Int. J. Pharm. Investigation, 2025; 15(1):19-29.
https://www.jpionline.org

Review Article

Unlocking the Potential of Purine Analogues: A Review on Novel Anticancer Strategies

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ABSTRACT

Cancer is one of the world's most prevalent causes of death; there is a constant need to find novel treatment medications with increased efficacy and reduced adverse effects. Cancer is a complex group of diseases characterized by the uncontrolled growth and spread of abnormal cells. These abnormal cells can invade and destroy surrounding healthy tissues, impairing the normal function of organs. Cancer can develop in virtually any part of the body and may arise from various factors, including genetic mutations, environmental exposures, lifestyle factors and infections. Purines are nitrogen-containing compounds that serve essential roles in biology, particularly in the context of nucleic acids and energy metabolism. They are heterocyclic aromatic organic molecules consisting of a pyrimidine ring fused to an imidazole ring. The two main purine bases found in DNA and RNA are Adenine (A) and Guanine (G). Purine analogues are synthetic compounds that structurally resemble purine nucleotides and are potentially harmful to the growth and survival of tumours due to their ability to impair key cellular activities. By concentrating on these crucial biological processes, purine analogues have the ability to induce cell cycle arrest, apoptosis and eventually limit tumour formation as established by *in vivo* and *in vitro* tests. It talks about their potential as a broad-spectrum anticancer drug and highlights the methodical design strategies that were employed to boost their effectiveness. Purine analogues show promise as anticancer medications overall, but more research is needed to develop targeted cancer treatments.

Keywords: Purine, Anti-cancer, Tumour, *9H*-purine, MCF7, Broad-spectrum.

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Received: 23-07-2024;
Revised: 22-09-2024;
Accepted: 09-11-2024.

INTRODUCTION

Cancer represents an extensive and complex spectrum of diseases capable of affecting any part of the body, manifesting in various symptoms. With over 100 different types, cancer includes both benign tumours, which do not spread and malignant ones that can metastasize. Signs and symptoms which indicates a potential tumour involves the appearance of a bumps, irregular bleeding, constant coughing, unusually decrease in weight and modifications in digestion.[1] The progression of cancer originates from the multistage transformation of normal cells into tumour cells, commencing with a precancerous lesion and evolving into a malignant tumour.[2] This evolution commonly involves the transition from a precancerous lesion to a malignant disease, influenced by the interplay between an individual's inherited characteristics and various foreign substances, such as:, Biological, Physical and Chemical a carcinogen substances.[3]

Physical carcinogens consist of ionizing radiation and ultraviolet light, which have the potential to induce cancerous changes in cells. Chemical carcinogens comprise substances such as asbestos, tobacco smoke, alcohol, arsenic and aflatoxin, all of which can contribute to the development of cancer. Biological carcinogens include bacteria, viruses, parasites and various other microorganisms that have the capability to initiate or promote the carcinogenic process within the host organism. The interaction between these diverse carcinogenic agents and an individual's genetic predisposition displays a crucial part in the initiation as well as progression of cancer.[4]

The most prevalent malignancies diagnosed in men were stomach, lungs and Cancer of the prostate, Cervical, colorectal; lungs and breast cancer are the four types of cancer that frequently afflict women. Brain tumours and acute lymphoblastic leukemia are the two malignancies that afflict youngsters most often.[5]

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DOI: 10.5530/jphi.20250020

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According to the WHO, there will be close to 10 million fatalities in 2020. The prevalent (in terms of brand-new cancer cases) in 2020 were represented in the Figure 1.

Chemotherapy is a popular therapeutic option; however, one unfavourable side effect is that cancer cells may develop a variety of defense mechanisms against traditional medications.[6] Human cancer cell lines are vital models in labs for studying cancer biology and testing anti-cancer drugs.[7]Top of Form The several human cell lines that were employed to investigate the cytotoxic actions were MCF-7 cell lines (breast carcinoma): reduced cell viability, induced apoptosis and had encouraging antitumor activity. Potent cytotoxic effects were observed, resulting in the elimination of A549 lung cancer cells and a deceleration in their growth. HCT-116, associated with colorectal cancer, exhibited robust inhibitory impacts, leading to reduced cell viability, cell cycle arrest and cell death. Remarkable cytotoxicity, diminished cell proliferation and potential efficacy in glioblastoma treatment were evident in U87MG cells (Glioblastoma). The sequence continued with significant anticancer activity in prostate cancer PC-3, marked by decreased cell proliferation and induced apoptosis.[8] The structural composition of purine involves a 6-membered pyrimidine nucleus and fused 5-membered imidazole nucleus. These two cycles collectively form purine, featuring four nitrogen atoms located at positions 1, 3, 5 and 9 the nomenclature of purine which is shown in Figure 2. The numbering of purines proceeds anticlockwise, starting from the first nitrogen of the 5 membered ring.[9]

