imaging agents in live-cell studies. To gain deeper insight into the sensing mechanisms, Density Functional Theory (DFT) calculations were carried out in the Gaussian 09 software suite.

Chapter 1 provides a brief introduction to the fundamental concepts of chemosensors, including their definitions, classifications, and the underlying principles of various non-covalent interactions. Additionally, a concise yet comprehensive literature review is presented, highlighting various reported chemosensors based on different molecular recognition mechanisms.

Chapter 2 outlines the detailed instrumentation techniques employed in the characterization and analysis of chemosensors, including ^{1}H and ^{13}C NMR, IR spectroscopy, HRMS, UV-Vis absorption, fluorescence spectroscopy, lifetime decay measurements, and single-crystal X-ray crystallography. This chapter also describes essential analytical methods such as quantum yield calculation, detection limit estimation, and association constant determination, which are crucial for the comprehensive evaluation of molecular sensing probes.

Chapter 3 represents with the fabrication and charecterization of a highly sensitive, reversible, reusable and fluorogenic ''turn-on'' probe (HBTC) for the sole detection of Al^{3+}. On incremental addition of Al^{3+} in a solution of HBTC in ACN: H_2O (4: 1), a sharp ''turn-on'' emission enhancement is observed. The reusability

and real-time application of the probe were also studied. Bioimaging study reveals that HBTC can detect Al^{3+} in human breast cancer cells (MDA-MB-231).

Chapter 4 presents the fabrication of a biphenyl thiosemicarbazide based chemosensor (HBMC) which showed specific detection of Cd^{2+} in MeOH: H_2O (4:1) solution. Where we observed a chromogenic change from colorless to light yellow colour, as well as it shows a "turn-on" fluorogenic change from non-fluorescent to blooming cyan colour. Moreover, In vitro detection of Cd^{2+} in human breast cancer cells (MDA-MB-231) by HBMC discloses its cell permeability and biocompatibility nature.

Chapter 5 deals with the fabrication of a new fluorescent organic probe DCMC (E)-2-((7-(diethylamino)-2-oxo-2H-chromen-3-yl) methylene)-N-methylhydrazine-1-carbothioamide. The systematic sensing studies of DCMC in DMSO/H_2O (9/1, v/v, pH = 7.2) by fluorescence and absorption method showed selectivity towards Hg^{2+}, Zn^{2+} and Cu^{2+} by different sensing modalities. A detailed investigation was performed on the detection mechanism by using Job's plot, ^{1}H-NMR, ESI mass analysis and density functional theory (DFT) calculations which established the 2:1 binding stoichiometry for all the three ions.

Chapter 6 introduces a novel triphenylamine benzimidazole based fluorogenic chemosensor (PBIA) which was successfully generated and characterized by varoius spectroscopic techniques. Among various screened anions only cyanide (CN^-) showed a distinct fluorogenic property towards PBIA. where we observed that, upon treatment of CN^- to probe solution, the orange fluorescence of ligand showed a blue shift and the orange fluorescence changed to greenish-yellow under UV lamp. Furthermore, the practical efficacy of the probe PBIA was established by dip-stick experiment along with cyanide detection in various natural water resources. Human breast cancer cells MDA-MB 231 makes it susceptible to CN^- sensing in biological system.

Chapter 7 reports synthesis of a new fluorescent ratiometric switch (BOHB) which showed swift and distinct detection of cyanide ion in aqueous media without any interference of other competitive anions. The blue shift in fluorescence intensity upon the addition of cyanide ion was attributed to the deprotonation mechanism of acidic protons present in BOHB. Triple negative breast adenocarcinoma (MDA-MB-231) cells were made susceptible to CN^- sensing in a biological system thereby making BOHB a biomarker tool.

Lastly, **Chapter 8** describes a biphenyl-benzoimidazole based (BPCI) chemodosimeter which displayed a rapid, sensitive and ratiometric detection towards lethal pulmonary agent phosgene. The chemodosimeter (BPCI) showed nucleophilic substitution reaction with phosgene followed by a ring closure to yield the carbamylated final product and showed an explicit ratiometric fluorescence response towards phosgene. This ratiometric switch which we developed, was used as a potential portable kit for detecting phosgene in vapour phase, as well as in solid phase when supported upon TLC plates.

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