Discovery of heterocyclic 4-arylamido 5-methylisoxazole analogues as selective FLT3 inhibitors by Conformational restriction of type II FMS inhibitor

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Abstract

A series of 4-arylamido 5-methylisoxazole derivatives incorporating heterocyclic aromatic ring were designed and synthesized by modifying type II FMS inhibitor. Kinase profiling of one compound revealed interesting features, with increased inhibitory potency toward FLT3 and concomitant loss of potency toward FMS. Therefore, more derivatives were synthesized and evaluated for their inhibitory activities against FLT3. Derivatives were made as several privileged heteroaromatic structure with hydrophobic moieties and one compound containing methyl piperazine among them exhibited the most potent inhibitory activity against FLT3 (IC50= 170 nM) with excellent selectivity profile.

Keywords: *FMS, heterocyclic aromatic ring, conformational restriction, FLT3*

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