Purine is ubiquitously present in nature and serves as a foundational structure in both RNA and DNA. The nucleotides of purine display significant positions as co-factors, substrates that were used in the operations of a variety of proteins, attracting biological interest to the vast significance of purines.[10] The modification of the natural purine structure, especially through the incorporation of ring structures, has been a focal point in numerous drug development programs. This is due to the fact that purine is considered one of the most prevalent molecules and is an essential component of cells, playing a Vitale role in transition of metabolic energy process, the protein nucleic acid production and various biochemical interactions.[11] The purine bases and nucleosides exhibit a diverse range of biological and pharmacological actions, including activities against viruses and cancers. Haematological malignancies are currently being treated with alternatives of purine nucleoside includes fludarabine, cladribine and pentostatin. Moreover, for a longer duration of sixty years, mercaptopurine and thioguanine have been employed as metabolic antagonists in the treatment of paediatrics acute lymphoblastic leukaemia.[12]

REVIEW LITERATURE

Salas Cris. O *et al.*, performed *in vitro* antitumour potency of 2, 6, 9-trisubstituted purine-based analogues. Among 3 of 31 compounds exhibit activity and of those three, compounds 2, 6, 9-trisubstituted purine derivative exhibits greater activity than the control, cisplatin. K562, NCIH-460, MCF7, HL-60 and CaCo-2 cell type were among the many cancer cells employed. In comparison to the standard medication, cisplatin, the compound 2, 6, 9-trisubstituted purine derivative IC_{50} value=1.3 µM triggered apoptosis and produced cell cycle arrest on HL-60 cells.[2]

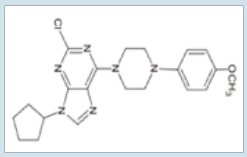
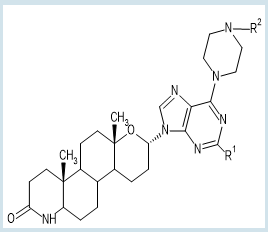
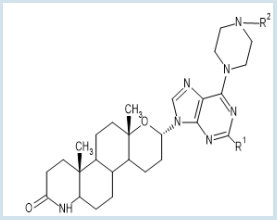
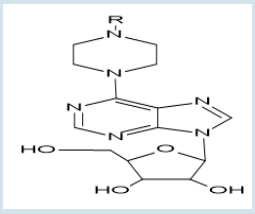
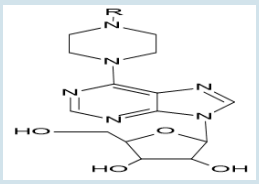
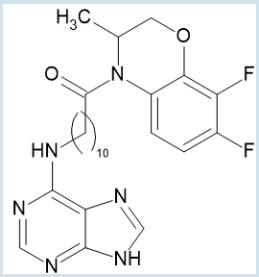
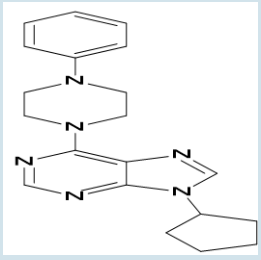
Huang Li *et al.*, performed *in vitro* anticancer activities of Carbon 6 of piperazine derived purine steroid-nucleosides compounds 2 to 9 and successfully demonstrated activity against the, PC3 and MCF7, HeLa cell types. The analogues 17-alpha fluoro-phenylpiperazine-1 phenyl purine derivative and 17-alpha 2 chloro-2 pyrimidinyl piperazine-1 phenyl purine derivative with IC_{50}=5.13 and 1.84 µM of the analogues from 2 to 9, showed strong and specific suppression of PC-3 cells, as well as reducing proliferation of tumour cell strains.[13]

