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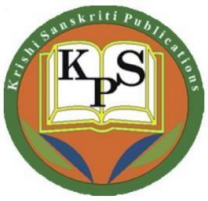

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Dihydrofolate Reductase as a Potential Therapeutic Target against Various Diseases

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Abstract—*Dihydrofolate reductase (DHFR) is a key enzyme in de novo synthesis of thymidylate, purine and several other amino acid synthesis, and therefore of DNA. It catalyses the NADPH-dependent reduction of dihydrofolate to tetrahydrofolate required for the biosynthesis of tetrahydrofolate cofactors. Inhibition of DHFR has been established as an attractive strategy for antibacterial, anti-inflammatory and antineoplastic drug development. Furthermore, cytostatic and immunosuppressive drugs target human DHFR. One of the reasons why DHFR became one of the most investigated proteins was because of its dual pharmacological target. DHFR has been a therapeutic target for more than 50 years. A wide number of pharmacological medicines have been developed to block DHFR activity. The challenges for DHFR inhibition-based disease treatment are now focused on overcoming the organism resistance to these medications as well as cross-reactivity as a single chemical species could have multiple targets, dynamically interfering with the distinct pathways, enzymes and metabolites. To design drugs that are specific to their targets and decrease the risk of cross reactivity, a better knowledge of difference in the structure of this enzyme in various organisms is required. The DHFR enzyme could possibly be used to treat a variety of other disorders linked to the folate cycle.*

Keywords: *Dihydrofolate Reductase; tetrahydrofolate; therapeutic target; Inhibitors; cross reactivity.*