PREFACE

Electron spin resonance spectroscopy is a powerful tool to study free radicals and paramagnetic metal ions in chemical and biological systems. It is the direct and definitive technique for measuring and characterizing molecules with unpaired electron spin. ESR spectroscopy can be applied to obtain spatial information by utilizing magnetic field gradients in a manner similar to that of NMR Imaging. The most common spin labels are nitroxyl radicals due to their high persistency, distinctive hyperfine and g values. ESR offers the unique opportunity to perform non-invasive studies in nontransparent samples both in vitro and in vivo and has entered the fields of medicine and pharmacy during the last decade. In detail, ESR was used to probe the microviscosity and micropolarity of systems, to characterize colloidal drug carriers, to monitor the microacidity in biodegradable polymers, and to follow drug release mechanisms.

Nitroxyl radicals have been widely used as antioxidants, contrast agents and spin probes. Spin labels are usually molecules containing the nitroxide moiety which possessed an unpaired electron localized on the nitrogen and oxygen atoms. These probes, or spin labels, are nitroxide derivatives containing an unpaired electron in the pp orbital of the N-O bond, the nitroxyl radical is stable owing to the presence of methyl groups on neighboring carbon atoms. The NO group is enclosed in either a six-membered piperidine or a five-membered pyrrole ring in order to limit flexibility. Pyrrole rings with an unsaturated bond are the least flexible. The unpaired electron in the pp orbital also interacts with the spin of the nitrogen nucleus, splitting the ESR signal into resonances corresponding to different nitrogen nuclear manifolds. Thus, the number of resonant peaks depends on the nitrogen isotope, three for ^{14}N and two for ^{15}N. The ^{15}N labels have the advantage of less spectral dispersion,

which increases the signal amplitude 1.5-fold in conventional ESR. Nitroxyl radicals have also been widely used as spin probes for low frequency in vivo electron spin resonance imaging (ESRI), and as contrast agents for Overhauser-enhanced magnetic resonance imaging (OMRI).

In this work, the ESR investigations are carried out on permeable, partially permeable and impermeable nitroxyl radicals in pure water, liposomal solution and high viscous medium using a multi frequency ESR spectrometer, which will be useful for optimizing the ESR/OMR imaging parameters. In addition, the DNP studies are also carried out for nitroxyl radical in high viscous medium.

Chapter I describes a brief introduction to the basic theory related to electron spin resonance spectroscopy and dynamic nuclear polarization. The scope of the thesis and literature review is also presented.

Chapter II presents the ESR and DNP measurements using multifrequency ESR spectrometers and Overhauser-enhanced magnetic resonance imaging technique. The nitroxyl radicals used in this work is also reported.

Chapter III describes the electron spin resonance (ESR) spectroscopy studies on the reduction process of nitroxyl radicals for 1mM concentration of ^{14}N-labeled nitroxyl radicals in 1 mM concentration of ascorbic acid as a function of time.

Chapter IV describes the electron spin resonance (ESR) studies for 2 mM ^{14}N-labeled deuterated 3-methoxycarbonyl-2,2,5,5-tetramethyl-pyrrolidine-1-oxyl (MC-PROXYL) and 3-carboxy-2,2,5,5,-tetramethyl-pyrrolidin-1-oxyl (carboxy- PROXYL) in pure water and various concentrations of liposomal solution by using an L-band ESR spectrometer.

C**hapter V** presents the electron spin resonance (ESR) studies for 2mM ^{14}N-labeled deutrated 3-methoxycarbonyl-2,2,5,5-tetramethyl-pyrrolidine-1-oxyl (MC-PROXYL) and 3–carboxy-2,2,5,5,-tetramethyl-1-pyrrolidinyloxy (carboxy-PROXYL) in pure water and various concentrations of liposomal solutions by using 300 MHz ESR spectrometer.

C**hapter VI** presents the mobility studies on ^{14}N-labeled TEMPONE, TEMPO, carbamoyl-PROXYL, carboxy-PROXYL in pure water and pure water/glycerol mixture in the ratio of 15:85.

Chapter VII describes the dynamic nuclear polarization (DNP) studies on ^{15}N labeled carbamoyl-PROXYL in pure water (1 cP) and pure water/glycerol mixtures of different viscosities (1.8 cP, 7 cP and 14 cP). The dependence of DNP parameters is also demonstrated over a range of agent concentration, viscosities, RF power levels and ESR irradiation time.

Chapter VIII presents the summary and conclusions of the thesis entitled “ESR studies on permeable and impermeable nitroxyl radicals used in imaging techniques”.