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BIOLOGICAL ACTIVITIES OF VARIOUS PYRROLOPYRIMIDINE DERIVATIVES: A MINI REVIEW

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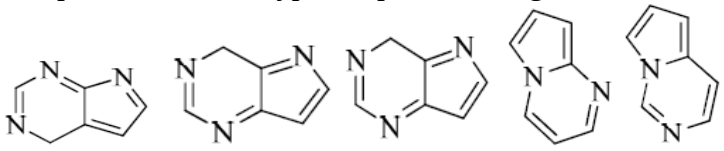
Abstract: The Pyrrolopyrimidine has gained much attention in the field of medicinal chemistry. Thus Pyrrolopyrimidine scaffold with various substituents is known to exhibit a wide range of biological activities. Pyrrolopyrimidine derivatives have captivated a great deal of interest owing to their pharmacological properties as they have wide range of interesting biological activities such as antimicrobial, diuretics, antioxidant, anti-inflammatory, analgesic, antidiabetic, antiviral and anti-cancer and other useful biological activities. These activities are described individually in this review.

Keywords: Pyrrolopyrimidine, biological activities, antimicrobial, antioxidant, anti-cancer

Introduction Heterocycles can meet many demands of biochemical systems due to its ease of its flexibility. As a result heterocycles have laid the platform fast exchange of research in the field of medicine, analytical chemistry, organic and pharmaceutical chemistry. Nitrogen heterocycles are of special interest as they constitute an important class of natural and non-natural products, many of which exhibit useful biological activities. The ambidextrous properties and captivating structures of *N*-heterocyclic compounds encourage chemists to keep on synthesizing new and novel nitrogen heterocycles with versatile pharmacological activities.

Pyrrolopyrimidine is a bicyclic nitrogen containing compound with the molecular formula $C_6H_5N_3$ where a pyrimidine nucleus is fused to a pyrrole, an electron rich ring fused to an electron poor ring. There are five different structural variations of a basic ring system i.e., [2,3-d], [3,2-d], [3,4-d], [1,2-a] and [1,2-c] are possible. Pyrrolopyrimidine derivatives have been posses different types of pharmacological and biochemical properties **[1-5].**



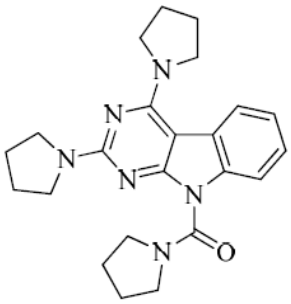
[2, 3-d] **[3, 2-d]** **[3, 4-d]** **[1, 2-a]** **[1, 2-c]**

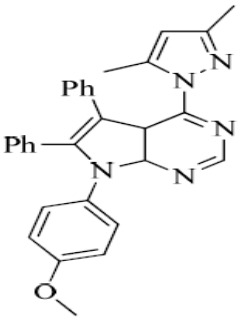
The natural occurrence and outstanding biological and pharmacological properties of pyrrolopyrimidine have been the logic for progressive study of their synthesis, their biochemical and physical properties, and their fusion into nucleic acids. Among them *7H*-

pyrrolo[2,3-d]pyrimidine and the *5H*-pyrrolo[3,2-d]pyrimidine based compounds occupy a particular place due to their very close structural analogy to the basic purine skeleton (these compounds can be viewed as 5-deaza- and 7-deazapurines, respectively). Pyrrolopyrimidine-containing compounds, also known as 7-deazapurines, have been a source of research interest since the discovery of toyocamycin in 1956 [6]. Secondary metabolites produced by various strains of *Streptomyces* have known to possess pyrrolopyrimidine functional groups. These act as the cofactors which are involved in the biosynthesis of tetracycline antibiotics [7] and DNA repair [8] to compounds with antoxoidant [9,10], diuretic [11,12], herbicidal, antifungal, antibacterial, anti-parasitic [13], antidiabetic [14], antineoplastic [15-17] and other anticipated biological activities [18-21]. Due to their structural resemblance to purines and owing to their interesting biological properties there has been an outpouring activity with increased interest in synthesizing these ring system in recent years. Pyrrolopyrimidine functional groups adorn a large number of compounds from marine or terrestrial sources, or as modified bases in t-RNA [22]. Pyrrolo[2,3-d]pyrimidine derivatives have captivated a great deal of interest owing to their pharmacological properties as they have wide range of interesting biological activities such as antimicrobial, antioxidant, antidiabetic, diuretics, analgesic, anti-inflammatory, antiviral, anti-cancer and other activities.

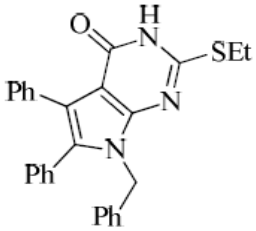
Anti-inflammatory activity: Inflammation is a normal protective response to tissue injury caused by several causes [23]. Inflammation is triggered by the release of chemical mediators from the injured tissue and migrating cells. In inflammation process prostaglandins play a very important role. In the past decade, efforts aimed at the discovery of therapeutically useful inhibitors of cyclooxygenase-2 (COX-2) have intensified. Conversion of arachidonic acid (AA) to prostaglandins is inhibited by almost all classes of non-steroidal anti-inflammatory drugs (NSAIDs). So NSAIDs are the most widely established and effective remedy for decreasing pain and inflammation. In search of new polyheterocyclic compounds with potential therapeutic value pyrrolopyrimidines are evolved as a promising anti-inflammatory drug. A series of novel pyrrolo[2,3-d]pyrimidine and fused pyrrolo[2,3-d]pyrimidine derivatives were evaluated for their anti-inflammatory activities *in vivo*. Some of the pyrrolo [2,3-d] pyrimidine compounds are promising anti-inflammatory agents. Among all the synthesized compounds, compound **(1)** (4-(3,5-Dimethyl-4*H*-pyrazol-1-yl)-7-(4-Methoxyphenyl)-5,6-diphenyl-4,7dihydro-3*H*pyrrolo[2,3-d]pyrimidine showed a promising anti-inflammatory activity which was comparable to the standard drug Ibuprofen [24].

