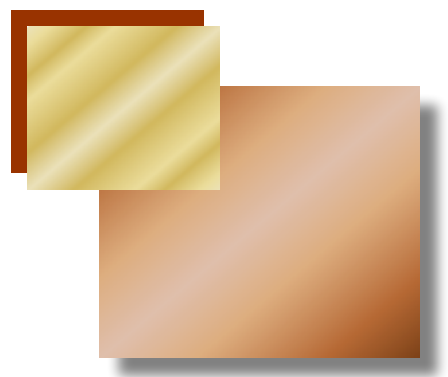


Synopsis



CHAPTER 1: Introduction & review of literature

The topic of the thesis is broadly related to the areas of nanomedicine research that includes the design and development of nanoparticles based drug delivery for cancer therapeutics and anti-bacterial activity. Over the past 10 years, nanomedicine has become an emerging field of nanotechnology applications to health. Recently, several groups including ours have extensively investigated for the development of metal nanoparticles based theranostics approaches for the treatment of several diseases including cancer, antibacterial activity and cardiovascular related diseases etc. Among several nanoparticles, gold, silver and platinum nanoparticles have been taken great attentions due to several advantages such as easy to synthesize, control their shape and size, easy to characterize, biocompatibility and easy to surface functionalization for drug delivery. Hence, design, development, fabrication and synthesis of gold, silver and other novel and smart nanomaterials/nanocomplexes through a simple, efficient and economically cheap method is very important area for nanobiotechnology research. In this context, we designed and fabricated metal nanoparticles (gold, silver, platinum, inorganic complex) based drug delivery systems using FDA approved anti-cancer drugs for cancer therapeutics and graphene oxides for angiogenesis study.

The introductory *Chapter 1* will address the scope and purpose of the present nanomedicine research. A brief overview of (i) the background and history of cancer, (ii) conventional treatment strategies and its limitations, (iii) alternative therapy: nanotechnology & nanomedicine, (iv) cancer nanotechnology, (v) passive targeting and active targeting, (vi) synthesis of inorganic nanoparticles & nanoconjugates (chemical & biological approach), (vii) advantages and applications of nanotechnology in drug delivery, (viii) FDA approved nanoparticles based medicine and nanomedicine in clinical trials, (ix) nanoparticles as antibacterial agent, (x) nanoparticles in angiogenesis & anti-angiogenesis, (xi) future challenges with nanomedicine: cost effectiveness, toxicity, immunogenicity, biodegradability and clearance from body will be elaborately explained with relevant references.

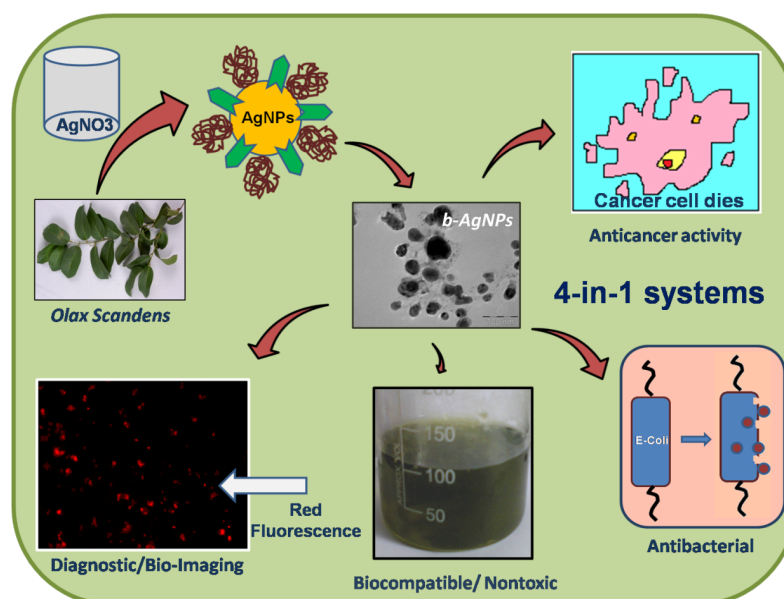
Considering these facts, the present research work was undertaken with the following objectives.

- Fabrication and characterization of novel inorganic nanoparticles/nanoconjugates (chemical synthesized and biosynthesized) based drug delivery systems (DDS).
- Thorough characterization of these nanoconjugates by several physico-chemical techniques.

- Detailed *In vitro* and *in vivo* toxicity studies of as prepared biomaterials. Functional activity of these nanoparticles/nanoconjugates for several *in vitro* and *in vivo* assays towards cancer theranostics, antibacterial activities and angiogenesis/anti-angiogenesis.