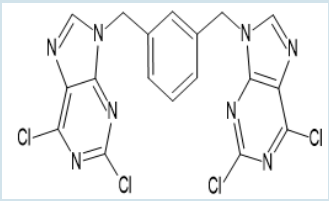
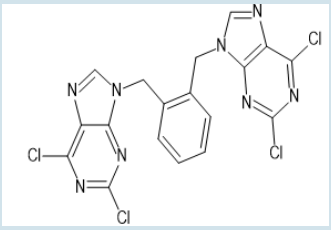
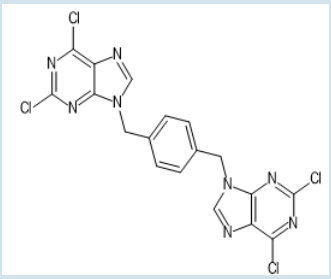
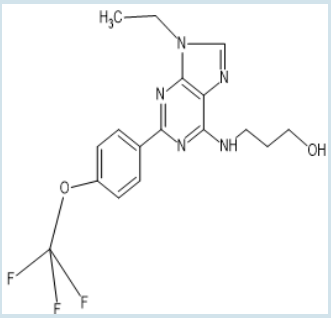
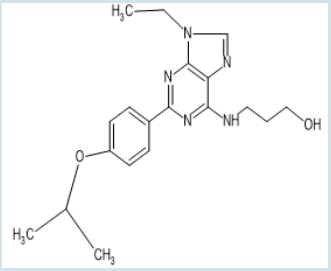
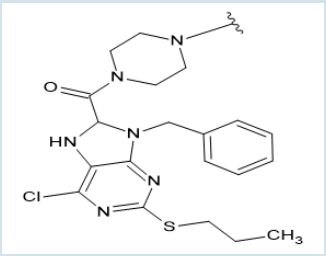
Tuncbilek.M *et al.*, Harmonized a fresh sequence of 6-[4-substituted piperazine-1-phenyl)-9-{D-ribo furanosyl} analogues of purine. Some Purine derivatives were assessed on cell lines, such as hepG2, FOCUS, HTC116 and MCF7 breast. The potential chemotherapy chemical ribofuranosyl analogues of purine blocks various kinase protein, which causes aging of cells followed by death, along with the purine analogues ribofuranosyl analogues by altering position exhibit cytotoxic activity on hepatoma cells, with IC_{50} values=5.2 and 9.2 µM, respectively.[10]

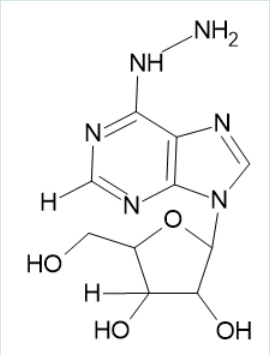
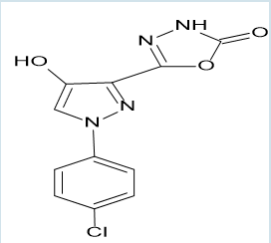
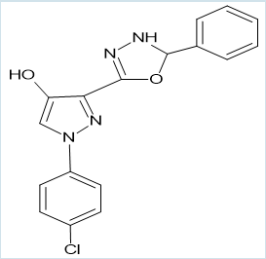
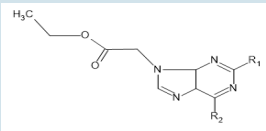
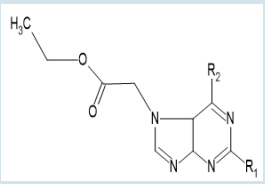
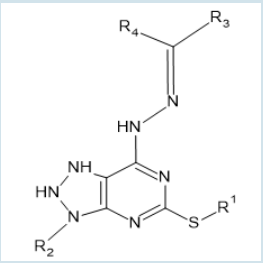
Victor P. Krasnov *et al.*, testing N-[omega-(purin-6-yl) aminoalkanoyl] derivatives of 7,8-difluoro-3,4-dihydro-3-methyl-2H-[1,4]benzoxazine revealed high cytotoxic activity against various tumor cell lines, notably 4T1, COLO201, SNU-1 and HepG2. Key to this activity is the difluorobenzoxazine fragment and a purine residue linked by a specific length. The most promising compound 1d inhibits DNA biosynthesis, suggesting potential for developing new antitumor agents.[14]

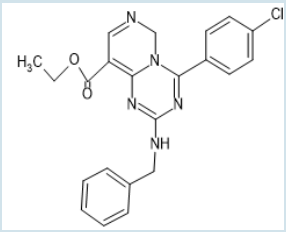
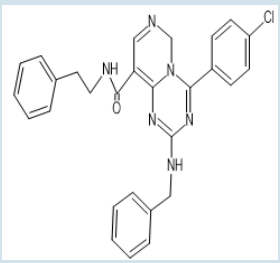
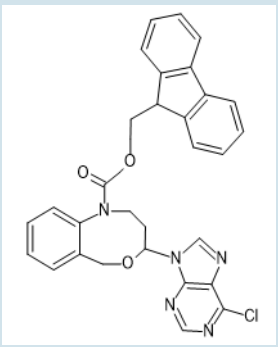
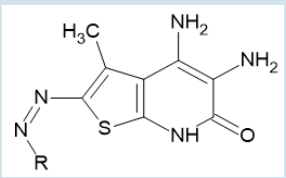
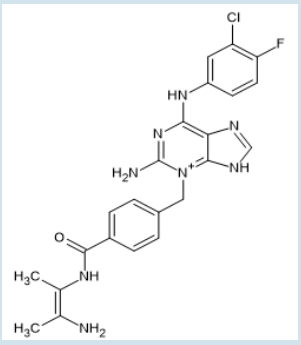
Ebru Bilget Guven *et al.*, newly synthesized 6-substituted piperazine/phenyl-9-cyclopentyl purine nucleobase analogs were tested for anticancer activity in human cancer cells. Compounds 15, 17-24, 49 and 56, with IC_{50} values under 10 µM, were further evaluated in liver cancer cell lines. Compound 19, with an IC_{50}<5 µM, induced apoptosis and showed high selectivity for Anaplastic Lymphoma Kinase (ALK) and Bruton's Tyrosine Kinase (BTK) with KINOME scan scores S35 of 0.02 and S10 of 0.01. Molecular docking revealed compound 19's extensive binding interactions with kinase activation sites, affecting signaling pathways and inducing apoptosis in liver cancer cells.[15]