PNU-142731A is a potent and efficient pyrrolopyrimidine inhibitor of eosinophilic lung inflammation that is currently in Phase II clinical evaluation for the potential treatment of asthma [25]. The new pyrrole derivatives and pyrrolo [2,3-d]pyrimidine derivatives were evaluated for their anti-inflammatory activity. Among these compounds, compound **(2)** showed a potent anti-inflammatory activity compared to the standard. The activity of the pyrrolopyrimidine compounds depends upon the nature of the side group on the C-2 at the



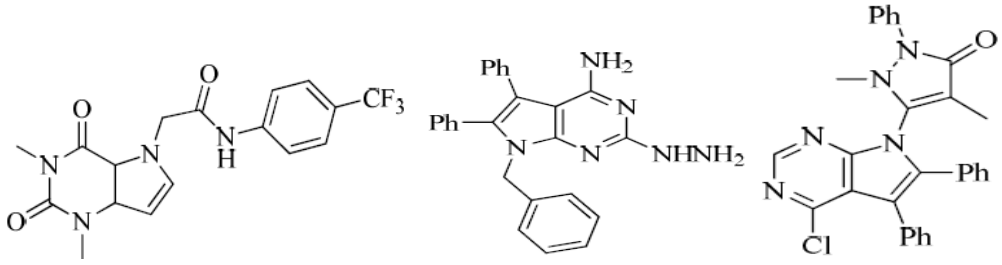


heterocyclic system [26].



PNU-142731A **1** **2**

Synthesis and functional evaluation of a series of 7-substituted-1,3-dimethyl-1,5-dihydro-pyrrolo-[3,2-d]pyrimidine-2,4-dione derivatives designed as TRPA1 antagonists was carried out. The transient receptor potential ankyrin 1 (TRPA1) channel is activated by a series of by-products of oxidative/nitrative stress, produced under inflammatory conditions or in the case of tissue damage, thus generating inflammatory and neuropathic pain and neurogenic inflammatory responses. These findings have identified TRPA1 as an emerging opportunity for the design and synthesis of selective inhibitors as potential analgesic and anti-inflammatory agents. The introduction of different substituted N7-phenylacetamide or N7-{4-(substituted-phenyl)-thiazol-2-yl}-acetamide chains, compounds were screened to estimate their ability to block acrolein-mediated activation of native human and rat TRPA1 channels employing a fluorometric calcium imaging assay. Among them compound **(3)** showed considerably improved potency (IC_{50}=400 nM) against human TRPA1 [27]. Using pyrrole as precursors pyrrolo[2,3-d] pyrimidine-2 and/or 4 thione derivatives were synthesized, Alkylation of the thione compounds in basic medium afforded the pyrrolo [2,3-d] pyrimidine and some 2-amino pyrrolo [2,3-d]pyrimidines. These compounds were evaluated for their *in vitro* anti-inflammatory and *in vivo* anti-microbial activity. Among the screened compounds, compound **(4)** showed a potent activity [28]. The Pyrrolo[2,3-d]pyrimidine derivatives, pyrrolo[3,2-e]tetrazolo[1,5-c]pyrimidine and pyrrolo[4,3e] [1,2,4]triazolo[1,5-c] pyrimidine derivatives were synthesized, the compounds were screened for both antimicrobial activity and anti-inflammatory activity. Compound **(5)** showed a promising activity compared to the standard drug [29].

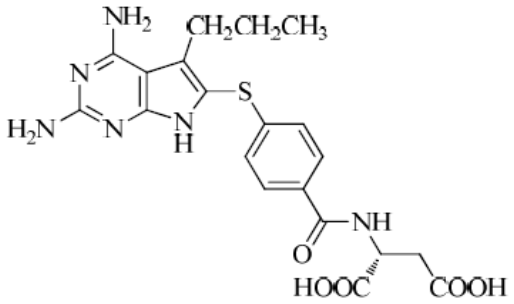


3 **4** **5**

Antitumor activity: Angiogenesis is the process by which new blood vessels broaden from established blood vessels [300]. Several mechanisms are involved in their cytotoxic activities as being dihydrofolate reductase inhibitors [31]. tyrosine kinase inhibitors [32] or adenosine receptor antagonist [33]. The emergence of tumor cells resistant to a range of cytotoxic drugs

is a serious problem in cancer chemotherapy. Pyrrolo[2,3-d]pyrimidine derivatives have aroused latest attention as potent anticancer agents [33]. Aleem Gangjee *et al.,* synthesized a novel classical and nonclassical antifolates by using 2,4-diamino-5-alkylsubstituted-7*H*pyrrolo[2,3-*d*]pyrimidines, they were evaluated for their antitumor activity. Among the synthesized compounds, compound **(6)** showed IC50 of 60 nM as a potent inhibitor of human DHFR, it inhibited tumor cells in culture with GI50 e 10-7 M [34].

