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NEW NON-CARBOXYLIC ACID CHALCONES AS ANTI-INFLAMMATORY AGENTS: MOLECULAR DOCKING, SYNTHESIS AND ADMET STUDIES

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Chalcones in combination with heterocyclic moieties have been reported to exhibit diverse biological activities. The present study was aimed to synthesize novel chalcones bearing pyrazoline moiety and Michael adducts. All the synthesized compounds were characterized by various spectral techniques, and screened for their anti-inflammatory potential. Most of the synthesized compounds exhibited good to moderate activity. The results of the experiment were statistically processed using GraphPad Prism 9.0. The compounds were also docked to get an insight of the binding interaction pattern with the active site of the target protein, and the results were found to be in consonance with the experimental findings. *In-silico* ADMET prediction was carried out for the title compounds. The study concludes that the synthesized compounds exhibit potential in supressing inflammation, and therefore can be considered for designing more such compounds as anti-inflammatory agents. Also, since the synthesized title compounds are non-carboxylic analogs, they may be considered as non-ulcerogenic, safe and effective anti-inflammatory agents.

Keywords: chalcones; pyrazoline; Michael adduct; *in-vivo;* anti-inflammatory; molecular docking; *in-silico* ADMET.

1. INTRODUCTION

Inflammation is the primary immune response of a body toward damage of its cells or tissues by external stimuli such as injury or pathogens [1]. A variety of chemical mediators from circulatory system, inflammatory cells, and injured tissue actively contribute towards inflammatory response. Some of the most strongly involved chemicals are the prostaglandins (PGs), leukotrienes (LTs), histamine, and bradykinin. More recently, platelet-activating factor (PAF) and interleukin-1 are also found to play a significant role in the process. However, the existing drugs such as NSAIDs including, selective COX-2 inhibitors [2] and the corticosteroids have unavoidable side effects [3], including incidences of stroke, heart attack, gastro-intestinal and renal damage [4]. Thus, there is a need in developing some new drug molecules with safer application as anti-inflammatory agents.

Heterocyclic ring systems such as pyridine have been found to display diverse pharmacological activities. Chalcones, i.e., 1,3-diaryl-2-propen-1-ones, may either be synthetic or natural in origin belong to the family of flavanoids [5]. Chalcones contain two aromatic rings linked by an aliphatic three-carbon chain [6]. These are useful synthons in the synthesis of a large number of bioactive molecules [7]. Pyrazolines are among them, and are well known nitrogen containing heterocyclic compounds [8]. Considerable attention has been focused on pyrazoline structure as it possesses a broad spectrum of biological activities such as anti-amoebic, anti-microbial, monoamine oxidase inhibitor, anti-mycobacterial, antidepressant, anticonvulsant and anti-inflammatory [3]. The nucleus is also found in niflumic acid and flunixin, the two traditional NSAIDs belonging to the class of fenamates. The presence of acetyl group in the pyridine makes it a versatile precursor for the synthesis of chalcones and pyrazoline derivatives. Also, the Michael addition is efficient reaction for the formation of C-C bonds. These diverse structures are either themselves vital drug analogs or can provide important building blocks for new drugs and bioactive moieties.

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