International Journal of Pharmacology and Pharmaceutical Sciences 2014; Vol: 2, Issue: 2, 1-8.

Home Page: http://ijppsjournal.org

International Journal of Pharmacology and Pharmaceutical Sciences

REVIEW ARTICLE **ISSN: 2394-613X**

Recent Advances in Cytotoxic Thiazole Derivatives: A Review

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Abstract

Heterocyclic nucleus imparts an important role in medicinal chemistry and it is a key template for the growth of various therapeutic agents. Heterocyclic compound is one which possesses a cyclic structure with at least one different kinds of hetero atoms in the ring. Nitrogen, oxygen, and sulphur are the most common heteroatoms. Thiazoles are a class of organic compounds related to azoles and it is aromatic, five membered molecular ring system. In this review we discuss about recently synthesized thiazoles possessing cytotoxic biological activities. The wide activity and synthetic possibilities of thiazole hold promise for the preparation of new thiazole derivatives and explain the range of application of these derivatives

Key Words: Heterocyclic, Thiazole, Cytotoxic, Synthesis, Heteroatoms

Introduction

Thiazoles are a class of organic compounds related toazoles with a common thiazole functional group. Thiazole is aromatic, heterocyclic organiccompound that have five membered molecular ringstructures, C_3H_3NS. Proper confirmed its structurein 1889. The numbering of thiazole starts from sulphur atom. There is larger Pi-electron delocalization inthiazoles as compared to corresponding oxazoles andhence have greater aromaticity which is evidenced by thechemical shift of the ring protons in proton NMRspectroscopy indicating strong diamagnetic current(The thiazole moiety is a crucial part of vitamin B1(thiamine) and epothilone, benzothiazoles areimportant thiazoles example eluciferin. Thiazoleshave been used to give N-S free carbenes andtransition metal carbene complexes. The amino atom can be alkylated to form a thiazolium cation, thiazolium salts are catalysts in the Stetter reactionand the Benzoin condensation. Thiazole dyes areused for dying cotton [1]. It has been observed over the years that thiazole nucleus possess different biological activities such as antihypertensive, anti-inflammatory, anti-schizophrenic, antibacterial, anti-HIV, hypnotic, anti-allergic and more recently analgesic fibrinogen receptor antagonists with antithrombotic activity that are inhibitors of bacterial DNA gyrase B and antitumor and cytotoxic activities [2].

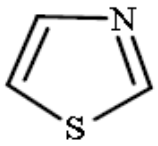

Fig. 1 Thiazole

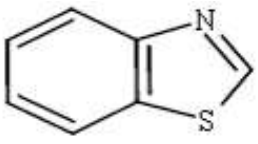

Fig.2 Benzthiazole

Thiazoles with Anticancer activity:

A series of7-(4-Chlorophenyl)-2-oxo-5-phenyl-N-(pyridin-2-yl)-3,5,6,7-tetrahydro-2H-thiopyrano[2,3-d][1,3]thiazole-6-carboxamide compound were synthesized. An anticancer *in vitro* assay was performed on the human tumor cell lines 27.11 (MOLT-4 / leukemia), 26.38 (HCT-116 / colon cancer), 32.89 (SF-295 / CNS cancer,) 35.53 (PC-3 / prostate cancer), 33.44 (MCF7 / breast cancer) and 33.81 (*T-47D* / breast cancer). The tested compounds showed different levels of activity on various cancer cell lines [3].

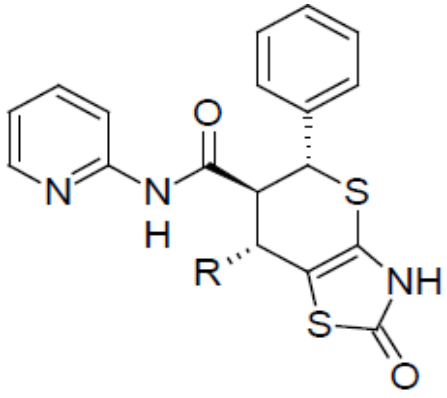

Fig. 3

A novel series of 2-oxo-5a,11b-dihydro-2H,5H-chromeno[4',3':4,5]thiopyrano–[2,3-d][1,3]thiazol-3(6H)-yl]acetate compounds (4a-d) were synthesized.The newly synthesized compounds were selected by the National Cancer Institute (NCI) within the Developmental Therapeutic Program for *in vitro* cell line screening and evaluated in vitro anticancer activity against human cell lines such as Ovarian cancer: OVCAR-3 (−16.33), Leukemia: SR (−12.33), K-562 (16.19), Renal cancer: CAKI-1 (−0.80), Breast cancer: MDA-MB-435 (2.23) and Colon cancer: HT-29 (15.51) [4].