The new HER2/EGFR dual kinase inhibitors, designed pyrrolo-[3,2-*d*]pyrimidine derivatives capable of fitting into the receptors' ATP binding site. Human epidermal growth factor receptor 2 (HER2) and epidermal growth factor receptor (EGFR) are involved in breast, lung, gastric, prostate, and other cancers; one, lapatinib, is currently approved for breast cancer. All the compounds were tested for antitumor activity. Among the screened compounds, compound **(7)** showed significant HER2 and EGFR (HER1) inhibitory activities as well as tumor growth inhibitory activity. Also the X-ray co-crystal structures of **(7)** with both HER2 and EGFR showed that **(7)** interacts with the expected residues in their respective ATP pockets. Moreover it reflected the good oral bioavailability, **(7)** exhibited potent *in vivo* efficacy in HER2 over expressing tumor xenograft models. So compound **(7)** (TAK-285) was a promising candidate for clinical development as a novel HER2/EGFR dual kinase inhibitor [35].



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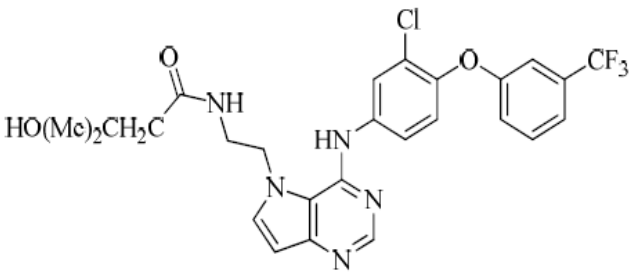

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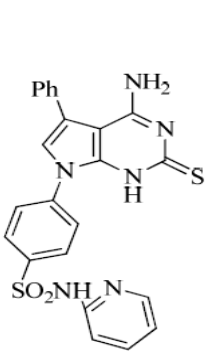
A series of 5-phenyl-pyrrolo [2,3-d] pyrimidine derivatives substituted at *N*-pyrrole by either sulfathiazole or sulfa pyridine moiety. The compounds were screened for anticancer activity. Also some compounds were evaluated as radio sensitizing agents to prove their ability to enhance the cell killing effect of gamma-radiation. The compounds were screened for their *in vitro* cytotoxicity against human liver and breast cancer cell lines (HEPG2 and MCF7). Among the compounds screened compound **(8)** showed a potent activity against both the cell lines HEPG2 and MCF7 [36]. The pyrrolopyrimidine inhibitors of the Akt kinase. Among the synthesized compounds, compound **(9)** possessed a strong inhibition towards Akt 1 kinase IC_{50} of 2.4±0.6 nM, Akt cell potency of 50±19nM, which inhibited the tumor growth about 68% of tumor growth in a mouse xenograft model [37]. The inhibition of the interactions between the tumor suppressor protein p53 and its negative regulators, the MDM2 and MDMX oncogenic proteins by carrying out molecular docking, molecular dynamics (MD) simulations, and molecular mechanics Poisson-Boltzmann and generalized Born/surface area (MMPB/GBSA) binding free energy of few pyrrolopyrimidine compounds. Among them compound **(10)** showed to the active compound. Detailed study of MM-PB/GBSA calculations on the MDM2–**(10)** and MDMX–**(10)** complexes revealed that the binding free energies are similar for the two complexes. Also the van der Waals energy is the largest component of the binding free energy for both complexes, which indicates that the interactions between the compound **(10)** and MDM2 and MDMX are dominated by shape complementarity. The obtained computational results indicated that the compound **(10)** can act as a dual inhibitor of MDM2–p53 and MDMX–p53 interactions [38].



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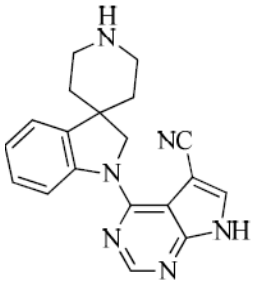

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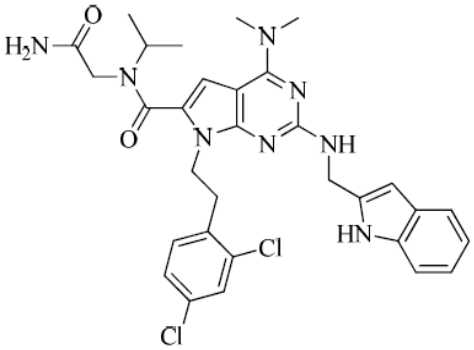

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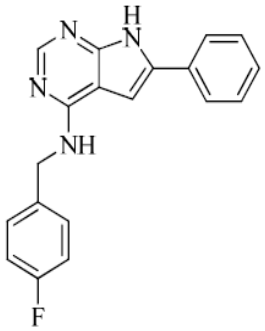
A series of 4-*N*-substituted 6-aryl-7*H*-pyrrolo[2,3-d]pyrimidine-4-amines was synthesized and were evaluated for *in vitro* EGFR (ErbB1) tyrosine kinase inhibitory activity. Eight of the new compounds had IC_{50} values in the range of 2.8-9.0 nM. The anticancer activity was tested using HELA cells. Compound **(11)** was a potent inhibitor of EGFR (ErbB1) tyrosine kinase [39]. Sulfur linked new pyrrolo[2,3-d]pyrimidines with heteroaryl substitution at 5th position were synthesized, by incorporating reputed pharmachoric moieties like benzimidazole and benzothiazole as heteroaryl groups. By using HCT116 colon cancer cell lines cytotoxic effect of synthesized compounds were estimated. Among all the compounds screened compound **(12)** showed the potent inhibition in a dose dependent manner [40]. A series of pyrrolopyrimidine derivatives were evaluated for Tie-2 kinase inhibitors compound **(13)** a ketophenyl pyrrolopyrimidine urea showed a potent *in vitro* attributes and stout oral tumor growth inhibition in animal models. Compounds **(14), (15), (16)** and **(17)** are few tie-2 active pyrrolopyrimidines which can inhibit the tumor growth [41].