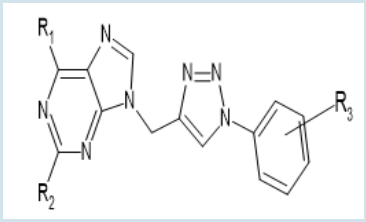
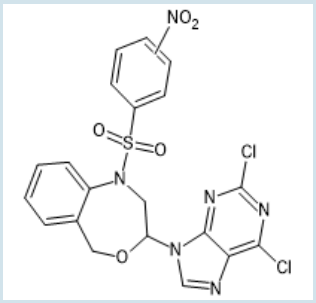
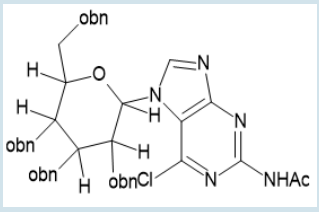
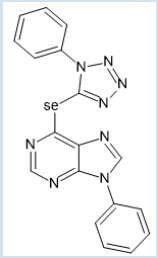
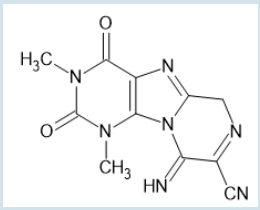
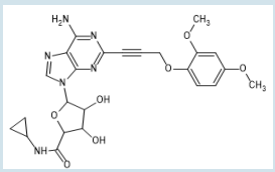
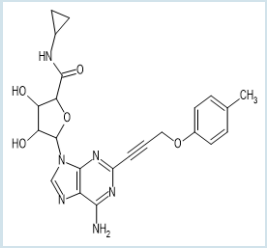
Table 1: Characterizing Antiproliferative Effects of Chemical Compounds on Multiple Cell Lines: IC_{50} and GI_{50} Analysis.

Sl. No.	Structures	Cell Lines	IC_{50} Value in μM	GI_{50}	Type of Assay	References
1.		HL-60	1.3		MTT Assay	2
2.		PC-3	5.13		MTT Assay	13
3.		PC-3	1.84		MTT Assay	13
4.		Hepatoma cell	5.2		SRB Assay	10
5.		Hepatoma cell	9.2		SRB Assay	10
6.		COLO201 MDA-MB-231	1±1 4±2		MTT assay	14
7.		Huh7	3±0.4		SRB colorimetric assay	15

Sl. No.	Structures	Cell Lines	IC_{50} Value in µM	GI_{50}	Type of Assay	References
8.		MCF-7	1.55		SRB Assay	16
9.		MCF-7	3.63		SRB Assay	16
10.		MCF-7	10.47		SRB Assay	16
11.		HeLa SiHa		30 50	MTT Assay	17
12.		HeLa SiHa		35 40	MTT Assay	17
13.		GES-1 A549	303.03 2.80		MTT Assay	18

Sl. No.	Structures	Cell Lines	IC_{50} Value in µM	GI_{50}	Type of Assay	References
14.		MCF-7 K562/S HeLa Caco-2 HT-29		6.1 2.0 5.0 5.0 8.2	RR Assay	19
15.		MG-MID		0.08	*In vitro* disease-oriented human cells screening pannel assay.	20
16.		MG-MID		0.20	*In vitro* disease-oriented human cells screening pannel assay.	20
17.		A375	1.18±0.03		AnnexinV-based Assay.	21
18.		A375	4.98±0.07		AnnexinV-based Assay.	21
19.		MGC-803 GES-1	0.85 56.17		MTT Assay.	11

Sl. No.	Structures	Cell Lines	IC_{50} Value in µM	GI_{50}	Type of Assay	References
20.		CDK2-inhibitors	1.85		KinaseGlo plus Illumination Kinase Assay.	22
21.		CDK2-inhibitors	2.09		KinaseGlo plus Illumination Kinase Assay.	22
22.		MCF-7	0.67±0.18		Micro Array	23
		HL-60	64.60±3.8		MTT Assay	24
		A549	80.22±4.1			
		SKBR3	42.96±3.2			
		MKN45	72.62±4.7			
		W138	>100			
		MDA-MB-231	1.48		MTT Assay	25
		MDA-MB-468	0.65			
		HepG2	12.44			