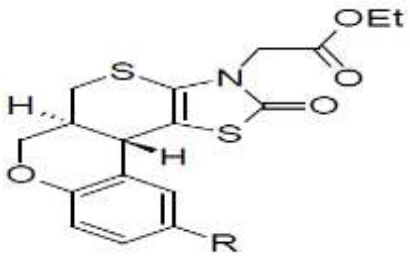

Fig.4 (a-d)

Compound	R
4a	H
4b	Br
4c	Cl
4d	F

A number of 3-Phenylimidazo [2,1-b]thiazol-6(5H)-one compounds (5a-c) have beensynthesized and evaluated by anticancer activity against the different human tumor cell lines, representing leukemia, melanoma and cancers of the lung, colon, brain, ovary, breast, prostate, and kidney [5].

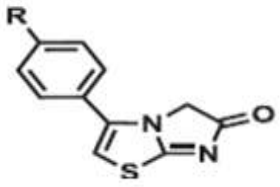

Fig.5

Compound	R
5a	H
5b	Cl
5c	CH_3

Synthesized a series of novel fluorinated thiazolo [4,5-d]pyrimidine derivatives and screened their anticancer activity against 60 human tumor cell lines. Compounds 6 and 7showed better anticancer activity against tumor cell lines [2].

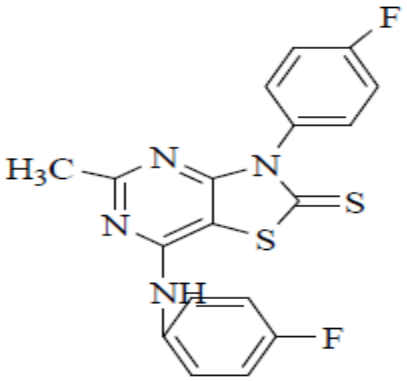

Fig.6

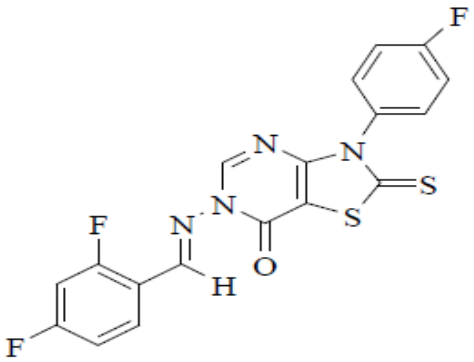

Fig.7

A novel series of o-aminophenols refluxed with substituted benzoic acid in presence of polyphosphoric acid at higher temperature to getaryl substituted benzothiazoles and evaluatedthem against Human Cervical Cancer cell lines as anticancer drugs [6].

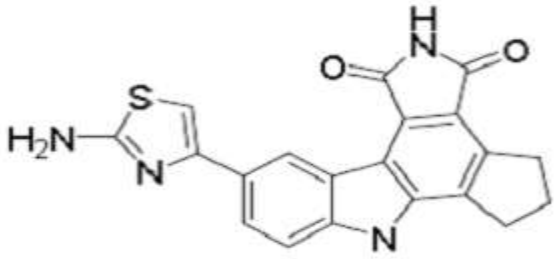

Fig. 8

A novel series of 2-arylthiazolidine-4-carboxylic acid amides forpossible cytotoxic activity in prostate cancer.Compound 15 was found to be most potent andselective cytotoxic agent with IC50 of 0.551 Mand 38-fold selectivity in PPC-1 cells [7].

