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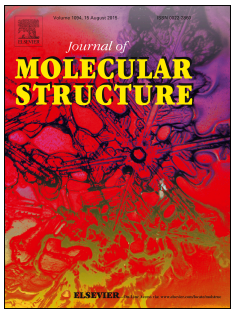

Synthesis, biological activities and molecular docking studies of some novel 2,4,5-trisubstituted-1,2,4-triazole-3-one derivatives as potent tyrosinase inhibitors

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Synthesis, biological activities and molecular docking studies of some novel 2,4,5-trisubstituted-1,2,4-triazole-3-one derivatives as potent tyrosinase inhibitors

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ABSTRACT

Tyrosinase plays a central role in the biosynthesis pathway of melanin pigment and its activity has also been linked to Parkinson's and other neurodegenerative diseases. Melanin functions in the formation of skin color and its unusual levels cause some skin disorders such as pregnancy scar, oldness spots and especially skin cancer (melanoma). In addition, melanin plays a critical role as a defense molecule for insects during molting process and wound healing and is important for their life. Therefore, determination of inhibitor molecules for tyrosinase activity has a promising potential for therapies of some disaeses and is an alternative method for keeping insects under control. In the present study, 4-amino-2-heptyl-5-methyl-2,4-dihydro-3H-1,2,4-triazole-3-on (**2**) was used as the starting materials to synthesize of 2-Heptyl-5-methyl-2,4-dihydro-3H-1,2,4-triazole-3-on (**3**) and 4-(substituebenzyl)-2-heptyl-5-methyl-2,4,-dihydro-3H-1,2,4-triazole-3-on (**4a-d**). Then, the synthesized compounds (**2-4**) were evaluated for their tyrosinase inhibiton efficiencies. **4b** compound among the synthesized molecules was found the most effective inhibitor with the smallest IC_{50} value (5 mM). Kinetic studies showed that the inhibition mechanism of **4b** compound on tyrosinase activity was reversible and uncompetitive. Molecular docking studies also indicated that **4b** compound could bind to the active site of the enzyme by weakly interacting with especially His244, His263, Phe264 and Val283.