Sl. No.	Structures	Cell Lines	IC_{50} Value in µM	GI_{50}	Type of Assay	References
		A-548	0.4		SRB Assay	9
		THP-1	0.08			
		MDA-MB-231	0.166		Apoptosis and Cytotoxicity Assay.	26
		HT-29		1.5	SRB Assay	27
		OV-90			Cytotoxic Assay	28
		MALME-3M	25.2		SRB-protein Assay	29
		HOP-92	31.8			
		T-47D	32.9			
		MDA-MB231	7.9		SRB Assay	30
		Caco-2	7.5			
		MDA-MB231	6.8		SRB Assay	30
		Caco-2	8.3			

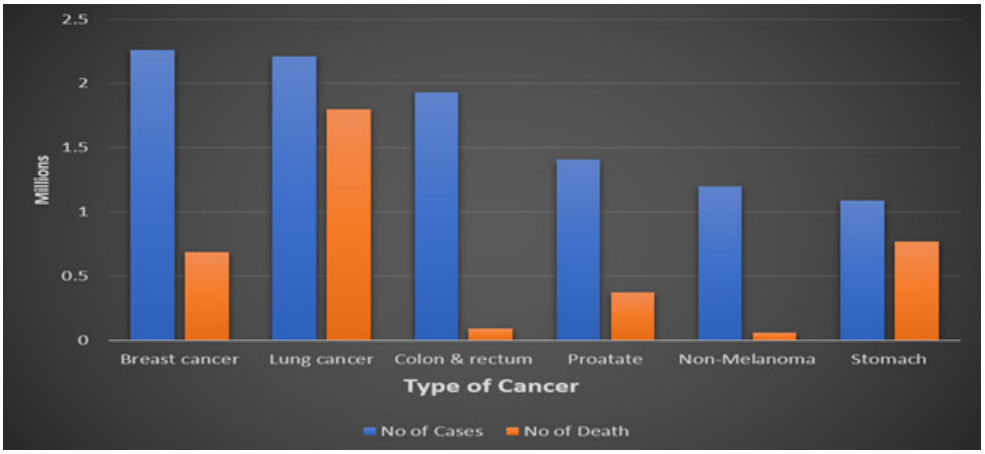


Figure 1: Number of cancer cases and death rate in millions.[5]

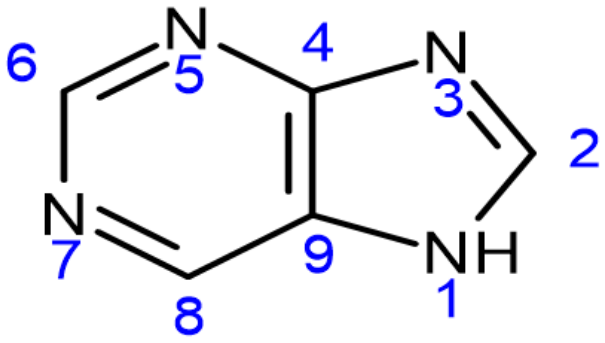


Figure 2: 7*H*-purine.

Kode. N *et al.*, conducted a synthesis on New Bis-N9-[methyl-phenyl-methyl]-purine derivatives 4 to 15 are examined for acute cell toxicity action towards a number of NCIH-460, MCF7 and SF268 cancer cell variants. Derivatives o-2,6-dichloropurine, m-2,6-dichloropurine, p-2,6-dichloropurine among which the analogue m-2,6-dichloropurine demonstrated the action on blood cancer and these 3 analogues also showed a significant tendency to cause cell line death in carcinoma of the breast.[16]

Ningegowda. R *et al.*, conducted a study on *in vitro* cancer fighting capacity of new derivatives of ethyl substituted 9H purine derivatives, by using Trypan blue exclusion and MTT assay method. The newer series of EPD act on different cell lines like siHa, LM8, SKOV3, OVSAHO, LM8G7, HeLa and caSki. The compound fluoro and methyl 9-ethyl substituted 9H purine derivatives shows activity against cervical cancer cells and shows inhibitory effects.[17]

