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# Synthesis and PASS-Assisted Evaluation of New Heterocyclic Compounds Containing Hydroquinoline Scaffold

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**Abstract :** There has been a significant surge in interest in the synthesis of heterocyclic compounds that contain hydroquinoline fragments. This surge can be attributed to the broad range of pharmaceutical and industrial applications that these compounds possess. The present study provides a comprehensive account of the synthesis of both linear and fused heterocyclic systems that incorporate hydroquinoline fragments. Furthermore, the pharmacological activity spectra of the synthesized compounds were assessed using the in silico method, employing the prediction of activity spectra of substances (PASS) program. Hydroquinoline nitriles 7 and 8 were prepared through the reaction of the corresponding hydroquinolinecarbaldehyde using a hydroxylammonium chloride/pyridine/toluene system and iodine in aqueous ammonia under ambient conditions, respectively. 2-Phenyl-1,3-oxazol-5(4H)-ones 9a,b and 10a,b were synthesized via the condensation of compounds 5a,b and 6a,b with hippuric acid in acetic acid in 30–60% yield. When activated, 7-methylazolopyrimidines 11a and b were reacted with N-alkyl-2,2,4-trimethyl-1,2,3,4-tetrahydroquinoline-6-carbaldehydes 6a and b, and triazolo/pyrazolo[1,5-a]pyrimidin-6-yl carboxylic acids 12a and b were obtained in 60–70% yield. The condensation of 7-hydroxy-1,2,3,4-tetramethyl-1,2-dihydroquinoline 3 h with dimethylacetylenedicarboxylate (DMAD) and ethyl acetoacetate afforded cyclic products 16 and 17, respectively. The condensation reaction of 6-formyl-7-hydroxy-1,2,2,4-tetramethyl-1,2-dihydroquinoline 5e with methylene-active compounds such as ethyl cyanoacetate/dimethyl-3-oxopentanedioate/ethyl acetoacetate/diethylmalonate/Meldrum's acid afforded 3-substituted coumarins containing dihydroquinolines 19 and 21. Pentacyclic coumarin 22 was obtained via the random condensation of malononitrile with 5e in the presence of a catalytic amount of piperidine in ethanol. The biological activities of the synthesized compounds were assessed using the PASS program. Based on the prognosis, compounds 13a, b, and 14 exhibited a high likelihood of being active as inhibitors of gluconate 2-dehydrogenase, as well as possessing antiallergic, antiasthmatic, and antiarthritic properties, with a probability value (Pa) ranging from 0.849 to 0.870. Furthermore, it was discovered that hydroquinoline carbonitriles 7 and 8 tended to act as effective progesterone antagonists and displayed antiallergic, antiasthmatic, and antiarthritic effects (Pa = 0.276–0.827). Among the hydroquinolines containing coumarin moieties, compounds 17, 19a, and 19c were predicted to be potent progesterone antagonists, with Pa values of 0.710, 0.630, and 0.615, respectively.

**Keywords :** heterocyclic compounds, hydroquinoline, vilsmeier-haach formylation, in-silico
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