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Anticancer Potential of Novel Pyrimidine Analogs: Recent Updates

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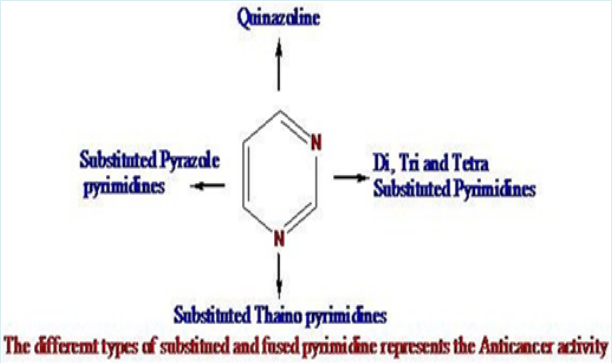
Abstract

Pyrimidine, having two nitrogen atoms, looks like pyridine and benzene. In nature, pyrimidine is present in different forms, such as the bases of DNA and RNA. Due to its structure, various kinds of biological activity have been observed. The substituted and fused pyrimidine derivatives were chemically synthesized and showed anti-cancer potential against cancer cell lines (SW480, A549, CCRF-CEM, THP-1, HepG2, HCT-116, PC3, Huh-7, CNE-2, MGC-803, and MDA-MB-435). Based on the experimental results, the substituted pyrimidines and fused derivatives showed remarkably enhanced anticancer activity, which may be due to the presence of Cl, F, Br, CH3O, aryl urea, indolyl pyrimidine, thienopyrimidine, benzyl amino pyrimidine and the pyrimidine moiety. In this article, recent anticancer research findings were highlighted.



Keywords: Pyrimidine Derivatives; Anticancer Activity

Introduction

Pyrimidine, having two nitrogen atoms, looks like pyridine and benzene. In nature, pyrimidine is present in different forms, such as the bases of DNA and RNA, which show various biological and pharmacological activities, such as di, tri, and tetra substituted pyrimidines, substituted pyrazole and thieno pyrimidines, and quinazoline, which represents potent anticancer activity. The experimental results of pyrimidine derivatives showed potent anticancer potential against all cancer cell lines (SW480, A549, CCRF-CEM, THP-1, HepG2, HCT-116, PC3, Huh-7, CNE-2, MGC-803, and MDA-MB-435). The brief observations are listed in the following.

Medicinal Significance

Anticancer Activity: Kilic-Kurt Z, et al. synthesized pyrimidine containing aryl urea moieties and showed potent anticancer activity (1&2) against colon and prostate cancer cell lines (SW480, IC_{50}: 11.08 µM, SW480) [1] (Figure 1).

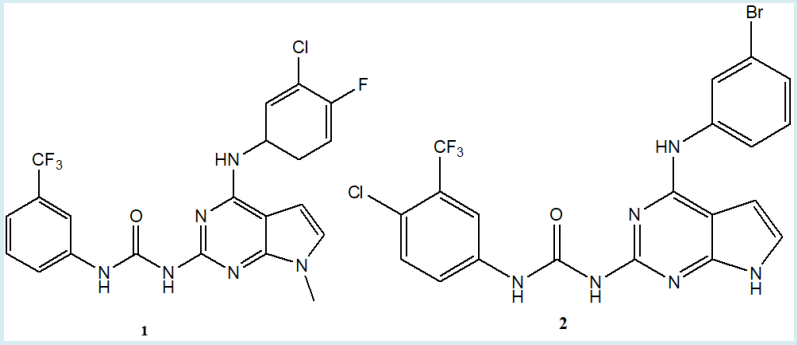


Figure 1: Shows potent anticancer activity (1&2) against colon and prostate cancer cell lines (SW480, IC50: 11.08 µM, SW480).

Tylinska, et al. developed 4-Chloro-6-[2-(6-methoxy-3,4-dihydronaphthalen-1(2*H*)-ylidene)hydrazinyl]pyrimidine and its derivative showed potent anticancer activity (3 & 4) against cancer cell (MCF-7, A549, HeLa) lines [2].