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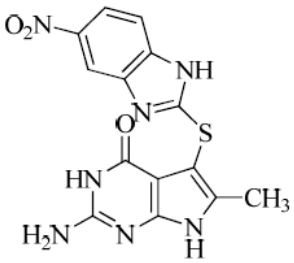

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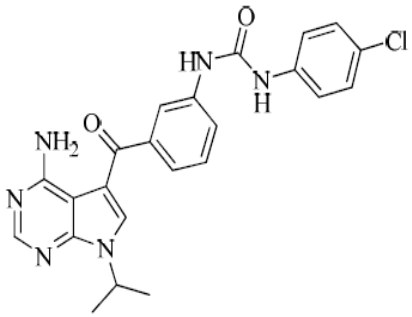

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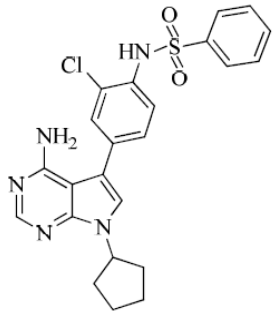

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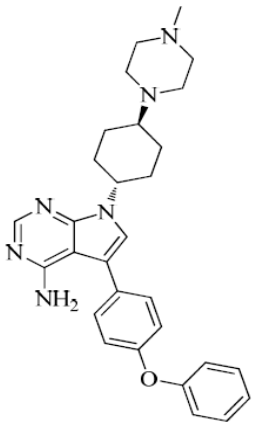

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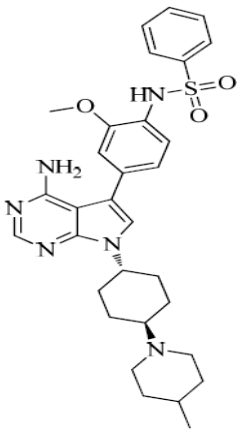

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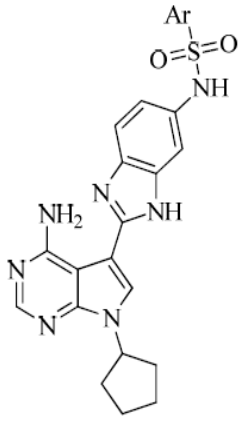

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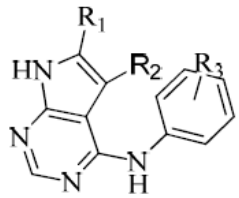
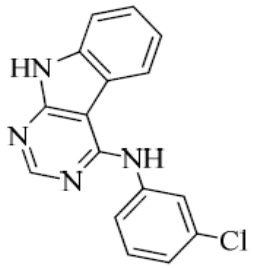
The 4-(phenylamino)-7*H*-pyrrolo[2,3-*d*] pyrimidines have been identified as a novel class of potent EGF-R protein tyrosine kinase inhibitors. Among the synthesized compounds, compounds **(18)**, **(19)**, **(20)**, and **(21)** showed inhibition of EGF-stimulated cellular tyrosine

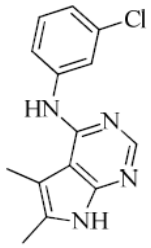
phosphorylation at the IC_{50} values between 0.1 and 0.4 μM, whereas PDGF-induced tyrosine phosphorylation was not affected by concentrations up to 10 μM [42].

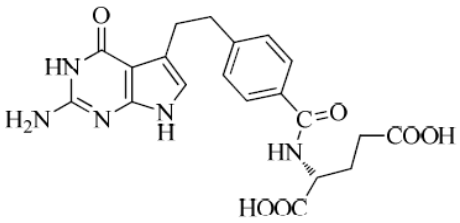




18 R1= Me; R2=Me; R3=3-Cl **21**
19 R1= H; R2=H; R3=3-Cl
20 R1=H; R2=H; R3= 3-Br

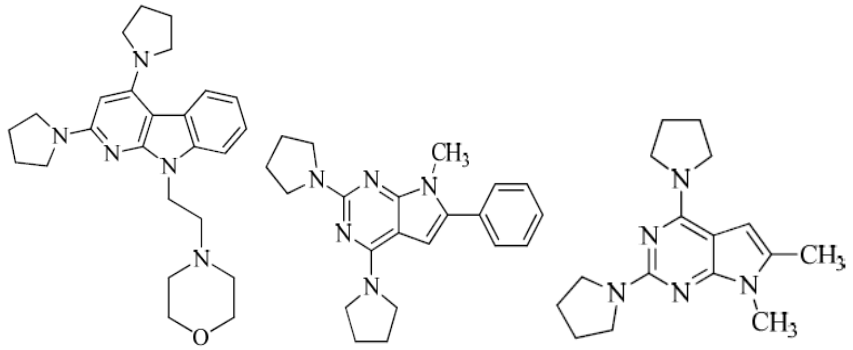
Optimization of selectivity and the biological profile of such pyrrolopyrimidine derivatives carried out at our research department, led to compound **CGP 59326** being promoted to development status as an antitumor agent, **Pemetrexed** is a pyrrolopyrimidine drug that is clinically used as antitumor agents [44].





