SYNTHESIS OF 3,3′-BISINDOLES AND İNVESTİGATİON OF THE EFFECT ON THE RAT ERYTHROCYTE 6PGD

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ABSTRACT: Many natural and synthetic biologically active compounds containing indole skeletons are being used as therapeutic agents. Therefore, a great deal of attention have been given to develop innovative synthetic strategies for the decoration of indole cores. The effect of a variety of indole derivatives containing bisindole moiety on the activity of some enzymes were tested and some intriguing results were obtained. The aim of this study was to investigate whether biologically active organic indole derivatives affects 6PGD enzyme activity in rat erythrocytes. In order to do that, the 3,3′-bisindole derivatives **3** and **4** were synthesized, the enzyme was purified from rat blood and its activity was spectrophotometrically measured. The studies of the effect of these compounds on the activity of rat 6PGD revealed that while the 3,3′-bisindole derivatives **3** inhibited the activity with an IC50 of 115.8 μM, the activity was increased in the presence of 3,3′-bisindole derivatives **4.**

Key words: Indole, 3,3′-bisindole derivatives, 6PGD, NADPH, reductive biosynthesis

INTRODUCTION

Indole and bisindole moiety are found in many natural products, fine chemicals, and pharmaceuticals. 3,3′-bisindole derivatives represent a particularly interesting class and are also known to possess a wide spectrum of biological activities in numerous natural products and pharmaceutical compounds [1]. Due to its multiple biological activities, the indole ring system has become an important building block or intermediate in the synthesis of many pharmaceutical agents (Figure 1). As a consequence of this, many researchers focused on developing new approaches for the designing of indole cores. Indole is an electron-rich hetero aromatic system, and although various methods for its alkylation at the C3-position are well established, its C2-alkylation remains to be a difficult task. While a number of methods have already been well documented for the derivate indole nucleus, there appear to be a few practical procedures available for the synthesis of 2-substituted indoles [2]. As an alternative solution to this problem, we focus on the reactions using 4,7-dihydroindole (**2**) derivatives as synthetic equivalents (synthons) for an easy access to 2-substituted indoles [3].