CHAPTER 2: Multifunctional theranostics applications of bio-synthesized gold and silver nanoparticles and their toxicity studies

The green synthesis approach for the synthesis of metal nanoparticles have several advantages over conventional chemical methods namely it is (i) a very simple, fast, clean & efficient method, (ii) eco-friendly & economically cheap method; and (iii) occurred at ambient temperature and pressure. **Chapter-2** will focus on the synthesis and fabrication of bio-synthesized gold (AuNPs) and silver nanoparticles (AgNPs) using plant extract (e.g. *Eclipta alba*, *Oxal scandens*, *Lantana montevidensis*, *Peltophorum pterocarpum* etc.) and their applications towards multifunctional activities (anti-cancer, anti-bacterial, fluorescence property etc.) [Mukherjee et al, *Nanotechnology*, 2012 (Highlighted in *Nature India, Global Medical Discovery Alert*)]; [Mukherjee et al, *RSC Advances*, 2013, (Highlighted in *Hindu, Early times*)]; [Mukherjee et al, *Theranostics*, 2014 (Highlighted in *Nature India*)] [Mukherjee, Sau and Madhuri et al, *Journal of Biomedical Nanotechnology*, 2015]; [Mukherjee et al, *J Mater B*, 2015]; [Patra and Mukherjee et al, *Material Science and Engineering C*, 2015]. Detailed *in vitro* and *in vivo* toxicity studies of green synthesized nanoparticles and their detailed mechanistic studies for anti-cancer and anti-bacterial activities will be demonstrated.



Scheme-1: Overall Scheme regarding the synthesis of biosynthesized silver nanoparticles and its multi-functional applications towards cancer theranostics and anti-bacterial activity.

CHAPTER 3: Design and fabrication of platinum nanoparticles and their detailed characterizations, *in vitro* and *in vivo* toxicity studies and development of Pt-nanoparticles based drug delivery systems (DDS) for cancer therapeutics

Chapter-3 will demonstrate the synthesis of poly ethylene glycol (PEG) stabilized highly stable 5-10 nm colloidal platinum nanoparticles (PtNPs) in aqueous medium at room temperature. Detailed characterization of these biocompatible Pt-nanoparticles and investigation of *in vitro* and *in vivo* toxicity of PtNPs will be discussed. We will demonstrate the design and development of platinum nanoparticles based stable drug delivery systems (Pt-DOX) using FDA approved anti-cancer drug (Dox: doxorubicin). Administration of Pt-DOX significantly inhibits the cancer cell proliferation (*in vitro*) as well as melanoma tumor growth (*in vivo*) compared to untreated group and group treated with pristine DOX. Finally, the detailed mechanistic studies behind the enhanced anti-cancer activity using Pt-DOX will be discussed in this chapter.

CHAPTER 4: Synthesis and fabrication of highly biocompatible prussian blue analogues nanoparticles and their application for cancer therapeutics and anti-bacterial activities

Prussian blue nanoparticles (PBNPs) have gained huge interests as an antidote for heavy metal toxicity. It has got FDA approval as it shows high biocompatibility. PBNPs and its analogs have been used for various biomedical applications including drug delivery, biomodal imaging, bio-sensing device, cancer theranostics due to unique physico-chemical properties and porous nature. *Chapter-4* will demonstrate the synthesis of poly(N-vinyl-2-pyrrolidone) (PVP) stabilized silver analogues of Prussian blue nanoparticles (SPBNPs), detailed characterization and biological activity studies for cancer therapy and anti-bacterial activities. SPBNPs showed high biocompatibility through *in vitro* and *in vivo* toxicity studies. Furthermore, it exhibited excellent antibacterial and anticancer efficacy towards *in vitro* and *in vivo* tumor model. Detailed mechanistic studies will be discussed for both anti-cancer and anti-bacterial activities.

CHAPTER 5: Graphene oxides and its role in angiogenesis and anti-angiogenesis

Chapter-5 will focus on the ROS (reactive oxygen species) dependent switchover role between angiogenesis and anti-angiogenesis of graphene oxides (GO) and reduced graphene oxides (rGO) and their detailed mechanistic studies [Mukherjee et al, *Adv. Healthcare Mater*, 2015 (Highlighted in *Nature India, Chemistry Views*)]. Angiogenesis, a process resulting in the formation of new capillaries from the pre-existing vasculature that plays vital role for the development of therapeutic approaches for cancer, atherosclerosis, wound healing, and cardiovascular related diseases. In this

Chapter, the synthesis, characterization, and *in vitro* and *in vivo* angiogenic properties of GO and rGO will be demonstrated. The formation of intracellular ROS, reactive

nitrogen species (RNS) and activation of phospho-eNOS & phospho-Akt might be the plausible mechanisms for GO and rGO induced angiogenesis. The results altogether suggest the possibilities for the future development of alternative angiogenic therapeutic approach for the treatment of cardiovascular related diseases where angiogenesis play a significant role.

Finally, we will conclude the overall thesis work with highlighting the possible outcome of the present thesis work. Also we will discuss the future translational directions and challenges of this nanomedicine research for cancer theranostics and other biomedical applications.