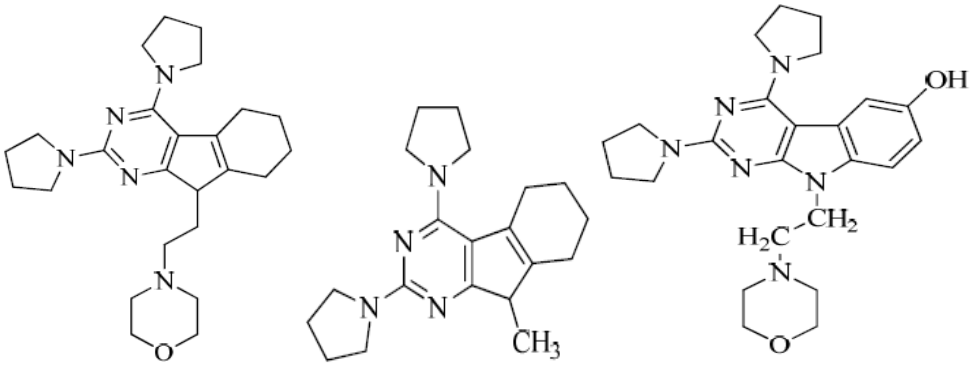
CGP 593261 **Pemetrexed**

Antioxidant activity: For the life of aerobic organisms oxygen is an essential component it may become toxic if supplied at higher concentrations. Dioxygen in its ground state is relatively unreactive; its partial reduction gives rise to active oxygen species (AOS) such as singlet oxygen, super oxide radical anion, hydrogen peroxide etc. Oxidative stress in the neurodegenerative cascades is linked to various central nervous system (CNS) disorders. This disfunction is associated with disorders such as Alzheimer's disease (AD) [45]. Antioxidants are reported to offer protection against oxidative damage in these disorders. These free radicals are mainly responsible for several diseases like arthritis, cancer, atherosclerosis etc. Damage to the critical cell biomolecules is caused by the presence of intracellular oxygen which is responsible to initiate a chain of unintentional reaction at the cellular level. Free radicals are highly reactive consisting of an odd or an unpaired electron. These free radicals can undergo fast chain reaction that results in the destabilization of the other molecules and produce many more free radicals. Two novel classes of antioxidant compounds that have been developed, namely the pyrrolopyrimidines and 21-amino steroids, inhibit lipid peroxidation and other biomolecular oxidation *in vitro* and *in vivo* [46,47]. Such compounds may be useful pharmacologically in a variety of pathologies involving oxidative stress, including Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, cancer, multiple sclerosis, muscular dystrophy, atherosclerosis, and diabetes mellitus [48] and they may also slow the degenerative processes of aging [49]. During chemical studies related to tirilazad mesylate, a series of novel 2,4-diaminopyrrolo [2,3-d pyrimidines and the compound was subjected to biological activities like antioxidant, CNS neuroprotective, and antiasthma agent. Among the compounds screened for antioxidant activity, compound **U-104067** manifested its ability to act as inhibitors of iron-induced lipid peroxidation and their activity in protecting mouse spinal neurons and human's astrocytes from oxidative injury [50].



U-104067 **PNU-87663** **PNU-89843**

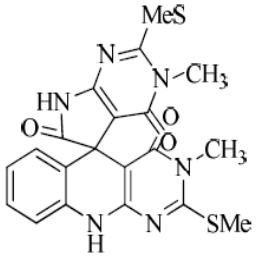
The antioxidant property of pyrrolopyrimidine compound, **PNU-87663** and **PNU-89843** which could readily diffuse across the blood-brain barrier and access intracellular sites was studied, the study revealed that the efficiency of extraction was dependent on serum protein binding, and *in situ* efflux confirms the *in vitro* data showing that **PNU-87663** is retained in brain longer than **PNU-89843** [51]. The measures of lipid and protein oxidation have been used to investigate the proposed antioxidant capacity of **U101033E**. The **U101033E** significantly ($P<0.005$) reduces the formation of the EPR active spin trap *N*-t-butyl-Kphenylnitrone (PBN)-radical adduct by 17.1% at a concentration of 1 mM, four orders of magnitude less than the concentration of PBN. In addition, **U101033E** partially prevents synaptosomal protein oxidation in the presence of Fe (II); however, **U101033E** demonstrates some protein oxidative effects itself. These results are supportive of the proposed role of **U101033E** as a lipid-specific antioxidant, especially for protection against lipid peroxidation that occurs deep within the membrane bilayer, but raise some potential concerns about the oxidative nature of this agent toward proteins [52]. The **U-94430** and **U-106311** also show potent antioxidant activity [53].



