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Drug repurposing of novel quinoline acetohydrazide derivatives as potent COX-2 inhibitors and anti-cancer agents

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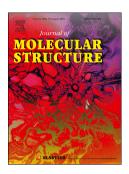
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CCEPTED MANUSCRIPT

Drug repurposing of Novel Quinoline Acetohydrazide derivatives as potent

**COX-2** inhibitors and anti-cancer agents

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**Abstract** 

Novel QuinolineAcetohydrazide (QAh) derivatives (9a-n) were firstly evaluated in silico to

determine their anti-inflammatory and anti-cancer efficacy via the mechanisms of COX1 and

COX2 inhibition, and NF-κB, HDAC and Human Topoisomerase I pathways respectively. In the

studied set, the trifluoro substituted QAh derivatives: (E)-N'-(4-(trifluoro methyl) benzylidene)-

quinolin-8-yl) (E)-N'-(3-(trifluoro 2-(7-fluoro-2-methoxy acetohydrazid and

benzylidene)-2-(7-fluoro-2-methoxy quinolin-8-yl) acetohydrazide are determined to be potential

leads, indicated from their best docked scores, relative ligand efficiency, and significant

structural attributes evaluated by ab initio simulations. The only setback being their partition co-

efficient that retrieved a red flag in the evaluation of their Lipinski parameters. The experimental

in vitro studies confirmed the significant enhancement as COX-2 inhibitors and appreciable

enhancement in MTT assay of breast and skin cancer cell lines. Significantly, trifluoro

substituent in the quinoline scaffold can be reasoned to note the excellent binding affinity to all

the evaluated drug targets.

**Keywords:** QuinolineAcetohydrazide; COX 2 inhibitors, Anti-inflammatory agents; Anti-cancer

agents; Drug Design; Molecular Docking study; Lipinski parameter.

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