Zhao. Tao *et al.*, synthesised and designed 6-chloro-2-propylthio substituted 7H-purine caboxamide derivative which shows anti-tumour properties on 4 cell strains of human were A549, MGC-803, PC 3 and TE1. Studies of Structural Activity Relationship have been carried out in 2nd positions for 7H-purine piperazine derivative. The analogue 7H-purine piperazine derivative, shows more potency towards PC3 cells when the substitution of thiophene at position 9 occurs and the 7H-purine piperazine derivative shows more effective ant-tumour action and better differentiation among the cancerous and beneficial cells with IC_{50} value of 2.80 µM in case of A549 and 303.03µM in case of GES1, consequently.[18]

Cappellacci. L *et al.*, synthesised N-6-aminopurine-9b-Deoxyribonucleosides and ribose modified 3-Carbomethyl derivatives, the small groups such as hydroxyl, methyloxy/amine groups were substituted at 6th positions and at Carbon-2 of N6 position were synthesised and investigated in connection to a group of leukemia and cancerous cell types. The derivative N6 hydrazino ribofuranosyl purine shows better antiproliferative activity in low micro molar range. The unsubstituted N6 of amino ending is required for the maximum cellular toxicity of 3-Carbomethyl-ribonucleoside in combating human carcinoma and cell types of the cancer, if any modification at Carbon 2 or 3-Carbomethylation in N6 derived adenosine compound led to reduce the action.[19]

Rostom. Sherif. A. F *et al.*, performed the synthesis of 1-[p-chlorophenyl]4-hydroxyl-1H-pyrazole carboxylic acid hydrazide analogues and a certain derived para substituted-1, 2, 4-triazoline thione, o-substituted 1, 3, 4-thiadiazole and o-substituted-1, 3, 4-oxadiazole against cancer. The 10 compounds are identified by *in vitro* disease oriented anti-cancer testing conducted by the NCI. P-chloro phenyl 1, 3, 4-oxadiazole derivative shows 50% growth inhibition [0.08 µM], tumour growth inhibition [15.8 µM] and shows LC_{50} [64.6 µM] for MG MID cell type respectively and the 2-phenyl 1, 3, 4-oxadiazole derivatives proposed 50% growth inhibition [0.20 µM], tumour growth inhibition [11.7 µM] and shows LC_{50} [87.1 µM] for MG MID cell type respectively.[20]

Morales. F *et al.*, worked on 7 hydrogen-purine compounds inhibit various carcinoma lines of cell in human. The compounds between 26 to 33 shows antiproliferative activity and partition co-efficiency opposed to the melanosarcoma cell strains like

G361and A375, the result shows that the 9H purine derivative and 7H purine derivative which are having high potency towards cancer and the compound 7H purine derivative is having capability to produce cell death versus individual's melanocarcinoma cell strain A375.[21]

Li1.Zhoung *et al*., designed and synthesised (1, 2, 3)-triazolo-(4, 5)-pyrimidine analogues possessing a hydra-zone molecule and this were examined for their anti-tumour effectiveness towards various cancerous cell strain utilizing MTT assay technique. The many of the analogues were exhibiting a better effectiveness towards cancerous line of cell, the pyrimidine derivative demonstrate a greater action along with favourable sensitivity among tumour and usual cells and IC_{50}=0.85μM against MGC 803 and 56.17 μM against GES 1, respectively and producing the cell death of MGC 803.[11]

Oudah. Khulood .H *et al*., performed synthesize and docked a new pyrazolo (1, 5)-(1, 3, 5)-triazine analogues which shows activity on CDK-2 inhibitory and anti-tumour activity. The CDKs were helps in the cell cycle progression and transcription so on. CDK-2 mainly hyper activation in human tumours, particularly in breast carcinoma, uterus cancer, respiratory cancer, endometrial tumour, melanocarcinoma and sarcoma of bone. The among synthesised compounds (1, 5)-(1, 3, 5)-triazine-8 carboxylate and (1, 5)-(1, 3, 5)-triazine-8 carboxamide shows better activity with percentage 82.38% and 81.96%, can observed by docking studies and having IC_{50} value=1.85 and 2.09 μM, respectively, by comparing with control compound roscovitine.[22]

Dıaz-Gavilan. M *et al.*, conducted a study on [1, 2, 3, 5-tetrahydro-4, 1-benzoxazepine-3phenyl]-pyrimidines and analogues of purine which shows anticancer activity against MCF7 cell lines by initial cyclicDNA chips investigation. Out of 51 compounds 9H purine derivative shows better action on MCF7 cells and also having ability to alters the function of genetics which are contributing in cell death, the IC_{50} value with regarding to the 9H purine derivative=0.67±0.18 μM.[23]

