New heterocyclic compounds as inhibitors of rat erythrocytes G6PD and 6PGD and docking studies

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Abstract— Glucose-6-phosphate Dehydrogenase (G6PD) is the rate-limiting enzyme of the pentose phosphate pathway. It catalyses the irreversible conversion of glucose 6-phosphate to 6-phosphoglucono-δ-lactone in the presence of NADP+ [1]. 6-phosphogluconolacton Dehydrogenase (6PGD) is the third enzyme in the pentose phosphate pathway. It is a well-known oxidative carboxylase that catalyses conversion of 6-phosphogluconate into ribulose 5-phosphate. In the absence of these enzymes the erythrocyte is susceptible to oxidative damage. G6PD is associated with some human diseases including cancer, metabolic disorders and cardiovascular diseases. It was also reported that suppression of 6PGD decreased lipogenesis and RNA biosynthesis and increased reactive oxygen levels in cancer cells, lessening cell proliferation and tumour growth suggesting that 6PGD could be an anticancer target. Therefore one aim of the work described in this paper is to investigate the effect of some biologically active indole derivatives on the activity of corresponding enzymes. The studies revealed that while the bisindole derivatives 1, 2 and 3 inhibited the activity of G6PD with an IC50 of 138 μM, 231 μM and 304 μM respectively, the studies of rat erythrocyte 6PGD indicated that the activity was increased in the presence of 1 and 2 and was inhibited in the presence of 3. Molecular docking studies were also carried out to understand the mechanism of inhibition/activation.

Keywords— carboxylase, heterocyclic, inhibition.

REFERENCES

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