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List of Abbreviations and Symbols

ABL	Abelson murine leukemia
AFM	atomic force microscopy
ALL	acute lymphocytic leukemia
AML	acute myeloid leukemia
AUC	area under the curve
BCR	breakpoint cluster region
Ch	chitosan
CI	confidence interval
Cmax	maximum plasma concentration
CML	chronic myeloid leukemia
CV	coefficient of variation
DIC	differential interference contrast
DLS	dynamic light scattering
DMSO	dimethyl sulfoxide
DNA	deoxyribonucleic acid
DOE	design of experiments
DSB	dasatinib
DSC	differential scanning calorimetry
EDXS	energy dispersive x spectroscopy
EPR	enhanced permeability and retention
EXAFS	extended x-ray absorption fine structure
FISH	fluorescence in situ hybridization
FTIR	Fourier transform infrared spectroscopy
GNP	gold nanoparticle
HR- SEM	high resolution scanning electron microscopy
IFN- α	interferon-alfa
MDR	multi drug resistance
mRNA	messenger ribonucleic acid
NIR	near infrared
NMR	nuclear magnetic resonance

NNI	National Nanotechnology Initiative
PAT	photoablation therapy
PBS	phosphate buffer saline
PDT	photodynamic therapy
PEG	polyethylene glycol
Ph	Philadelphia chromosome
PLGA	poly lactic-co-glycolic acid
PTT	photothermal therapy
PVP	poly vinyl pyrrolidone
QbD	quality by design
RPMI	Roswell park memorial institute
RT- qPCR	reverse transcriptase quantitative polymerase chain reaction
SAED	selected area electron diffraction
SAXS	small-angle x-ray scattering
SERS	surface-enhanced Raman scattering
SPR	surface plasmon resonance
Src	sarcoma
STM	scanning tunneling microscopy
TEM	transmission electron microscopy
TGA	thermo gravimetric analysis
TKI	tyrosine kinase inhibitors
Tmax	time to reach maximum plasma concentration
US FDA	United States food and drug administration
UV	ultraviolet
UV- Vis	ultraviolet-visible
WBC	white blood cells
XPS	x-ray photoelectron spectroscopy

Preface

In recent years, the development of various nanoparticulate drug delivery systems has gained significant interests for cancer theranostics. These nanocarriers are targeted specifically to the tumor cells either actively or passively based upon their mode of action. In this targeted drug delivery system, the drug gets confine and delivers to the targeted site in a greater amount without affecting the surrounding healthy cells. The idea to work for the present thesis was conceived from drug and dose-related problems associated with the available antineoplastic drugs. Dasatinib (DSB) is an antineoplastic drug approved as a first-line drug for the treatment of chronic myeloid leukaemia (CML). During chemotherapy, large doses are recommended for treatment, which may induce adverse effects to normal cells and the surrounding healthy organs. Thus, the objective of this study was to design and develop a new targeted delivery system comprising of polymer stabilized chitosan capped gold nanoparticles (Ch-GNPs) loaded with DSB with the aim of restricting high dose administration and reducing the dose related adverse side effects and also the frequency of dosing. For a drug to be clinically effective, it needs to be suitably protected in the biodegradable and biocompatible polymeric vesicles till its delivery to the targeted site. The novelty of the present research work lies in the synthesis and stabilization of potent, non-toxic, cost-effective, eco-friendly, selectively targeted, sustained release drug loaded gold nanocarriers by green reduction method utilizing minimum raw materials and time, and preserving its stability and bioactivity during fabrication and release.

The design, development, and optimization of nanoformulations were done by employing systematic design of experiments (DOE), which has attracted attention in

the pharmaceutical sector to simultaneously attain multiple objectives with minimal consumption of time and resources. DOE involves stepwise assessment of critical quality attributes, factor screening, experimental design and optimization. BBD (Box-Behnken design) was employed to evaluate the effect of independent factors on the dependent responses. The effect of independent variables on the responses was illustrated by 3D response surface methodology. A graphical and numerical optimization procedure was carried out to obtain the predicted value of various factors and responses. The final optimized batch of the nanoformulation was evaluated and validated.

Further, the nanoformulations were subjected to detailed evaluations for solid state characterization, physicochemical characterization, stability studies, *in vitro* drug release, drug release kinetic studies, hemocompatibility study, cellular uptake study by confocal fluorescence microscopy, *in vitro* cytotoxicity assay in K562 cell lines, cell apoptosis assay and *in vivo* pharmacokinetic study in Sprague Dawley rats and the results have been discussed in detail. These results indicate that the newly developed nanoparticulate system could prove to be a promising drug delivery system for prolonging the drug release and achieving the desired drug concentration at the tumor site for longer duration resulting in improved therapeutic efficacy of the drug in the treatment of CML.