Review Article

A Review on Biological Activities of Thiazine Derivatives

Girly Vincent*, Baldwin Mathew V, Jini Joseph, Meena Chandran,

AR. Bhat and K. Krishna Kumar

Department of Pharmaceutical Chemistry, ST. James college
of Pharmaceutical Sciences, Chalakudy-680 307, Kerala, India.

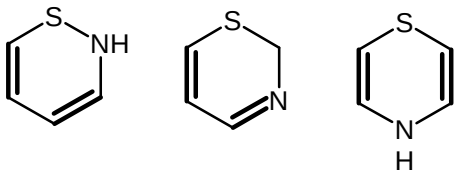
ABSTRACT

Now a days heterocyclic compounds analogues and derivatives have become strong interest in pharmaceutical research area because of their useful biological and pharmacological properties. Heterocyclic compounds are abundant in nature and have acquired more importance because their structural subunits are exhibit in many natural products such as vitamins, hormones, antibiotics etc. Thiazine nucleus present in compounds possess variety of pharmacological activities such as anti-tumor, anti-microbial, antipsychotic, anti-mycobacterial, antifungal, antiviral and anti- inflammatory. The present review focuses on thethiazine derivativeswithpotential activities that are now in development.

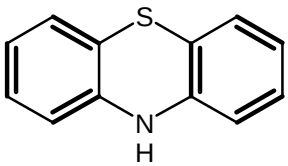
Keywords: Thiazine, Anti–Tumor,Anti-Mycobacterial agent.

INTRODUCTION

Thiazines are organic compounds with molecular formula C4H5NS**.** Thiazine is a six member heterocyclic ring system, which contains two heteroatoms (N & S) placed in the heterocyclic ring. Thiazine derivatives may be 1, 2-thiazine, 1, 3-thiazine or 1, 4-thiazines[1, 2].



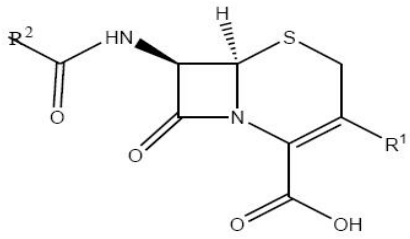
The heterocyclic compounds which contain nitrogen and sulphur possess an enormous significance in the field of medicinal chemistry. Many researchers have synthesized different thiazines derivatives that exhibit various biological activities such as anti-tubercular, anti-fungal, anti-bacterial, analgesic, anti-inflammatory etc. Through this review I tried to expose some thiazine derivatives in the development phase due to their versatility of the thiazine skeleton, its chemical simplicity and accessibility. Manycompounds of thiazines were known as phenothiazines. Phenothiazines are used as vermifuge for liver stock and also as an insecticide[3].



