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STUDY OF THIAZINES AS POTENTIAL ANTICANCER AGENTS

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Abstract

Anticancer properties of heterocycles containing nitrogen, sulphur and oxygen are the supreme dominating stuffs which can be employed in medicinal and pharmaceutical field. More importantly, their widespread cytotoxic effects in contradiction of various forms of cancer cells, except this their behaviour as receptors as kinase inhibitors, make them additional valuable material. In present days, thiazines derivatives have often involved the attentiveness of medicinal chemist for their exceptional anticancer stuffs. The present article is a review carried out by medicinal and pharmaceutical chemist in the discovery of new potential anticancer agents.
Keywords: Thiazines; Anticancer activities; Heterocycles; Benzothiazines; Phenothiazines; Antitumor; Carcinogens.

Introduction

Now a day heterocycles play a very vital role as medicinal material and can be extracted either from natural substance or synthesized by the use of chemical substances using various methods. Recent literature revels that heterocycles with nitrogen, oxygen and sulphur atom are a chief set of drugs exhibiting very gifted anticancer, antitumor and antibacterial activities (Kaur *et al.,* 2017; Manhas *et al.,* 2017; Sharma *et al*., 2016, 2017, 2018, 2019; Mudilla *et al*., 2018, 2019). Based on structure activities relationship studies scientists in present time work on two important modification strategies; either introduction of a new element in parent heterocyclic compounds or substitution of one or two rings containing heteroatoms which will make them potential pharmaceutical or medicinal agents. Keeping in view all these observations and our continuous interest this review summarizes the latest research in the fields of heterocycles consider as potential anticancer agents (Sharma *et al.,* 2018; Kumar *et al*., 2010, 2013, 2014, 2015, 2016, 2017, 2018, 2019).

Review of Literature

Synthesized azaphenothiazines tetracyclic quinobenzothiazines, and their substitutes compounds were confirmed for cytotoxicity. Synthesized azaphenothiazines tetracyclic quinobenzothiazines effects on PHA (phytohemagglutin A) stimulated proliferative reaction of PBMC and LPS stimulated TNF-A secreted by mentioned cells were also studied. Azaphenothiazines tetracyclic quinobenzothiazines showed differential inhibitory activities in trials and considerably diverse for cytotoxicity. Azaphenothiazines tetracyclic quinobenzothiazines were also tested for growth inhibition of epidermal carcinoma, colon cancer and showed better anticancer activity (Jelen *et al.,* 2013; Singh *et al*., 2014, 2015, 2016, 2017, 2018, 2019; Kaur *et al*., 2015, 2017, 2018, 2019).

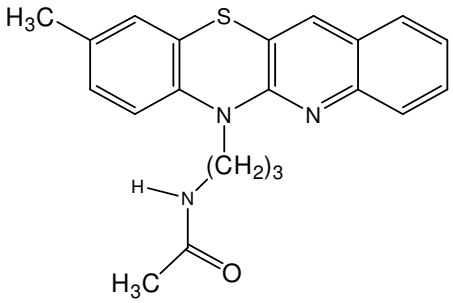

Figure 1 Synthesized azaphenothiazines tetracyclic quinobenzothiazines

Substituted dibenzothiazines are important and well known anticancer agents. Specially Fluoro derivatives such as 5-fluoro-uracil and 5-fluorotryptamine are most effective anticancer agents.Trifluoromethyl substituted 1,4-benzothiazines also consider as effective antitumour agents (Gupta *et al.,* 1985).

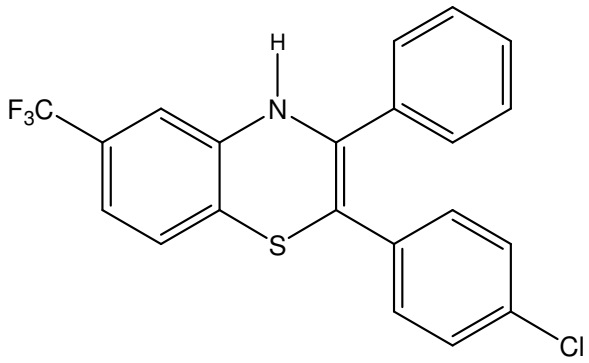

Figure 2 Substituted dibenzothiazines

The synthesis of S-alkenyl derivatives of (trifluoromethyl)-4H-1,2,4-triazole-3-thiol by alkenation reaction along with diverse alkenyl halides. Literature revels that 1,2,4-triazole ring systems have been considered for anticancer activities and consider as anticancer agents(Ilinykh *et al.,* 2013).

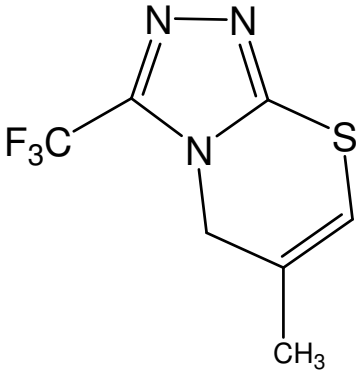

Figure 3 1,2,4-triazole ring systems

Isothiocyanates based heterocumulenes having -N=C=S group that is of vast meaning in synthesis(organic) and exhibit anticancer activity in animals treated along with chemical carcinogens due to their inhibition of carcinogen metabolic activation (Bedane *et al.,* 2015).

