

# Dihydrofolate reductase (DHFR) inhibition and molecular modeling study of some 6-bromo- or 6,8-dibromo-quinazolin-4(3H)-ones

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## Abstract

**Objectives:** The dihydrofolate reductase (DHFR) inhibitory activity of 6-bromo- and 6,8-dibromo-quinazolin-4(3H)-ones were studied to define the structural features and requirements that enhance selectivity and specificity for the proper binding to the enzyme active site. **Methods:** Compounds were tested for their in vitro DHFR inhibition. As an application of the use of DHFR inhibitors, in vitro antitumor activity using disease-oriented human cell lines assay was performed. **Key findings:** Compounds 19, 20, and 22 showed remarkable DHFR inhibitory activity, 17, 18, 20, and 24 proved to be broad spectrum antitumor with median IC<sub>50</sub> values revealed that the active DHFR inhibitors 22 and 20 bind to DHFR with similar amino acid residues as methotrexate, especially Arg 28. **Conclusions:** The mono-bromo series proved to be more active than the di-bromo counterparts and the 3-(2-hydrazinyl-acetyl)- is more active than its 3-(acetohydrazide) isoster. The investigated compounds could be used as template model for further optimization.

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