Phenothiazine

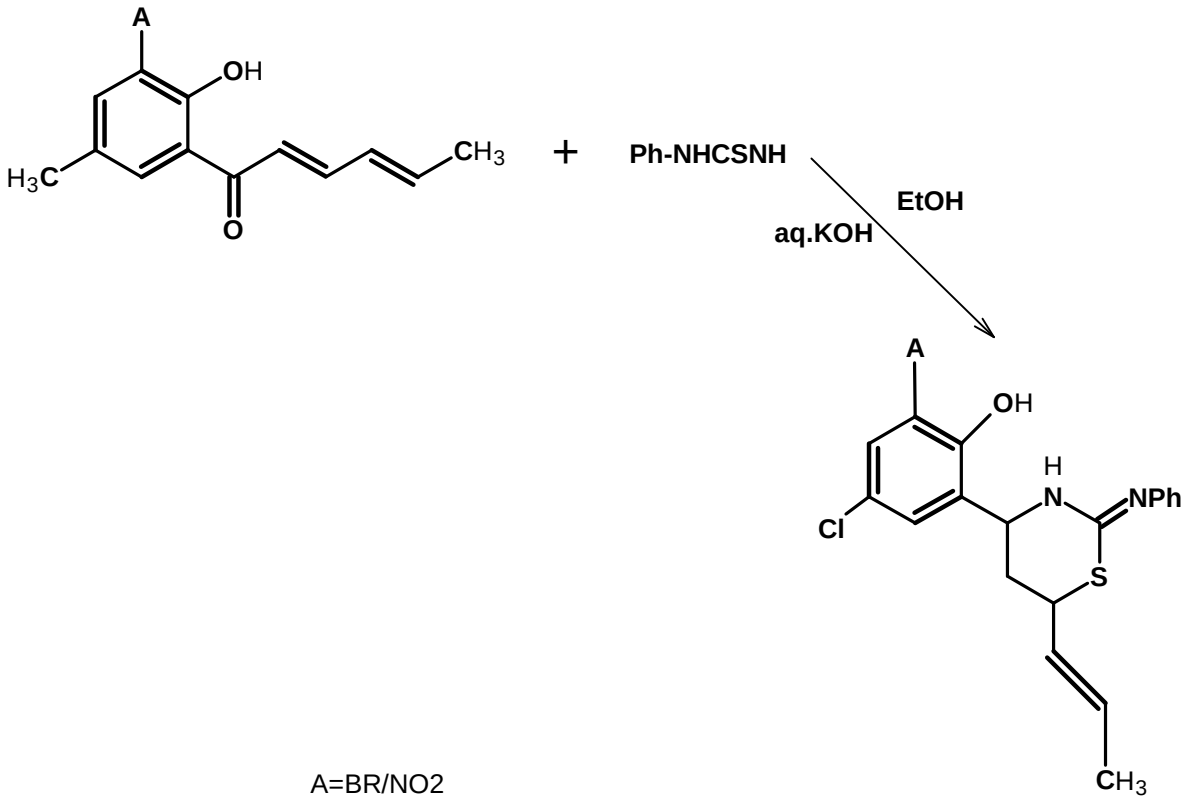
The 1,3 thiazine nucleus is active core of Cephalosporin which are among the widely use β lactam antibiotics A large group of dyes has phenothiazine structure ,including methylene blue thiazine are used for dyes,tranquillizers. Thiazine can help reduce some of that extra water weight you may be

holding on to in stomach .Thiazine is a fairely basic diuretic supplement ,it reduces water and increase vascularity, so it is also use as anabolic agent in medicine[4].



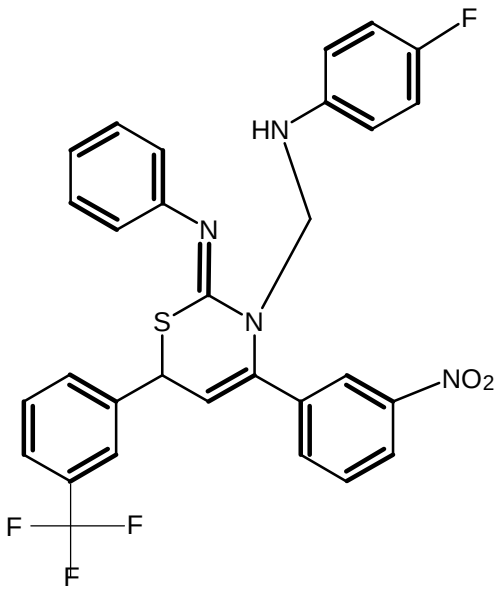
BIOLOGICAL EVALUVATION OF THIAZINE DERIVATIVES

Ram S G et al; (2013) synthesized 1, 3 thiazines by refluxing the mixture of 2-Hydroxy-3-bromo/nitro -5-chlorochalcone and phenyl thiourea in alcohol and aq.KOH. It was screened against anti-bacterial and anti-fungal activity[5].

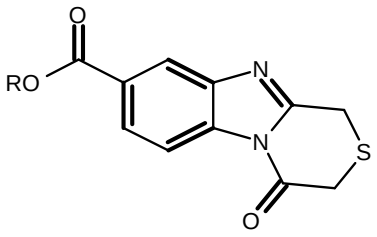


A=BR/NO2

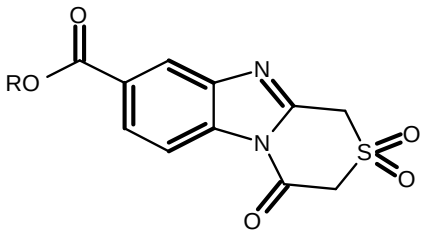
Dipansu G S et al; (2012) has synthesized a series of substituted phenyl[2-(phenylimino)-2H-1,3-thiazine -3-(6H)-yl]methanone and evaluated for their in vitro antibacterial activity against three Gram positive bacteria and gram negative bacteria.CF_3 substituted compound produces the most potent activity[6].