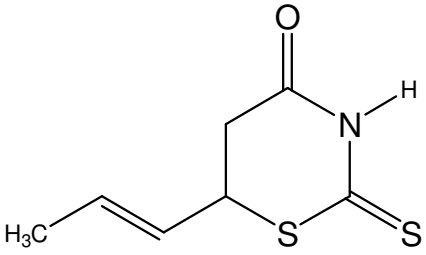

Figure 4 Isothiocyanates based heterocumulenes

Metal complexes $[ML(H_2O)(CH_3OH)x]\cdot nH_2O\cdot(CH_3OH)y(NO_3)z$ [M=Cu, Co, Ni, Cr, VO, Zn, Cd etc) from condensation of substituted 2H-1,3-thiazine-2,6(3H)-dione with thiosemicarbazide exhibit anticancer and antitumor activities (Adly *et al.,* 2011).

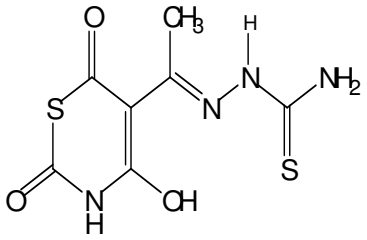

Figure 5 Metal complexes [ML(H2O)(CH3OH)x]·nH2O (CH3OH)y(NO3)z [M=Cu, Co, Ni, Cr, VO, Zn, Cd etc) from condensation of substituted 2H-1,3-thiazine-2,6(3H)-dione with thiosemicarbazide

Synthesized substituted pyrimido-thiazine derivatives, containing thiazine moiety which consider as potential anticancer agents (Baharfar *et al.,* 2011).

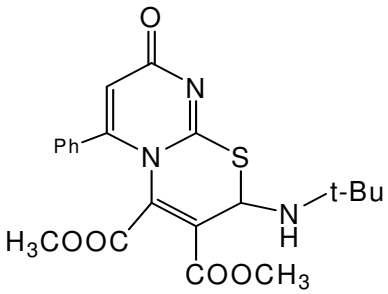

Figure 6 synthesized substituted pyrimido-thiazine derivatives

Heterocycles: primarily O and *N* atom containing heterocycles indicate advantaged structural subunits in living organism materials with considerable biological activities equivalent as anticancer activities (Banerjee *et al.,* 2016).

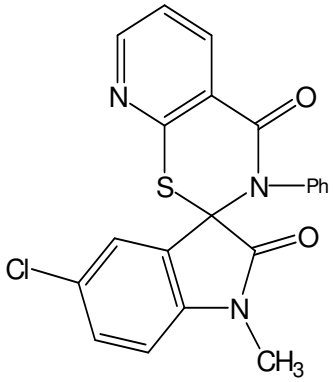

Figure 7 Heterocycles: primarily O and N atom containing heterocycles

Literature revel's that synthesized thiazine's are among the greatest prevailing properties that can be made use of as potential antitumor and anticancer agents (Bozorov *et al.,* 2015).

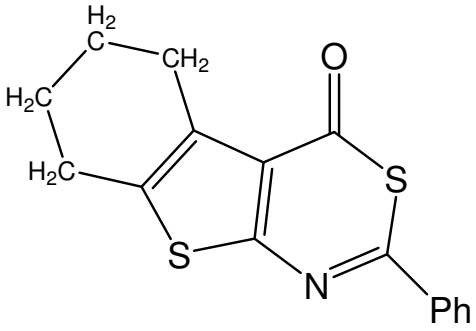

Figure 8 synthesized thiazine's

Indole having pyrido-thiazine diones, are of recent interest due to their excellent activities in biological systems such as anticancer, antitumor, potential CNS activities and antioxidant (Dandia *et al.,* 2004).

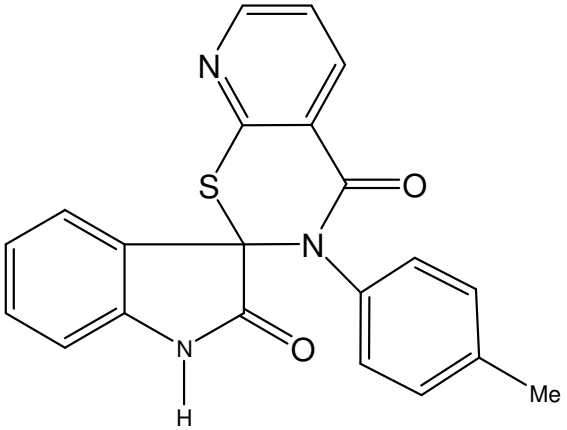

Figure 9 Indole having pyrido-thiazine diones

Synthesized substituted pyrazolo-pyridine were evaluated for antiproliferative activity against HCT-116, PC-3, and HePG-2 cell lines. As well as for anticancer activities and consider as potential anticancer agents (Eissa Ibrahim *et al.,* 2016).

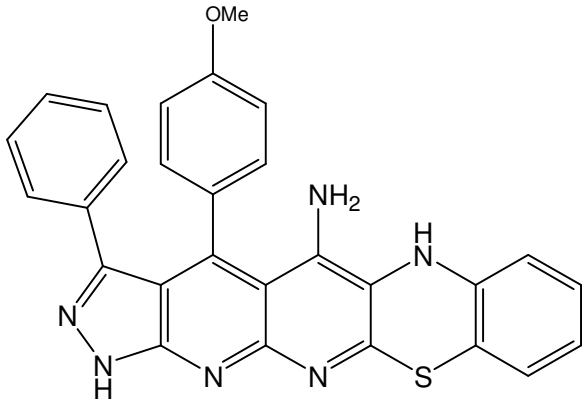

Figure 10 Synthesized substituted pyrazolo-pyridine

Conclusion

Cancer has been still accepted as major health problems which are consider as the basis of mortality and morbidity worldwide in the present time. Thus it's very necessary to develop new anticancer agents possessing different mechanisms of action to remove this problem completely. This review paper is a step in the discovery of new anticancer agents.

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