"Synthesis and Photophysical Studies of Fluorescent Probes for Nitric Oxide and Nitroxyl with Bio-imaging Applications"

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Nitric Oxide (NO) a diatomic gaseous radical acts as a signaling molecule in several physiological and pathological processes with a half-life of a few seconds in the blood. Crucial roles in vascular and neuronal signal transduction, smooth muscle relaxation, platelet adhesion and aggregation, bioenergetics, immunity, and cell death regulation are actively played by NO. Due to its immense importance in neuroscience, physiology and immunology, NO was proclaimed as "Molecule of the Year" in 1992. Nitroxyl (HNO) is an evasive protonated redox cousin of NO. Like NO, HNO also regulates cellular function and acts as an important alternative of NO in therapeutic application. Due to its high chemical reactivity, HNO can avidly react with thiols to provide either disulfides or sulfinamides and inhibit the enzyme's activity. As a result, monitoring the concentration of NO/HNO in a biological system is crucial and a unique challenge for chemists/biologists. Among the plethora of detection methods like electro-chemical, electron spin resonance, chemiluminescence, the fluorescence technique is of gold standard in terms of sensitivity, selectivity, spatiotemporal resolution for the detection of endogenous/exogeneous NO and HNO.

Till date, chemists have designed and developed a plenty of organic and metal complex based probes for the detection of these biomolecules using fluorescence spectroscopy. Among all the type of fluorescent NO sensors, *o*-phenylenediamine (OPD) based organic probes have been considered as one of the pioneering and key strategies for nitric oxide detection. Though with time these probes are highly modified and tuned for enhanced selectivity still they are suffering from serious interferences from species like AA, DHA and RNOs, which are endogenously present in the biological system.

So, in this research endeavor, we have judisiously designed some NO and HNO probes which can detect these reactive biomolecules devoiding of any interferences from other reactive species. All these probes were thoroughly characterized by using standard analytical tools and spectroscopic techniques. Probe **PQPY**, was synthesized by embedding phenanthroquinone and pyridoxal moiety which exhibits ICT process based fluorescence enhancement (9 fold) upon reaction with NO at 505 nm due to the N-nitrosation at secondary amine moiety. PQPY is least cytotoxic, cell permeable and suitable for living cell imaging application. Another NO probe **BCM** is composed of simple Benzo-coumarin moiety connected with the acyl-hydrazide, a NO recognition unit. This probe is highly selective and sensitive exhibiting 123 fold fluorescence enhancement due to the formation of electron deficient 1,2,3,4-oxatriazole which inhibits the PET process giving 16 nM detection limit. Last one is based on fluorescent probe containing dansyl-quinoline platform, **DQ_{468}**, which on complexation with Cu^{2+} forms $[Cu^{II}(DQ_{468})Cl]^{+}$ - a paramagnetic non-fluorescent species. However, on further treatment with HNO the fluorescence is regenerated due to the formation of $[Cu^{I}(DQ_{468})]^{+}$, a diamagnetic species. This probe shows 0.41 μM detection limit with negligible cytotoxicity, good biocompatibility.

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