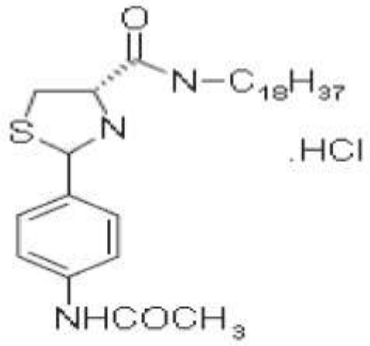

Fig.9

A series of synthesized benzothiazole containing phthalimide andstudied their anti-cancer activity on humancarcinoma cell lines [8].

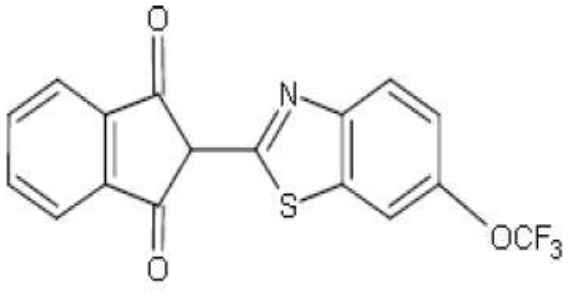

Fig.10

A novel series of N-(4-{2-[2-(Substituted-phenyl)-4,5-diphenyl-imidazol-1-yl]-thiazol-4-yl}-phenyl)-acetamide compound were synthesized.Anticancer activities of the synthesized compounds were evaluated by determining the percentage inhibition of DLA cells and EAC cells by tryphan blue dye exclusion technique [9].

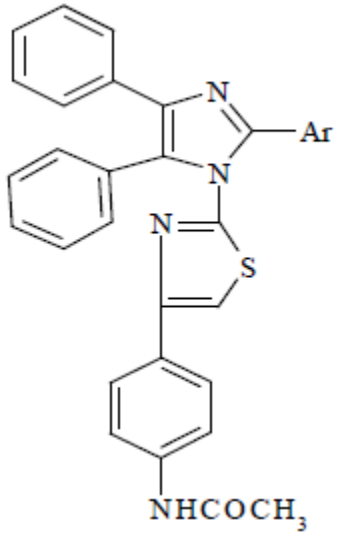

Fig.11

A successful series of 3-[2-(4-Fluorophenyl)-2-oxoethyl]-3,5a,6,11b-tetrahydro-2H,5H-chromeno[4',3':4,5]thiopyrano[2,3-d][1,3]thiazol-2-one compound were synthesized. The cytotoxic and/or growth inhibitory effects of the most active selected compounds were tested in vitro against the full panel of about 60 human tumor cell lines at 10-fold dilutions of five concentrations ranging from 10−4 to 10−8 M. A 48-h continuous drug exposure protocol was followed and an SRB protein assay was used to estimate cell viability [4].

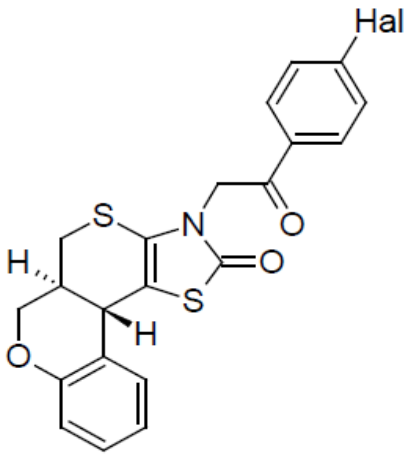

Fig.12

A novel synthesis of 2-(4-amino-2-arylamino thiazole-5-oyl)-N methyl benzimidazolecompounds (13a-e) were synthesized and evaluated for their anticancer activity against cell lines are: leukemia(CCRF-CEM, HL-60 (TB), K-562, MOLT-4);nonsmall cell lung cancer (A549/ATCC, EKVX, HOP-62), colon cancer [10].

