

Design and Synthesis of Phthalazine Based Compounds as Possible Anticancer Agents

Thesis

Presented by

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List of Abbreviations:

5-aza-CdR : 5-Aza-2'-deoxycytidine

5-aza-CR : 5-Azacytidine

ADDM: Azodicarbonyl dimorpholide

ALL: Acute lymphoblastic leukemia.

Asp: Aspartate

ATP : Adenosine triphosphate

BAECs: Bovine aortic endothelial cells

Bcl-2 : B-cell lymphoma-2

BET: Bromodomain and extraterminal domain family

Bim: Bcl2-interacting mediator of cell death – a membrane-bound “death ligand” inhibited by Bcl2.

BPS: Bioscience Corporation

CDK: Cyclin dependent kinase

c-FLIP: Cellular FLICE like inhibitory protein

CHARMm: Chemistry at Harvard macromolecular mechanics

CML : Chronic myeloid leukemia

CRD: Cysteine-rich domains

CrK: Creatine kinase

DD: Death domain

DFG: Asp-Phe-Gly

DMF:Dimethylformamide

DMSO: Dimethyl sulfoxide

DNA: Deoxyribonucleic acid

DNMT: DNA methyltransferase

DTP: Development therapeutic program

EC: Endothelial cells

EGFR : Epidermal growth factor receptor

ER : Estrogen receptor

Fas: Fragment, apoptosis stimulating. Fas is actually a cell receptor.

FDA: Food and Drug Administration

FGF: Fibroblast growth factor

FGFR-1: Fibroblast growth factor receptor 1

FITC: Fluorescein isothiocyanate

FLT-4: fms related tyrosine kinase 4

GI₅₀: 50%Growth inhibition concentration;

HCC: Hepatocellular carcinoma

HCC: Hepatocellular carcinoma

HDAC: Histone deacetylases
HRD: His- Arg-Asp
Hrs: hours
HTS: High-throughput screening
HUVEC: Human umbilical vein endothelial cells
Hz: Hertz
IAPs: Inhibitor of apoptosis
IC₅₀: Half-maximal inhibitory concentration
IC₅₀: Half-maximal inhibitory concentration
KAT: Histone acetyltransferases
KDM: Histone demethylases
KDR: Kinase insert domain receptor
KMT: Histone methyltransferases
L2987 : Lung adenocarcinoma cells.
MAPK: Mitogen-activated protein kinase
MD: Molecular dynamics
MDAMB-231: Breast adenocarcinoma
MET: Hepatocyte growth factor receptor
MHz: Mega hertz
Mmol: Millimole
m-RNA : Messenger ribonucleic acid
MS: Mass spectroscopy
NCI: National Cancer Institute
NF- κ B: Nuclear factor κ -light-chain-enhancer of activated B cells
NIH: National Institutes of Health
NMR: Nuclear magnetic resonance
NRTK: Non-receptor tyrosine kinase
NSCLC : Non small cancer lung cancer
PD-1 : Programmed cell death protein 1
PDB: Protein data bank
PDGFR : Platelet derived growth factor receptor.
PGF: Placental Growth Factor
Ph+ : Philadelphia chromosome-positive
PI: Propidium iodide
PIGF: Placental growth factor
PPB: Plasma protein binding
PR : Progesterone receptor
PS: Phosphatidylserine

Pt NWs: Platinum nanowires
Raf-1: v-Raf murine sarcoma viral oncogene
Ras: Rat sarcoma
RCC: Renal cell carcinoma
RET: Rearranged during transfection (Proto-oncogen).
RMSD: Root mean square deviation
RNA: Riboneucleic Acid
rt: Room temperature
RTKs : Receptor tyrosine kinase.
SAR: Structure activity relationship
Smac/DIABLO: Second mitochondria-derived activator of caspase/direct inhibitor of apoptosis-binding protein with low pI
SRC: Sarcoma (Schmidt-Ruppin A-2) Viral Oncogene
T315I: Threonine being substituted by Isoleucine at that position
TEA: Triethyl amine
THF: Tetrahydrofuran
Tie-2: Tyrosine kinase with immunoglobulin-like and EGF-like domains.
TK: Tyrosine kinase
TLC: Thin layer Chromatography
TNF: Tumor necrosis factor
TP53: Tumor protein 53
TRAIL: TNF-related apoptosis-inducing ligand
VEGF: Vascular endothelial growth factor
VEGFR: Vascular endothelial growth factor receptor
VEGFR-2: Vascular endothelial growth factor receptor-2