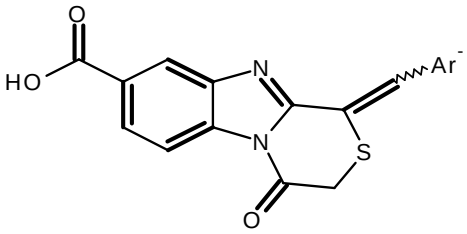
Shadia A G et.al; **(2011)** investigated 1,3-dihydro-4H-benzo[4',5']imidazole [2,1 c][1,4]thiazine -4-one-8-carboxylic acid derivatives. Tested against antiviral activity of compound (78-86) were tested against their herpes simplex virus 1. Compounds (80 and 84) have possessed potent activity as they inhibited virus propagation by 94.7% and 91.3 % at a dose of 50mg respectively. Compound 80 and 84 showed higher potentssive than acyclovir at dose of 20mcg and 50 mcg[7].



(78)R=H
(79)R=C 2H5



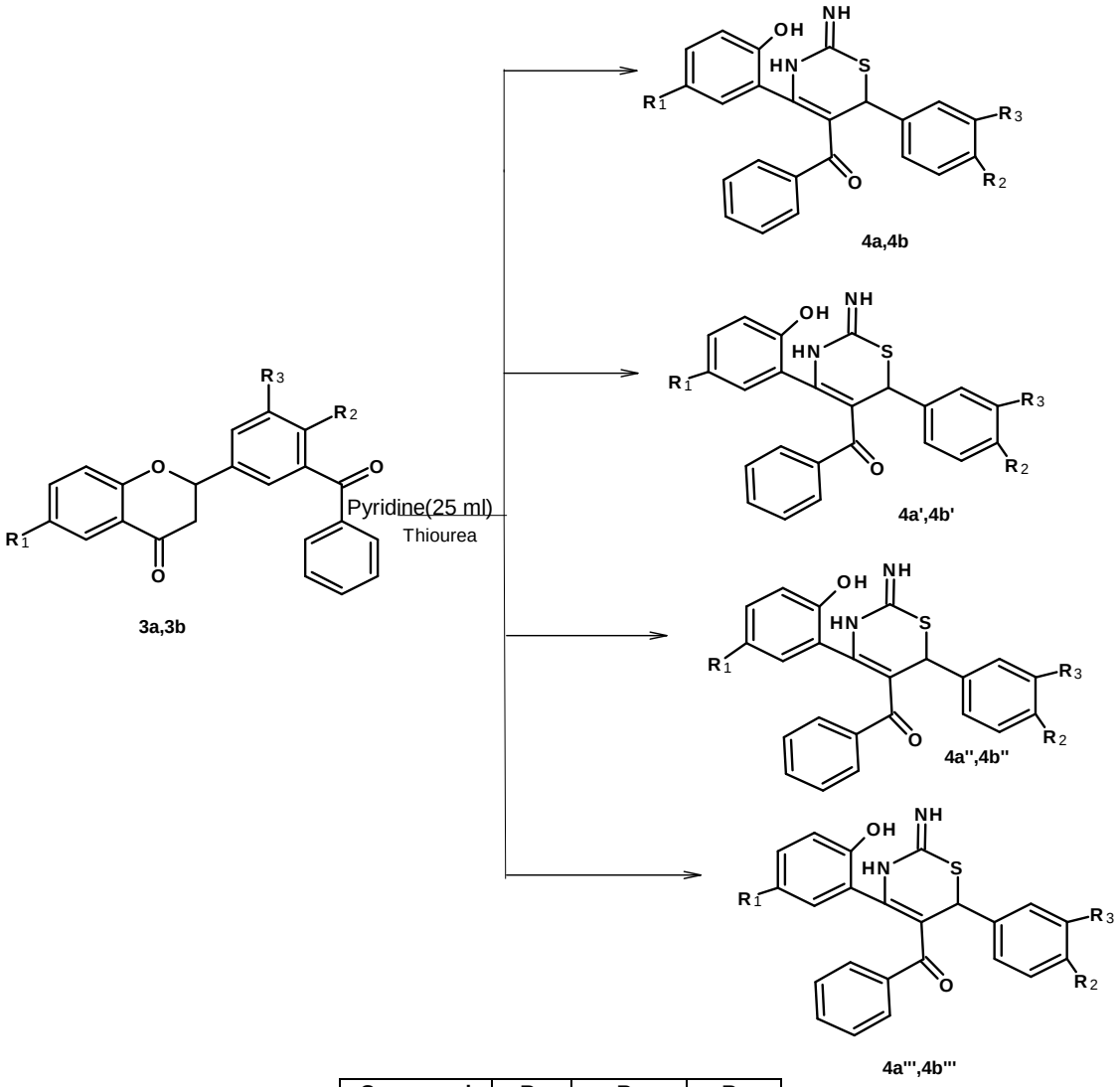
(80)R=H
(81)R=C 2H5



(82)R=-3 -Pyridinyl
(83)R=-Benzo[1,3]dioxol
(84)R=-1H -3- indolyl

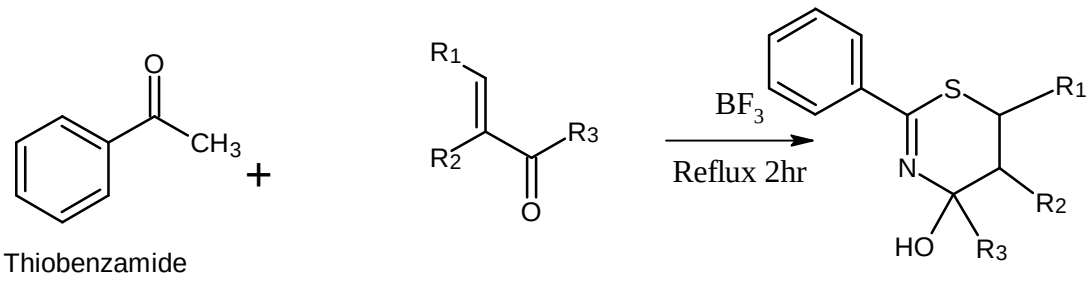