U101033E **U-94430** **U-106311**

Antimicrobial activity: The pyrrolopyrimidine antibiotics, tubercidin, toyocamycin and sangivamycin have accelerated noticeable interest because they are powerful antibacterial, antifungal and cytotoxic agents. Since then pyrrolo[2,3-*d*]pyrimidines are known to exhibit a very reasonable antimicrobial activity. The *in vitro* antibacterial activity of spiro[pyrimido[4,5-*b*]quinoline-5,5-pyrrolo[2,3-*d*]pyrimidine] were evaluated. The compounds were tested against *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginusa* (ATCC 85327) (Gram-negative bacteria), *Bacillus subtilis* (ATCC 465), *Staphylococcus aureus* (ATCC 25923) (Gram-positive bacteria).Among all the screened compound, compound **(22)** showed a potent zone of inhibition [54]. Antibacterial and antifungal activity of a series of pyrrole derivatives, pyrrolo[2,3-d]pyrimidine derivatives, pyrrolotriazolopyrimidines and pyrrolotetrazolopyrimidines were checked out against *S. aureus*, *E. coli*, and *Candida albicans*. Among the screened compounds, compound **(23)**, **(24)**, and **(25)** showed exceptional activity than the standard drug flucanozole (MIC 1.5

mg/mL) and against *S. aureus* (MIC 0.31 mg/mL) and the rest of the compounds were inactive against bacteria and fungi. Compounds containing electron withdrawing groups showed a better activity [55].



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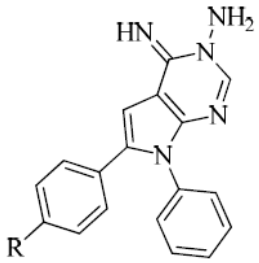
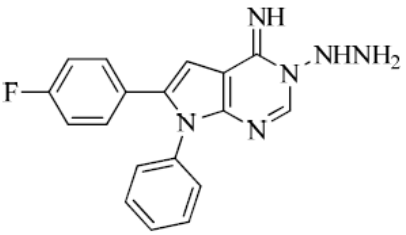
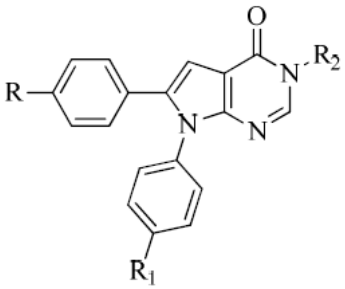


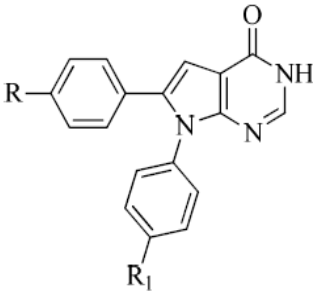
23; R=Br **24**; R=Cl

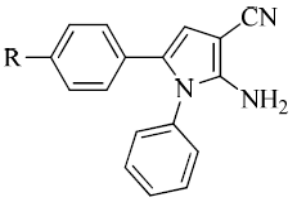


25

Novel pyrrolo [2,3-*d*] pyrimidine derivatives were synthesized, concerning the activity of these new class of pyrrolo[2,3-*d*]pyrimidine derivatives against highly pathogenic avian influenza (HPAI) H5N1 and highly virulent new castle disease virus (NDV). The antibacterial activity against *Escherichia coli* and *Salmonella typhimurium* strains. Among them, compounds **(26), (27), (28), (29)** showed dynamic activity against destructive pathogenic avian influenza (HPAI) H5N1 virus and **(30)** were dominant against highly virulent Newcastle disease virus (NDV) compounds **(26,27,29)** and **(30-34)** were showed a maximum activity against enterobacteriases [*E. coli* and *S. typhimurium*] strains [56].

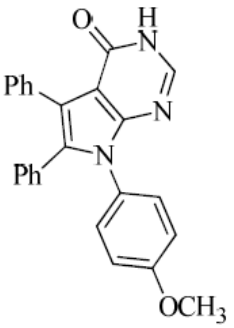






26; R=H; R_1=H; R_2= $CH_2CH_2OCH_2CH_2OH$ **30;** R=H; R1=H **32**; R=H
27; R=H; R_1=H; R_2=$CH_2CHOHCH_2OH$ **31;** R=4-Cl; R1=H **33**; R=4-Cl
28; R=4-Br; R_1=H; R_2=$CH_2CH_2OCH_2CH_2OH$ **34**; R=4-Br
29; R=4-Br; R_1=H; R_2=-$(CH_2)_8CH_3$

Antimicrobial activity of pyrrolo[2,3-*d*]pyrimidines derivatives were evaluated on gram positive (*S. aureus* and *B. subtilis*), gram-negative (*E. coli* and *P. aeruginosa*) and fungal strain *C. albicans*. Compounds **(35), (36)** and **(37)** showed a charismatic microbial activity comparable with the standard drugs amoxicillin and fluconozol [57].



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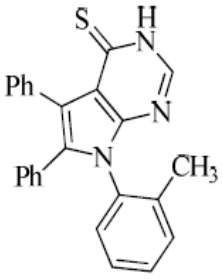

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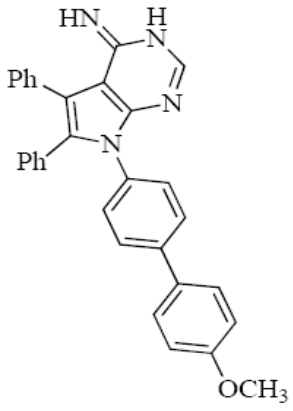
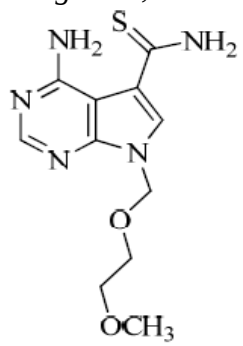


