Design and Synthesis of Phthalazine Based Compounds as Possible Anticancer Agents

Thesis
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The candidate got the Master degree in Pharmaceutical Sciences (Organic Chemistry), Faculty of Pharmacy, Cairo University, and the master thesis was equivalent by Council of Faculty of Pharmacy, Ain Shams University.

Besides the work presented in this thesis, the candidate successfully passed special PhD courses in Pharmaceutical Chemistry for one year during academic year 2011/2012 with the following grades:

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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: Fluorescin isothiocyanate
FLT-4: fms related tyrosine kinase 4
GI_{50}: 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
IC_{50}: Half-maximal inhibitory concentration
IC_{50}: Half-maximal inhibitory concentration
KAT: Histone acetyltransferases
KDM: Histone demethylases
KDR: Kinase insert domain receptor
KMT: Histone methyltransferases
L2987 : Lung agenocarcinoma 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-κB: 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: Protien data bank
PDGFR : Platelet derived growth factor receptor.
PGF: Placental Growth Factor
Ph+ : Philadelphia chromosome–positive
PI: Propidium iodide
PlGF: 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