List of Figures

Figure 1: Pathophysiology of inflammation……2
Figure 2: Reported cancer cases i) Worldwide, ii) India (men and women) ……...8
Figure 3: Kinases; catalysed the phosphorylation of substrate……..16
Figure 4: Phosphorylation with PI3K enzyme in cell……..…..20
Figure 5: PI3K activation pathway……..……...22
Figure 6: Isoform-specific inhibitors……...…27
Figure 7: Dual PI3K/mTOR inhibitors……..…….28
Figure 8: Pan-PI3K inhibitors…….....29
Figure 9: PI3Kδ crystal structure complexed with a) IC-87114 (PDB ID: **2WXK**) and b) Idelalisib (PDB ID: **4EX0**) ……..…….31
Figure 10: Potent PI3Kδ inhibitors with similar structural features…….…..….32
Figure 11: Imidazo-quinoline derivatives…….…..34
Figure 12: INK-654 and INK-666 co-crystal with PI3Kδ enzyme (PDB ID: **2WXK**) ……....35
Figure 13: Benzofuran and 2,4-disustituted quinoline derivatives as PI3Kδ inhibitor…….….36
Figure 14: Quinoline and imidazo-quinoline based PI3K inhibitors. ……..…..37
Figure 15: Designing strategy using imidazo-quinoline pharmacophore……..…….39
Figure 16: Imidazo-quinoline based antibacterial agents……..….41
Figure 17: Imidazo-quinoline based antimalarial agents……..…..42
Figure 18: Imidazo-quinoline based anthelmintic agent…….....42
Figure 19: Imidazo-quinoline based anticancer agent……..…..43
Figure 20: Imidazo-quinoline based β-lactamase inhibitors…….….43
Figure 21 (a): Imidazo-quinoline: different isomers…….…….....45
Figure 21 (b): Common routes for the preparation of imidazo-quinoline……..…45
Figure 22: Effect of Compound **10h** and **Dactolisib** in CIA mice model. ……....85
Figure 23: *In vivo* anti-tumor activity of Compound **10h**……..….86
Figure 24: The Glide docking studies of Compounds **9c**, **10h**, **10k** and Dactolisib into site of PI3Kδ (PDB ID:4XE0). Compounds are shown as sticks. Hydrogen bonds are shown as yellow dash lines. ……....89
Figure 25: a) INK-666 co-crystal with PI3Kδ enzyme. b) Docking image of INK-666 (PDBID: **2WXK**) ……..…..91
Figure 26: Designing strategy using benzofuran bioisoster. ……..…93

Figure 27: Benzofuran bioisoster of quinoline (PDE4 inhibitors) ……..95
Figure 28: Benzofuran bioisoster of quinoline (FadD32 inhibitors) ……..96
Figure 29: Benzofuran as therapeutic agent……...97
Figure 30: Natural products containing benzofuran ring. ……..……97
Figure 31. Benzofuran as antiparasitic and antifungal agents. ……..……..98
Figure 32: Benzofuran as anti-inflammatory agents……..….98
Figure 33: Benzofuran as anti-cancer agent……....99
Figure 34: Benzofuran as anti-oxidant…….…..99
Figure 35: Perkin benzofuran synthesis…….…..100
Figure 36: Benzofuran synthesis from salicylaldehyde……100
Figure 37: Benzofuran synthesis through McMurry reaction……...101
Figure 38: Docking of INK-666, INK-654, Compound 26b, 26c, 26g and 26h (PDB ID: **2WXK**)……131
Figure 39: Designing strategy for 2,4-disubstituted quinoline…….…....133
Figure 40: Overlay of INK-654 and 2,4-disustituted quinoline derivatives (PDBID: **2WXK**)….……..134
Figure 41: *ortho*, *m*eta and *para* NOSH aspirin. …….…..…136
Figure 42: Benzotrizole (*1N* and *2N*) derivatives as antibacterial agents. …….…..….137
Figure 43: Docking image of INK-654, **37a** and **37h** (PDBID: **2WXK**) …….…...158
Figure 44: Hit to lead optimization in imidazo-quinoline series (Chapter II) …….…...161
Figure 45: Lead compounds form benzofuran series (Chapter III) ……....162
Figure 46: Proposed imidazo-quinoline based, orally bioavailable PI3Kδ selective inhibitors…….….164