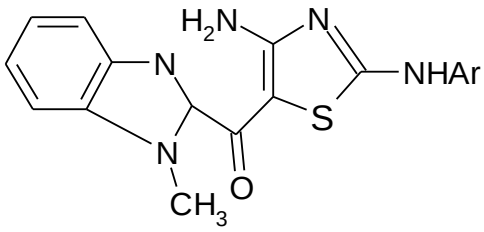

Fig.13

Compound	Ar
13a	C_6H_5
13b	4-Cl C_6H_4
13c	4- CH_3O C_6H_4
13d	4-$C_2H_5OC_6H_4$
13e	4-$CH_3C_6H_4$

A novel series of synthesized a variety of 1-substituted-2-methyl-5-nitrobenzimidazoles and evaluated them for anti-tumor activity. The anti-tumor effect of compound was found to be significant [11]

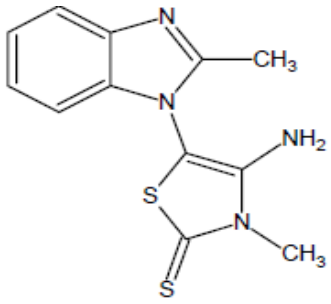

Fig.14

Synthesis and activity of a series of 4-thiazolyl substituted analogs of novel pyrrolocarbazole as Poly(ADP-ribose) polymerase-1-(PARP-1) inhibitors havebeen disclosed.Among these compounds, (15) found to be more potent [12]

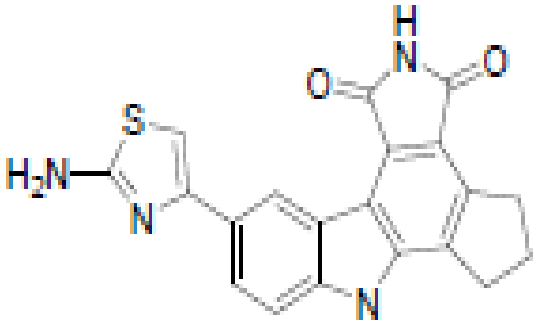

Fig.15

A novel synthesis of 3- and 5-substituted pyrones, which show remarkable inhibitory activity against bacteria, yeast and fungi, and 3-Octenyl and 5-octanyl 2-pyrones, shows anticanceractivity against human ovarium carcinoma and human chronic myelogenousleukaemia cell lines at the micromolar level.

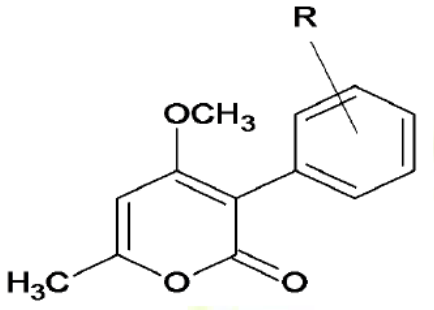

Fig .16

A novel synthesis of 4-(2-Aminothiazol-4-yl)-2,3-dimethyl-1-phenylpyrazol-5-one.In addition, 1,3,4-thiadiazoles were recently reported by us and others as highly anti-inflammatory and anticonvulsants well as anticancer agents , reporting their inhibitoryprofile against human hepatocellular carcinoma cell line, HepG2.Furthermore, several 1,3-thiazole scaffolds have been reported as potent anticancer agents . For example, 1,3-thiazolestructures (17) and (18) exhibited potentialanticancer activity against various cancer types.

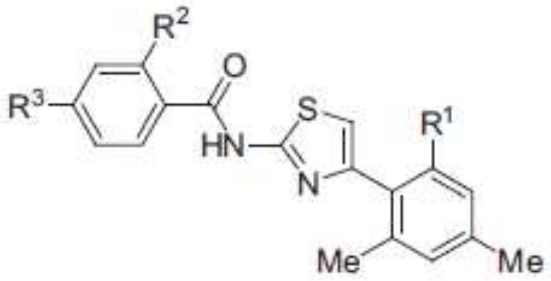

Fig.17

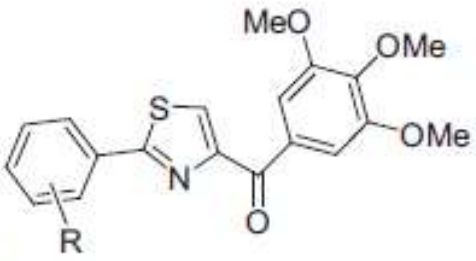

Fig. 18

A novel series of synthesized carbon 11 labeled fluorinated2-aryl benzothiazoles used for protein emission tomography(PET) to image tyrosine kinase in cancer [13]