37

Three active analogs series of nonnucleoside pyrrolo[2,3-*d*]pyrimidines were taken from the prior study of this series as inhibitors of human cytomegalovirus (HCMV). Compounds **(38)**, **(39)**, and **(40)** showed 50% inhibitory concentrations (IC50s) of 0.4 to 1.0 mM for HCMV plaque-reduction assay. HCMV enzyme-linked immunosorbent assay (IC50s 51.9 and 0.4 mM, respectively) for 828 and 951 and viral DNA-DNA hybridization assay (IC50 51.3 mM) for **(38)** also demonstrated the same values. The activities of three compounds were comparable with the activity of ganciclovir (GCV; IC50 0.2 mM). Compound **(38)** was equally competent against GCV-sensitive GCV-resistant HCMV clinical isolates [58]. *Pneumocystis carinii, Toxoplasma gondii,* and *Mycobacterium avium*, are few opportunistic pathogens to which AIDS patients are highly susceptible because of their immune compromised state. Compounds **(41), (42)** and **(43)** showed good activity against these strains [59]. Compound **(44)** showed a potent antibacterial activity against *E. coli*, *E. entericus*, *P. aeruginosa*, and *B. subtilis* than the standard ampicillin [60].



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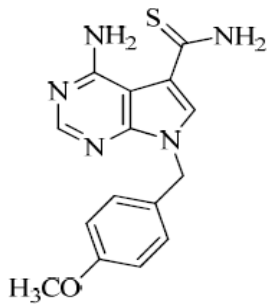

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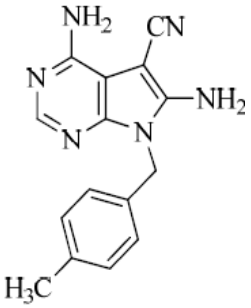

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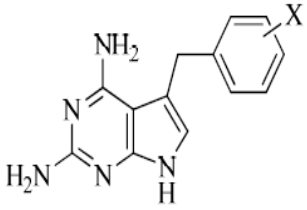
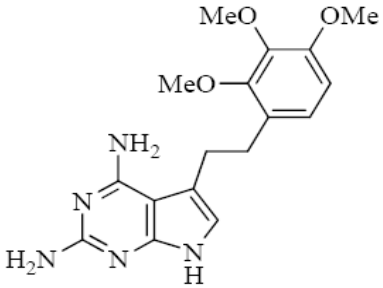


41; X=3', 4'-Cl2
42; X=3',4',5'-(OMe)



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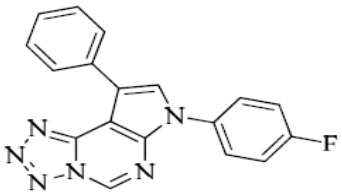
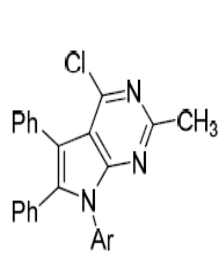


144

Pyrrolopyrimidine containing compounds which are purine based metabolites isolated from the biological sources are known to exhibit good antibiotic property and few compounds isolated from terrestrial sources and marine sources are listed [122].

Anti-diabetic activity: Diabetes mellitus is metabolic disease characterized by increased blood sugar levels for a prolonged duration. In recent years pyrrolopyrimidines show a good anti-diabetic activity. Mohamed *et al.,* synthesized and estimated a novel pyrrole and pyrrolopyrimidine compounds as anti-hyperglycemic agents. Among the screened compounds, compound **(45)** showed a good anti-hyperglycemic activity [60]. The novel pyrrolopyrimidine analogues as a potent dipeptidyl peptidase IV inhibitors, wherein compound **(46)** showed potent anti-diabetic activity compared to alogliptin [61].



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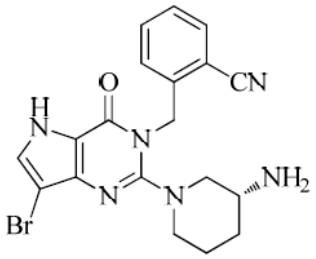
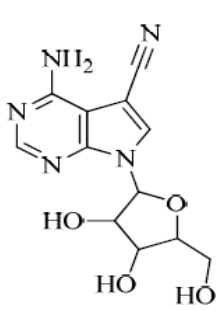
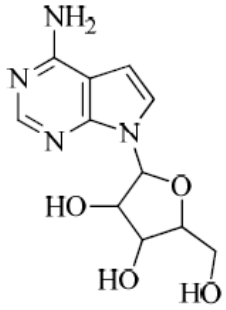