Farooque H Z H et al; (2012) synthesized 1,3 thiazine derivatives from thiourea first by using 2-Hydroxy acetophenone as starting material and second by using 2-Hydroxy 5-methyl acetophenone as starting material. Got 4-(2-Hydroxy phenyl)-5-benzoyl-6-phenyl or 4-alkoxy phenyl or 4-dimethyl amino phenyl or 4-dimethyl amino phenyl-2-imino -6-H-2,3 dihydro 1,3 thiazine

(4a,4a',4a'',4a''').second series starting material is 2-hydroxy -5-methylacetophenone and got 4-(2-Hydroxy-5-methyl phenyl)- 5-benzoyl -6-phenyl-2-imino-6 H-2,3 dihydro 1,3 thiazine(4b,4b',4b'',4b''') all these compounds are analyzed by melting points ,IR,NMR.All these compounds are tested against anti-microbial studies. The antimicrobial activity increased with increasing thenumber of heterocyclic ring[8].



Compound	R_1	R_2	R_3
4a	H	H	H
4a'	H	OCH_3	H
4a''	H	OCH_3	OCH_3
4a'''	H	$N(CH_3)_2$	H
4b	CH_3	H	H
4b'	CH_3	OCH_3	H
4b''	CH_3	OCH_3	OCH_3
4b'''	CH_3	$N(CH_3)_2$	H