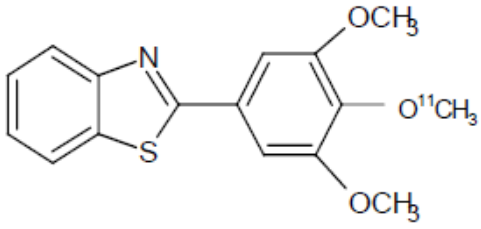

Fig.19

A novel series of 2-[4-[2-substituted 4-methylthiazole-5-yl] thiazole-2-yl] amino-5-arylidenethiazoline-5-onederivatives have been synthesized by applying known synthetic routes with minor modifications. The cytotoxic and/or growth inhibitory effects of the selected compounds were evaluated in vitro against approximately sixty six human tumour cell lines derived from nine neoplastic diseases. It is reported that some of the compounds showed anticancer activities [17]

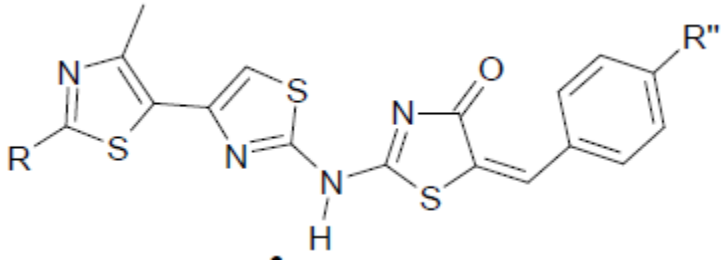

Fig.20

A novel series of synthesized benzothiazole derivatives andevaluated for *in vitro* cytotoxic activity against HL-60 and U-937 cell lines using 5-flurouracil and cisplatin as standard drug,*In silico* pharmacokinetic study revealed that benzothiazole dimere were free from teratogenicity, irritation and sensitivityproperties than monomers. The QSAR study showed thatincrease in hydrogen donor count is conductive for cytotoxicactivity of benzothiazole derivatives against HL-60 cell line [14].

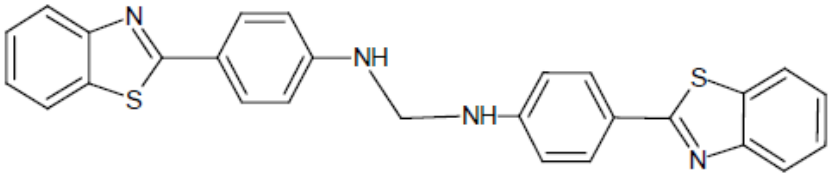

Fig.21

A series of Isonicotinic acid hydrazide (INH) incorporated derivatives of thiazolidin-4-onewere synthesized with good activity [15]. A series of novel fluorinated thiazol (4,5)-dipyrimidine derivatives and screened their anticancer activity against 60 human tumor cell lines. Compound (22) and (23)showed better anticancer activity against tumor cell lines [16].

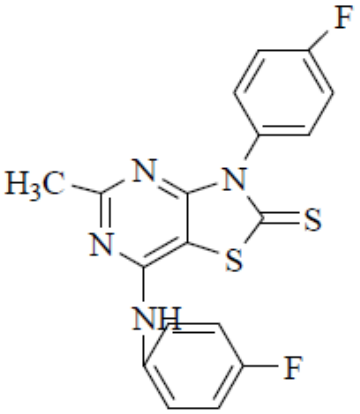

Fig.22

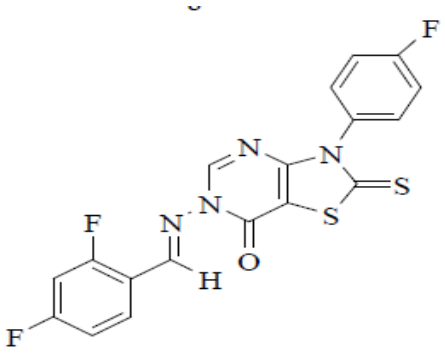

Fig. 23

Acknowledgement:

Authors are thankful to President and Hon. Secretary of Khalsa College Charitable Society, Amritsarand Director-Principal, Khalsa college of Pharmacy, Amritsar for their inspiration, encouragement and support.

Conflict of Interest: No conflicts to declare.

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