Design and Synthesis of New Barbituric- and Thiobarbituric Acid Derivatives as Potent Urease Inhibitors: Structure Activity Relationship And Molecular Modeling Studies

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ABSTRACT

In this study 36 new compounds were synthesized by condensing barbituric acid or thiobarbituric acid and respective anilines (bearing different substituents) in the presence of triethyl orthoformate in good yields. In vitro urease inhibition studies against jack bean urease revealed that barbituric acid derived compounds (**1**–**9** and **19**–**27**) were found to exhibit low to moderate activity however thiobarbituric acid derived compounds (**10**–**18** and **28**–**36**) showed significant inhibition activity at low micro-molar concentrations. Among the synthesized compounds, compounds (**15**), (**12**), (**10**), (**36**), (**16**) and (**35**) showed excellent urease inhibition with IC_{50} values 8.53 ± 0.027, 8.93 ± 0.027, 12.96 ± 0.13, 15 ± 0.098, 18.9 ± 0.027 and 19.7 ± 0.63 μM, respectively, even better than the reference compound thiourea (IC_{50} = 21 ± 0.011). The compound (**11**) exhibited comparable activity to the standard with IC_{50} value 21.83 ± 0.19 μM. In silico molecular docking studies for most active compounds (**10**), (**12**), (**15**), (**16**), (**35**) and (**36**) and two inactive compounds (**3**) and (**6**) were performed to predict the binding patterns.

KEYWORDS: Urease; Barbituric; Thiobarbituric; Jack bean; In silico; Triethyl orthoformate

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