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Synthesis and Characterization of Some New Pyridine and Pyrimidine Derivatives and Studying Their Biological Activities

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Abstract:

Heterocyclic systems, which are essential in medicinal chemistry due to their promising cytotoxic activity, are one of the most important families of organic molecules found in nature or produced in the laboratory. As a result of coupling *N*-(4-nitrophenyl)-3-oxo-butanamide (**3**) using thiourea, indole-3-carboxaldehyde, or piperonal, the pyrimidine derivatives (**5a** and **5b**) were produced. Furthermore, pyrimidine **9** was synthesized by reacting thiophene-2-carboxaldehyde with ethyl cyanoacetate and urea with potassium carbonate as a catalyst. The chalcones **11a** and **11b** were synthesized by reacting equal molar quantities of 1-naphthaldehyde and 2-quinoline carboxaldehyde with 4-Bromo acetophenone and 4-fluoro acetophenone respectively. Pyrimidine **13** was synthesized by reacting chalcone **11a** with guanidine hydrochloride in the presence of potassium hydroxide. Pyridine derivative **14** was prepared from the reaction of chalcone **11b** with ethyl cyanoacetate and ammonium acetate in glacial acetic acid. In addition, the reaction of 4-methyl benzaldehyde and 4-fluoro acetophenone with ethyl cyanoacetate and ammonium acetate in n-butanol gave pyridine derivative **16**. Spectral investigations (FT-IR, ^{1}H, and ^{13}C-NMR) and EI-MS spectra were used to determine the structure of the prepared compounds. The synthesized derivatives were tested in vitro for their potential cytotoxicity against two different human cancer cell types, MCF-7 (breast cancer cell) or HepG2 (liver cancer cell). Compounds **5a** and **14** displayed cytotoxic activity versus HepG2 cell line with IC_{50} values of 43.84 and 57.14 µg /mL, respectively. Furthermore, the pyridine compound **14** demonstrated cytotoxic action versus MCF-7 with an IC_{50} value of 50.84 g/mL. The antibacterial and anti-parasitic properties of the synthesized derivatives have also been described.

Keywords: Anti-bacterial, Anti-parasitic, Cyanopyridine, cells (HepG2, MCF-7), Pyrimidine.

Introduction:

Nitrogen-based heterocyclic compounds are regarded as an extremely important class of compounds that play an important role in health care and pharmaceutical drug design [1, 2]. Chalcones have been linked to a variety of biological activities. Furthermore, they are well-known intermediates in the synthesis of various heterocyclic compounds such as pyrimidines and pyridines [3-6]. Pyrimidines are the most significant six-membered heterocyclics, with two nitrogen atoms in positions 1 and 3. The pyrimidine was obtained from nucleic acid hydrolyses and is a substantially weaker base than pyridine and water soluble[7]. Pyrimidines are essential biologically because they are connected to nucleic acids and are used to construct DNA and RNA[8]. Pyrimidine derivatives, such as cytarabine and 5-fluorouracil, are widely used as anticancer drugs because their toxicity is expressed in the S phase of the cell cycle, which kills only actively dividing cells [9]. Chalcones and pyrimidines have been linked to a variety of biological and pharmacological activities, including antibacterial, anti-inflammatory, analgesic, anti-hypertensive, and CNS effects [10-12]. Additionally, Pyridines are an organic heterocyclic compound with a six-member ring with five carbons and one nitrogen atom. Pyridine and its derivatives are antimicrobial, antiviral, antioxidant, antidiabetic, anticancer, antimalarial, anti-inflammatory, analgesic, anti-convulsant, and anti-parkinsonian properties [13, 14]. Cyanopyridines have piqued the interest of medicinal chemists due to their heterocyclic