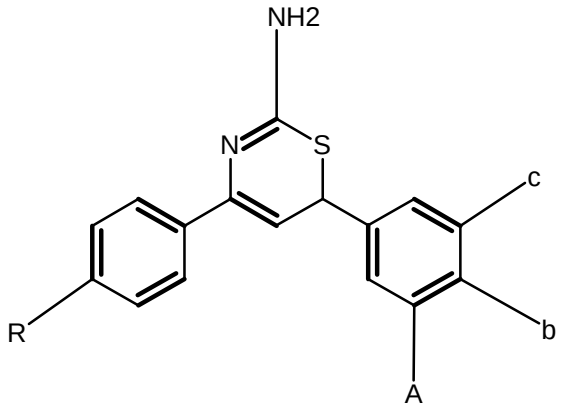
Mamoru koketsu et al; (2002) synthesized a series of eight 5,6 –dihydro -4-H-1,3 thiazine derivatives by BF_3Et_2O-catalysed reaction of selected an α, β unsaturated ketoneswith thiobenzamide at room temperature .The anti-mycobacterial activities of these compounds are determined against Mycobacterium tuberculosis $H_{37}R_v$ using Alamar blue method.(3a got 97 % of ant mycobacterial activity at 6.25mg/ml)[9].



Thiobenzamide

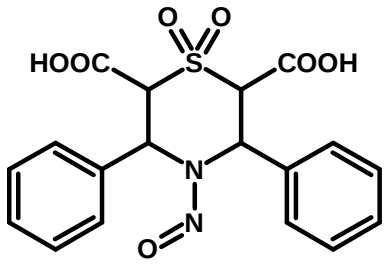
Chalcone

Varalakshmi et al; (2011) synthesized a series of novel chalcones from different benzaldehydes with various Acetophenones .The resulted chalcones weretreated with thiourea leading to the formation of corresponding thiazines in good yields. All the compounds synthesized have been characterized by IR, 1H NMR, MS and elementalanalysis. The compounds were screened for the antibacterial activity[10].

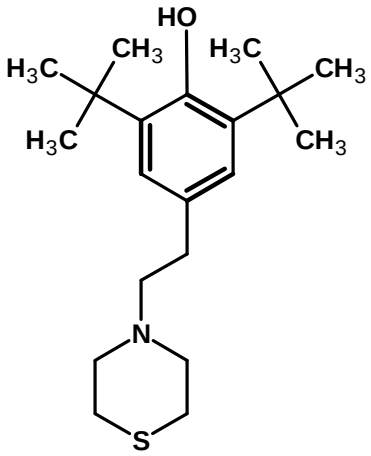


COMPUNDS	SUBSTITUTION			
	R	A	B	C
34	H	H	H	H
35	H	H	Cl	H
36	H	H	OCH_3	H
37	H	OCH_3	OCH_3	H
38	H	OCH_3	OCH_3	OCH_3
39	Cl	H	H	H
40	Cl	H	Cl	H
41	Cl	H	OCH_3	H
42	Cl	OCH_3	OCH_3	H
43	Cl	OCH_3	OCH_3	OCH_3
44	CH_3	H	H	H
45	CH_3	H	Cl	H
46	CH_3	H	OCH_3	H
47	CH_3	OCH_3	OCH_3	H
48	CH_3	OCH_3	OCH_3	OCH_3

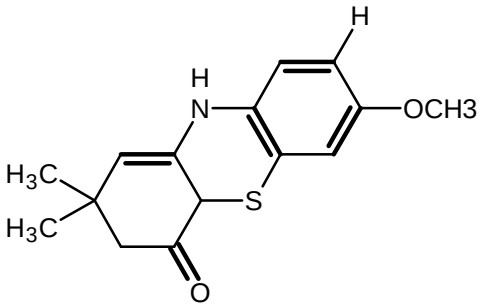
Naushad E et al; (2012) synthesized N-nitroso-2, 6-dicarboxy-3, 5 diaryltetrahydro-1,4 thiazine-1,1 dioxides and tested against anti-bacterial and antifungal activity. The compound exhibits potent antifungal activity[11].