Khalifa. Moh. E *et al*., synthesised and molecular docked nine new purine-based compounds by using compound 8-amino substituted purine as starting material. All compounds were examined for their excellent anti-tumour activity towards various cell lines using *in vitro* method, such as HL60, A549, SKBR3 and MKN45. The purine hybrid 8 substituted diazinyl purine derivatives undergo docking study and shows higher value when interacting with serine kinase, result that explained that imidazole contained purine hybrid 8 substituted diazinyl purine derivatives gives promising score with in the others, with IC_{50} value, HL60=64.60± 3.8 μM, A549=80.22±4.1 μM, SKBR3=42.96±3.2 μM, MKN45=79.62±4.7 μM, W138=>100 μM.[24]

Nepal. K *et al*., conducted study on purine and purine isoster as novel analogues of benzoylamide catogery of Histone deacetylase blockers, where *in vitro* cytotoxic studies shows that benzamide compound 14 inhibits the triple-negative mammary cancer cells multiplication with IC_{50} value=1.48 μM, MDA-MB 468 IC_{50} value=0. 65 μM and hepatic cancerous cells Hep G2 IC_{50} value=2.44 μM and also compound 9H purine aminophenyl benzamide derivatives shows more potent than Chidamide (6) and MS-275 (5). Contrast with HDAC inhibitor SAHA, with enhance sensitivity IC_{50}=0.33 μM in 3 blood cancer cell strains, KG-1 THP-1 and K-562.over all the compound 9H purine aminophenyl benzamide derivatives shows potent anticancer activity in individual's MDA MB 231 breast carcinoma xenograft mice model, respectively.[25]

Khazir. J *et al*., synthesised 1, 2, 3 triazole derivatives of 2, 6, 9-trisubstituted purine are filtered for *in vitro* anticancer action on different cell line HCT-1, A-549, THP-1 and IMR-32. Some derivatives like 9a, 9b, 9e are showing better potency against different cell lines by conducting bioassay. The compound 2, 6, 9-trisubstituted analogue purine shows better IC_{50} values against two cell lines rather than others, THP 1=0.08 μM, A548=0.4 μM.[9]

López Cara. L.C *et al*., conducted a SAR experiment with RS-6-substituted [7/9(1, 2, 3, 5-tetra-hydro-benzoxazepine 3 phenyl)-7H/9Hydrogen-purines possess antitumor action against human ductal carcinoma cell strains MCF 7 and MDA MB231. Regarding to MCF7, compound (RS)-14 induces apoptosis until 52.50% of cell proliferation after 48 hours, which is more activity than clinically used medication 43% paclitaxel. Compound benzoxazepine 9H purine having IC_{50} value for the MDA MB231 cell strains is 0.166 μM.[26]

Schwarz.S *et al*., Conducted research on 6-chloropurine nucleosides, which have anticancer action, induce apoptosis and block the G2 cell cycle. The series of nucleosides was tested on cell lines from melanoma, lung and ovarian cancer. The compound beta-D-mannopyranosyl-purine derivative exhibits superior action with GI_{50} 1.5 μM, when compared with compound betulinic acid or tamoxifen and stop the cell cycle and inducing apoptosis after being examined for its cytotoxic activities.[27]

Dilek. G *et al*., prepared a newer selenotetrazole analogues of purine 4a to 4h as efficient anti-cancer activity. And the synthesised analogues are examined for their chemotherapeutic action. The synthesised compounds undergo spectro-photometric and agarose-gel-electrophoresis techniques and also *in vitro* tissue culture studies shows that all the compounds were drastically decreased the production of DNA and shows anti-tumour influence on cancerous cell strains. Over all the compound 9 benzyl 1H -tetrazole-9H purine analogue act as most potential agent against OV90.[28]

Ashour. F. A *et al.*, synthesized a novel tri-azino and tri-azol-o-[4,3] purine analogues were screened for its *In vitro* antineoplastic, antiHIV-1 and anti-microbial actions. The compound 4 imino 6, 8 dimethyl dihydro 1, 2, 4 triazino purine carbonitrile derivative

showed potency towardsHOP-92, T-47D and, MALME 3 M with GI_{50} values=25.2, 31.8 and 32.9 µM, appropriately.[29]

Mohan. Arasavelli. A *et al.*, performed a preparation, differentiation and biological activity of carbon5-N-cyclo-propyl-carboxamido alkynylated purine nucleic acid derivatives. 11a to 11g are examined for its *in vitro* anticancer and antibacterial properties. The compound 2, 4 dimethoxy phenoxy 5-N-cyclopropyl carboxamido adenosine and 3-p-tolyloxypropynyl 5-N-cyclopropyl-carboxamido show essential anti-cancer activity IC_{50}=7.9 and 6.8 µgmL^{-1}, appropriately, v/s MDA MB-231 cell strains of 7.5 and 8.3 µgmL^{-1}, correspondingly, towards the CACO-2 cell strains. The 11c and 11g showed more potent antibacterial activity against *S. aureus* and *P. aeruginosa* bacterial strains.[30]

CONCLUSION

In this review, we analysed the proofs, that purine analogues may be effective cancer-fighting agents. Efforts were made by many of researchers to find novel methods for synthesizing purine analogues and have been made worthwhile by their diverse pharmacological actions. Although the preclinical research results showed seems to be encouraging and to perform clinical studies it is difficult due to differences in safety and effectiveness profiles of purine samples were seems to be different.

