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Short communication

Design and synthesis of pyrimidine molecules endowed with thiazolidin-4-one as new anticancer agents

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ABSTRACT

Design and synthesis of new pyrimidine derivatives clubbed with thiazolidin-4-one from 4-(2-chlorophenyl)-6-(2,4-dichlorophenyl)pyrimidin-2-amine and their *in vitro* anticancer activities were screened at National Cancer Institute (NCI), USA against full NCI 60 cell lines. Compound **2** (NSC: 765735) exhibited remarkable growth inhibition at single dose (10 μM) and encourage chosen for broadcast at 10-fold dilutions of five different concentrations (0.01, 0.1, 1, 10 and 100 μM). The compound **2** was found better quality for Lung cancer cell line (HOP-92) by viewing growth inhibition (GI_{50} 0.52) and no cytotoxicity seen (LC_{50} > 100). Molecular docking study was performed using Maestro 9.0 (Schrodinger Inc. USA) to provide binding mode into binding sites of CDK2. Compound **2** could be used as a lead compound for developing new potential anticancer agents.

1. Introduction

The cell cycle is a highly proscribed and prearranged mechanism which is fundamental in each cell of an organism. A term of the cell cycle malady in which cells carve up mitosis without manage called as cancer and it's not only affect the appropriateness but also financial system of the patient. Therefore, it is buildup a monetary shock and amplified financially viable load for family as evenly for patient to be exact with a lot of panic and hopelessness everywhere [1–3]. The value of many accessible anticancer molecules is restricted by their toxicity to usual quickly growing cells in the intestinal and bone marrow areas. The solemn difficulty of on hand anticancer agents is that the cancerous cells which are primarily covered up by a precise medicine may buildup resistance for that exact medicine. While foremost altered have been ended in the accessible chemotherapeutic through molecular biology, empirical screening, rationale drug discovery and development and up till now nonstop painstaking duty of medicinal chemistry for pointed new anticancer agents [4–6].

At the moment more than 60% of the medicines, which are in practice, are synthetic molecules and step by step the scale of synthetic medicinal chemistry is widened. In the middle of the extensive series of heterocyclic and fused heterocyclic compounds were evaluated as prospective anticancer agents, the derivatives of pyrimidine heterocyclic compounds are of immense significant in their biological plus synthetic loom of medicinal chemistry essentially subsequent to the finding of Fluorouracil (**1**) [7], Tegafur (**2**) [8], NU6027 (**3**) [9], Uramustine (**4**) [10], Cytarabine (**5**) [11], Thiarabine (**6**) [12], Ara-C (**7**) [13], Gemcitabine (**8**) [14], CNDAC (**9**) [15], Capecitabine (**10**) [16], CGP60474 (**11**) [17], Nimustine (**12**) [18], Trimetrexate (**13**) [19], ClNK4 (**14**) [20] and some other related heterocyclic moieties for example; Troxacitabine (**15**) [21], Decitabine (**16**) [22], Forodesine (**17**) [23], Mercaptopurine (**18**) [24] and Olomoucine (R_1 = H, R_2 = Me), *N*-9-Isopropylolomoucine (R_1 = H, R_2 = iPr) (**19**) [25] as revealed in Fig. 1. The chemically pinched of recently geared up compounds as lucid drawing with Fluorouracil and additional interrelated heterocyclic compounds structurally shown in Fig. 2.

In excess of the pasted few years, pyrimidine has been given a great deal curiosity and reported to have prospective antitumor/antiproliferative/anticancer activity [26–32] along with antimicrobial [33,34], antiviral including anti-HIV [35], anti-inflammatory including analgesic and ulcerogenic [36,37], antidiabetic [38], anti-parkinsonism [39], antipsychotic [40], anticonvulsant [41], antihistaminic [42], antinociceptive [43], molluscicidal [44], herbicidal [45], steroidal like compound [46] and anthelmintic activity [47]. In persistence of our earlier and ongoing research works on the heterocyclic and fused heterocyclic compounds as new anticancer