46

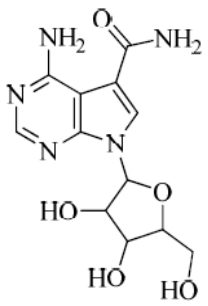
Pyrrolopyrimidine compounds isolated from terrestrial sources: Selective IRE1α inhibitor. Adenosine (ab120498) analog. PI3-kinase inhibitor. Inhibits RNA self-cleavage. Induces apoptosis in cancer cell lines. Suppresses thapsigargin-, **tunicamycin**- and 2-deoxyglucose-induced XBP1 mRNA splicing and showed antitumor and antimicrobial effects *in vivo.* ***Streptomyces tubercidicus*** is a bacterium species from the genus of *Streptomyces* which has been isolated from soil in Japan. *Streptomyces tubercidicus* produces tubercidin and ascomycin. **7-Deazaadenosine** (Tubercidin): Adenosine (ab120498) analog antibiotic agent. Inhibits RNA processing, nucleic acid and protein synthesis. Shows antiproliferative, antiviral, antiparasitic and antifungal effects. **Sangivamycin** is a cytotoxic purine nucleoside active against human cytomegalovirus (HCMV). Sangivamycin is also a selective and potent PKC (protein kinase C) inhibitor. The inhibition is competitive with respect to ATP and non-competitive with respect to histone and lipid cofactors. The phosphorylation of histone H1 protein is a mechanism by which Sangivamycin prevents the cell growth and acts as cytotoxic agent against a variety of human cancers. The **dapiramicin A** is a novel nucleoside antibiotic. **Echiguanine A** is a Inhibition of phosphatidylinositol 4-kinase in human A431 cell membrane and Inhibition of Phosphatidylinositol 4-kinase of human epidermoid carcinoma A431 cells. A new aminonucleoside, **kanagawamicin (IA)**, is produced by a strain belonging to *Actinoplanes kanagawaensis.* A new herbicidal antibiotic, **SF2**494 (**5'-o-sulfamoyltubercidin**) produced by Streptomyces mirabilis.



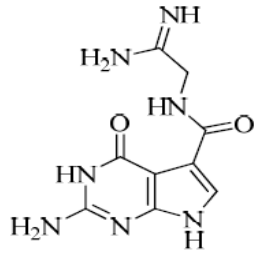
Toyocamycin



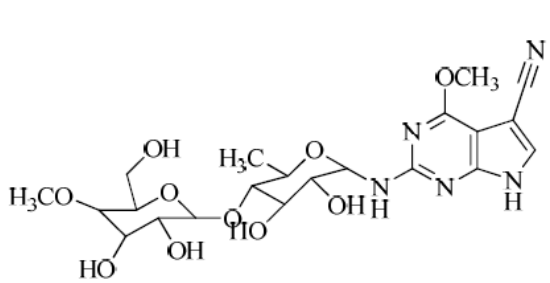
Tubercidin



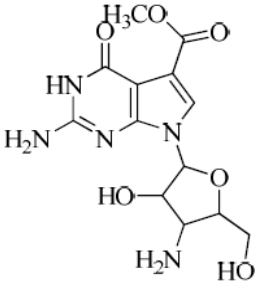
Sangivamycin

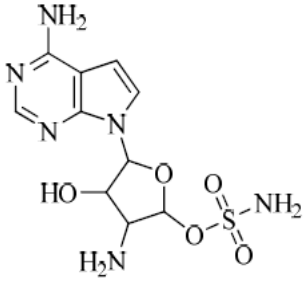


Echiguanine A



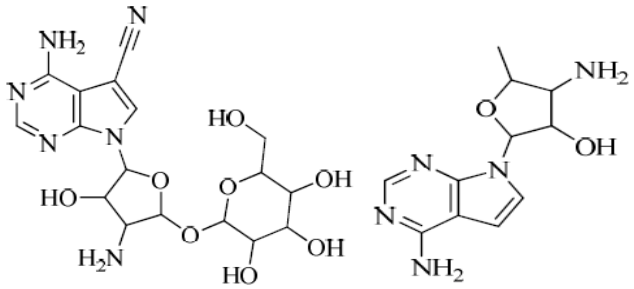
Dapiramicin A



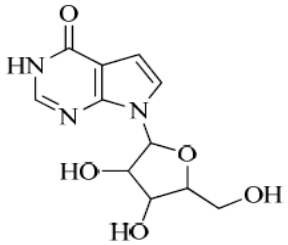


Kanagawamicin 5'-*O*-sulfamoyltubercidin

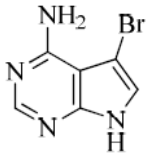
Pyrrolopyrimidine compounds isolated from marine sources: Tubercidin-5'-α-D-glucopyranose is the major cytotoxic and fungicidal nucleoside in Tofypothrix distorta (BL-11-2). Its structure was elucidated by spectral analysis and enzymatic degradation to tubercidin, which was first isolated from Streptomyces tubercidicus, and D-glucose. **5'-Deoxy-5-iodotubercidin**, a novel nucleoside recently isolated from a marine source, has been synthesized in four steps from tubercidin. The synthesis of model **7 deazapurine** derivatives related to tubercidin and toyocamycin has been performed. Tubercidin derivatives were obtained by simple conversion of the amino group of the heterocyclic moiety of the starting 7-deazadenosine compounds, into a hydroxyl group. A nucleoside 3',5'-cyclic phosphorothioate having 7-bromo-7-deazaadenine as the nucleobase (the Sp-stereoisomer).



Tubercidin-5'-(alpha-D-glucopyranose) 5'-deoxytubercidin



7-deazainosine



7-bromo-7-deazaadenine

Conclusion: The Pyrrolopyrimidines fictionalization at various positions of ring and found considerable biological interest as bio-active compounds. Biological activity of Pyrrolopyrimidines ring mainly focusing on potential biological activities [62-67]. This ring became interesting in search of new and more potent drugs with lesser side effect. The need arose to prepare Pyrrolopyrimidines compounds which bearing various substituents at the ring system. It can be concluded that Pyrrolopyrimidines have a great potentials which remain to be disclosed till date. The biological profile of Pyrrolopyrimidines represents much progress with this regards.

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