Design and Synthesis of Quinazoline Based Compounds as Tyrosine kinase Inhibitors with Anticipated Anti-Proliferative Activity

Thesis
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Pre-requisite Predoctoral Courses and Exams

In addition, to the work presented in the thesis, the candidate has attended and passed the following Pre-requisite predoctoral courses:

- Pharmaceutical chemistry
- Drug design
- Stereochemistry
- Selected topics

Moreover, the candidate has passed a comprehensive exam in organic and Pharmaceutical chemistry and presented a research proposal with the title of "**Design, Synthesis and Evaluation of Novel Tyrosine Phosphatase Inhibitors".**

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List of Abbreviations

3D: 3-Dimensional

2D: 2-Dimensional

Å: Angstroms

A-loop: Activation loop

Abl: Abelson tyrosine kinase

Arg: Arginine

Asn: Aspargine

Asp: Aspartate

Asp-Phe-Gly : Aspartate-Phenyl alanine-Glycine

AT: Adenine thymine

ATP: Adenosine-5'-triphosphate

BBB: Blood brain barrier level

BSA: Bovine serum albumin

CYP2D6: Cytochrome P450 2D6

DFG: Aspartate-Phenylalanine-Glycine sequence

DIPEA: N,N Diisopropylethylamine

DMA: Dimethylacetal

DMF: Dimethyl formamide

DMSO: Dimethylsulfoxide

DNA: Deoxyribonucleic acid

EGFR: Epidermal growth factor receptor

FAK: Focal adhesion kinase

FDA: Food and Drug Adminstration

FGFR: Fibroblast growth factor receptor

List of Abbreviations

FRET: fluorescence resonance energy transfer

G-loop: glycine rich loop

Glu: Glutamate

Gly: Glycine

HIA: Human intestinal absorption

HIV: Human immunodeficiency virus

HPLC: High-performance liquid chromatography

IC50: Half maximal inhibitory concentration

Ig: Immunoglobulin

L858R: Leucine858Arginine

Lck: Lymphocyte-specific protein tyrosine kinase

Leu: Leucine

Lys: Lysine

mAB: Monoclonal antibody

MAPK: Mitogen activated protein kinase

MEK: Map kinase kinase

Met: Methionine

Mp: Melting point

MS (ESI): Electrospray ionization mass spectrometry

NRTK: Non-receptor tyrosine kinase

NMR: Nuclear magnetic resonance

NSCLC: Non-small cell lung cancer

NRTK: Non- recptor tyrosine kinase

PBS: Phosphate buffered saline

PDB: Protien Data Bank

PDGFR: Platelet derived growth factor receptor

PI3K: Phosphatidylinositol-3-kinase

List of Abbreviations

ppm: part per million

Pred: predicted

PSA: Polar surface area

PPB: Plasma protein binding

RMSD: Root mean square deviation

RNA: ribonucleic acid

RPMI: Rosewell Park Memorial Institute

RT: room temperature

RTK: receptor tyrosine kinase

SAR: Structure activity relationship

Ser: serine

S phase: Synthesis phase

SRC: Sarcoma (Schmidt-Ruppin A-2) Viral Oncogene

S/TKs: Serine-threonine kinases

T790M: Threonine790Methionine

TBST: Tris-buffered saline, 0.1% Tween 20

TEOF: triethyl orthoformate

TFA: Trifluoroacetic acid

TGF: Transforming growth factor

THF: Tetrahydrofuran

TK: Tyrosine Kinase

TKI: Tyrosine kinase inhibitors

TLC: Thin Layer Chromatography.

TMS: Tetramethylsilane

TNF: Tumor necrosis factor

List of Abbreviations

Val: valine

VEGFR: Vascular Endothelial growth factor

Abstract

Title of thesis:

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