Ahmed NM, et al. synthesized the indolyl pyrimidine hybrids (5, 6 & 7) and showed potent antitumor activity in the following cancer cell (HepG-2, HCT-116 and MCF-7) lines [3] (Figure 2).

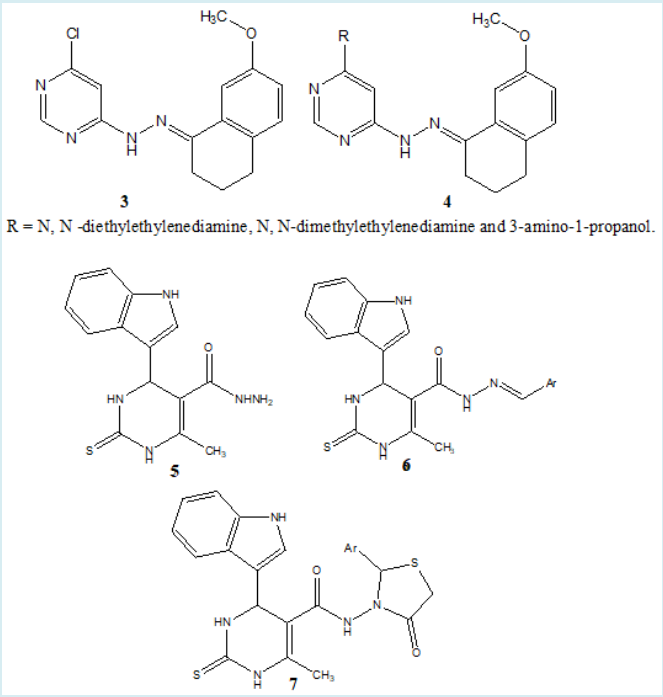


Figure 2: Shows potent antitumor activity in the following cancer cell (HepG-2, HCT-116 and MCF-7) lines.

Safinaz ESA, et al. developed fused pyrimidines, and the experimental results revealed that Compounds 8 & 9 showed significant anticancer potential in the following cancer cell (MCF7, PC3, and A549) lines [4]. Ahmed NM, et al. observed the experimental results of pyrimidine pyrazoline anthracene (10) derivatives showed potent activity against HepG-2 and Huh-7 (hepatocellular carcinoma-HCC) cell lines [5] (Figure 3).

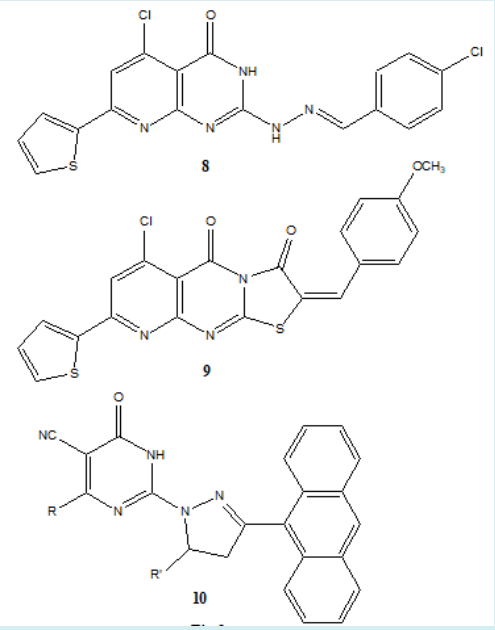


Figure 3: Compounds 8 & 9 showed significant anticancer potential in the following cancer cell (MCF7, PC3, and A549) lines.

Abu-Hashem, et al. synthesized the tetra-alkyldihydropyrimidopyrazine-triones (11 & 12) and showed potent anticancer activity [6].

Abu-Hashem, et al. synthesized the polycyclic pyrimidine derivatives and 1,2,4-triazoloimidazo-pyrrolotriazolothienopyrimidindiones among all compounds 13 & 14 showed significant anticancer potential against human cancer cell (CNE2, KB, MCF-7, and MGC-803) lines [7] (Figure 4).