In continuation to that of purine analogues were also vital since they hold promising results of cancer therapies as analysed and mentioned in the Table 1. Throughout our review, we have observed compelling evidence of their potential in disrupting cancer cell growth, inducing apoptosis and interfering with cancer-related signalling pathways.

However, it's crucial to acknowledge that the effectiveness of purine analogues can vary considerably based on factors such as the specific compound (substitutions in the various positions of purine nuclei) and types of the cancer.

Therefore, we are attempting to communicate to the scientific community that there is still opportunity to conduct a variety of investigations on purine nuclei using a 360° strategy. Additionally, we believe that this review may help the scientific community to uncover fully effective compounds that may be used as anticancer drugs.

ACKNOWLEDGEMENT

The authors extend their appreciation to Mr. Madhu BL, In-charge of Library, Faculty of Pharmacy, Adichunchanagiri University, BG Nagara for providing access to few important journals and also submit thanks to department faculty members for clarifying the doubts during the review process.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

IC_{50}: Half-Maximal Inhibitory Concentration; **GI_{50}:** Growth Inhibition of 50%; **MTT:** 3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide; **SRB:** Sulforhodamine B; **RR:** Resazurin Reduction; **CDK2:** Cyclin-Dependent Kinase 2; **ALK:** Anaplastic Lymphoma Kinase; **BTK:** Bruton's Tyrosine Kinase; **HDAC:** Histone Deacetylase; **NCI:** National Cancer Institute; **MG-MID:** Mean Graph Midpoint; **MALME-3M:** Melanoma Cell Line; **HOP-92:** Non-Small Cell Lung Cancer Cell Line; **T-47D:** Breast Cancer Cell Line; **MDA-MB-231:** Triple-Negative Breast Cancer Cell Line; **MDA-MB-468:** Breast Cancer Cell Line; **HepG2:** Liver Cancer Cell Line; **A-548:** Lung Cancer Cell Line; **THP-1:** Acute Monocytic Leukemia Cell Line; **HT-29:** Colorectal Cancer Cell Line; **OV-90:** Ovarian Cancer Cell Line; **COLO201:** Colorectal Cancer Cell Line; **SNU-1:** Gastric Cancer Cell Line; **4T1:** Breast Cancer Cell Line; **MCF7:** Breast Cancer Cell Line; **HL-60:** Acute Promyelocytic Leukemia Cell Line; **PC-3:** Prostate Cancer Cell Line; **A549:** Lung Cancer Cell Line; **HCT-116:** Colorectal Cancer Cell Line; **U87MG:** Glioblastoma Cell Line; **SKBR3:** Breast Cancer Cell Line; **MKN45:** Gastric Cancer Cell Line; **W138:** Normal Lung Fibroblast Cell Line; **CACO-2:** Colorectal Cancer Cell Line; **HepG2:** Liver Cancer Cell Line; **GES-1:** Normal Gastric Epithelial Cell Line; **MGC-803:** Gastric Cancer Cell Line; **PC3:** Prostate Cancer Cell Line; **FOCUS:** Hepatocellular Carcinoma Cell Line; **SKOV3:** Ovarian Cancer Cell Line; **OVSAHO:** Ovarian Cancer Cell Line; **LM8:** Osteosarcoma Cell Line; **LM8G7:** Osteosarcoma Cell Line; **CaSki:** Cervical Cancer Cell Line; **G361:** Melanoma Cell Line; **A375:** Melanoma Cell Line; **MGC-803:** Gastric Cancer Cell Line; **TE1:** Esophageal Cancer Cell Line; **KG-1:** Acute Myeloid Leukemia Cell Line; **K-562:** Chronic Myelogenous Leukemia Cell Line; **IMR-32:** Neuroblastoma Cell Line; **HCT-1:** Colorectal Cancer Cell Line; **THP-1:** Acute Monocytic Leukemia Cell Line; **A-549:** Lung Cancer Cell Line; **OV90:** Ovarian Cancer Cell Line; **HOP-92:** Non-Small Cell Lung Cancer Cell Line; **T-47D:** Breast Cancer Cell Line; **MALME-3M:** Melanoma Cell Line.

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Cite this article: Deepika DU, Purushotham KN, Kumar LK. Unlocking the Potential of Purine Analogues: A Review on Novel Anticancer Strategies. Int. J. Pharm. Investigation. 2025;15(1):19-29.