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Quinazoline fused 1,2,4-triazoles: PIDA-mediated synthesis, characterization, anti-breast cancer agents, ABTS radical scavenging efficacy, molecular docking, and DFT studies

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The present work demonstrates the PIDA-mediated mild synthesis of 3-aryl-5-phenyl-[1,2,4]triazolo[4,3-c]quinazolines **5a-n** through an intramolecular oxidative-cyclization of twelve electronically dissimilar and newly prepared (*E*)-4-(2-benzylidenehydrazineyl)-2-phenyl- quinazolines **4a-n** as key precursors. Structural confirmation of quinazoline-hydrazone and triazole has been established based on ^{1}H and ^{13}C NMR, IR, and HRMS data. Antiproliferative activity examination has led to the identification of 5-phenyl-3-(2,3,4-trimethoxyphenyl)-[1,2,4] triazolo[4,3-c]quinazoline **5g** and 3-(2,3-dichlorophenyl)-5-phenyl-[1,2,4]triazolo[4,3-c] quinazoline **5j**, as most active (less than and comparable to standard), which exhibit cytotoxicity with IC_{50} value of 1.14 mM and 1.39 mM, respectively against MCF-7 cell line. **5g** and **5j** also show significant potential against MDA-MB231 cell line with IC_{50} of 2.79 mM and 1.95 mM, respectively. Additionally, molecular modeling studies have been conducted to support the results and to study the binding interaction of the compound **5g** and **5j** with VEGFR-2 kinase enzyme (PDB ID:3U6J). Furthermore, systematic screening of **5a-n** for ABTS radical scavenging activity, displays that 3-(4-fluorophenyl)-5-phenyl-[1,2,4]triazolo[4,3-c]quinazoline **5h**, has the highest antioxidant efficacy with IC_{50}= 11.2 ± 0.14 µg/mL. The antioxidant efficacy of **5a-n** is also supported by DFT studies.

Keywords: [1,2,4]Triazolo[4,3-c]quinazolines, Hypervalent Iodine(III) Reagent, VEGFR-2 Inhibitors, Antiproliferative Activity, Antioxidant Activity