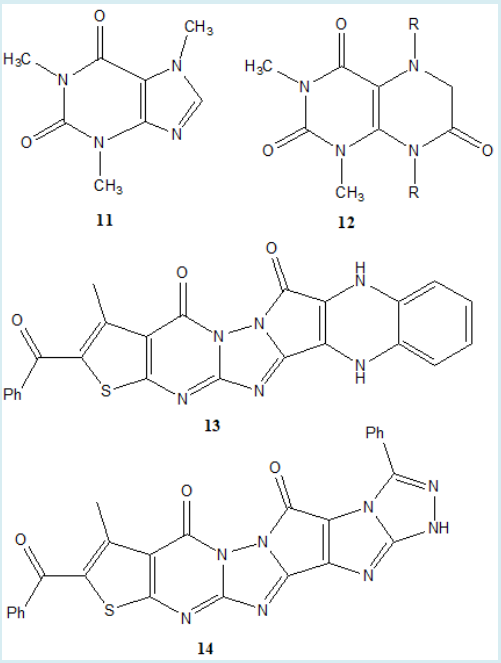


Figure 4: Synthesized the tetra-alkyldihydropyrimidopyrazine-triones (11 & 12) and showed potent anticancer activity & Compounds 13 & 14 showed significant anticancer potential against human cancer cell (CNE2, KB, MCF-7, and MGC-803) lines.

Samvel SN, et al. developed the pyridothienopyrimidines among all compounds (15) showed anticancer potential against the cancer cell (HeLa) line [8]. Shyyka O, et al. synthesized the new thienopyridine-ones and benzylaminopyrimidinone among all compounds (16) and showed potent anticancer potential against cancer cell (MDA-MB-435) lines [9] (Figure 5).

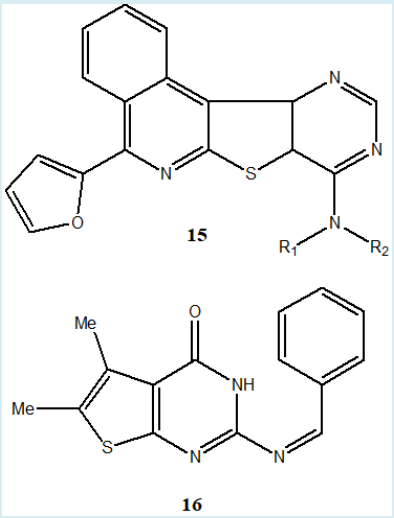


Figure 5: Compound (15) showed anticancer potential against the cancer cell (HeLa) line & Compound (16) and showed potent anticancer potential against cancer cell (MDA-MB-435) lines.

Abbas N, et al. studied the SAR of fused and substituted pyrimidine, and eco-friendly synthetic approaches and tiny molecules fused with a pyrimidine moiety showed potent anticancer activity [10]. Huang T, et al. synthesized the oxacalix[2]arene[2]pyrimidine derivatives exhibit anticancer potential in the following cell lines (HepG-2, HeLa, MCF-7, and A549) MTT assay used [11]. Mounir A, et al. synthesized S-glucoside derivatives and showed potent anticancer activity against (HePG-2, HCT-116, HePG-2, and PC3) cancer cell lines [12]. Mghwary, et al. developed thienopyrimidine derivatives with different substituent's showed poor to potent anticancer potential against MCF-7 cancer cell line [13]. Huang Tonghui, et al. synthesized oxacalix[2]arene[2] pyrimidine derivatives and showed significant anticancer potential against human cancer (MCF7, HeLa, A549, and HepG2) cell line [14].

The recent review of pyrimidines reveals that pyrimidine moiety is a versatile compound for constructing and designing new novel derivatives for medicinal applications. Recent review articles of our group on the medicinal plants & other heteroatom reveals the broad spectrum of therapeutical applications [15-32].

Conclusion

Different series of novel fused, substituted pyrimidine derivatives showed moderate, equipotent, potent, remarkable anticancer activity against cancer cell (SW480, A549, CCRF-CEM, THP-1, HepG2, HCT-116, PC3, Huh-7, CNE-2, MGC-803 and MDA-MB-435) lines. The Structure activity relationship may be due to presence of Cl, F, Br, CH_3O, aryl urea, indolyl pyrimidine, thienopyrimidine, benzyl amino pyrimidine and the pyrimidine moiety.

Conflict of Interest

The authors declare that there is no conflict of interest.

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