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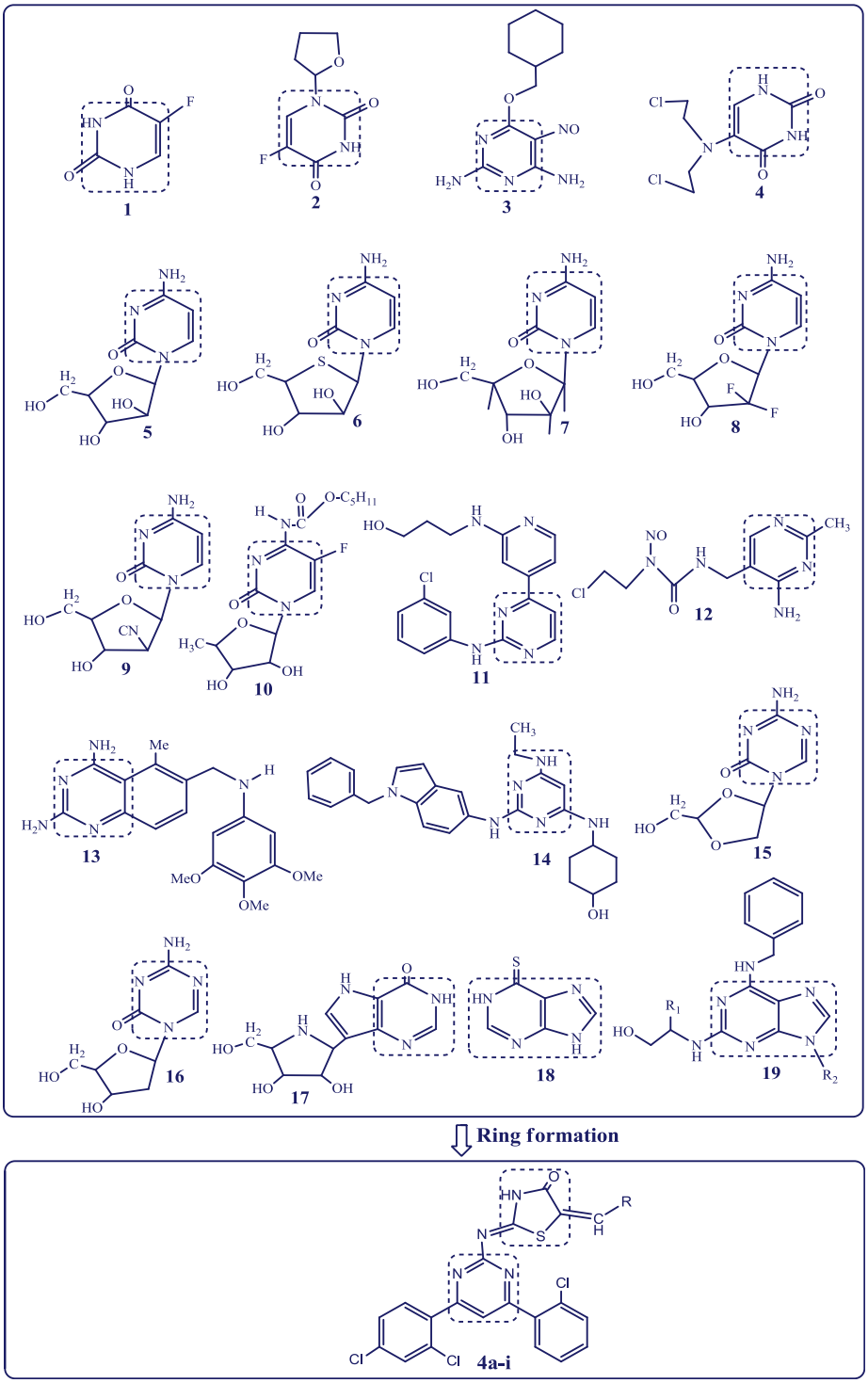

Fig. 1. Reported structure (**1**–**19**) of some anticancer agents having pyrimidine ring and other related heterocyclic scaffold and rationally design target compounds (**4a**–**i**) having above hybrid ring system.

agents was found to be reasonable choosy towards Leukemia cancer with mean growth inhibition (GI) as GI_{50} 6.59, GI_{50} 12.62 and GI_{50} 1.04 [48–51]. In sight of these points, it was consideration important to design and synthesized new molecules that to have substituted pyrimidine. The pyrimidine molecules were also clubbed with other heterocyclic ring like thiazolidinone, thiazolo-pyrimidine and thiazolo-isoxazoline with a glance forward to produce capable anticancer agents. For that reason, a number of new compounds were synthesized and screened for their *in vitro* anticancer activities at Development Therapeutic Program, National Cancer Institute (NCI), Chemotherapeutic Research division, USA, on nine human systems (Leukemia, Melanoma and cancers of Lung, Colon, Brain, Breast, Ovary, Kidney and Prostate) against full NCI 60 cell line panel according their applied protocol.