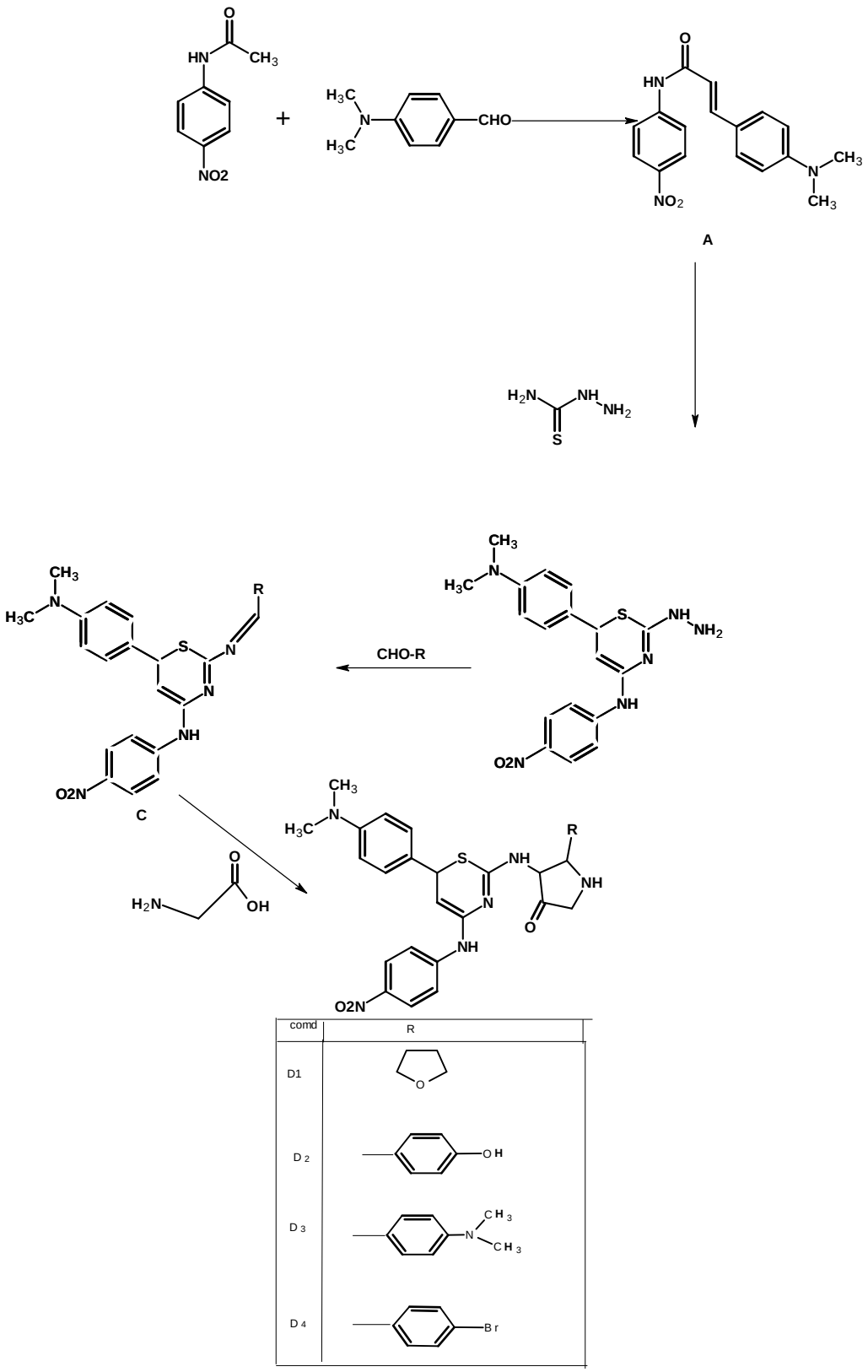
Eleni A. R et al; (2006) was synthesized an amine and amide derivatives having 2, 6-di-tert-butyl phenol moiety, all most all are anti-oxidants and it reduces acute inflammation and inhibit COX-1 and lipoxygenase activity. 2, 6-di-tert-butyl 1, 4-thiomorpholine-4-yl methyl phenol is having most potent anti-inflammatory activity[12].



VIJAY V.D et al; (2013) synthesizeda Series of chalcones and substituted guanidino-4-(2'-amino-5'-substitued phenyl) mercapto-6-phenyl-1, 3-thiazineand it was studied by IR, NMR and Mass spectroscopy. The new synthesized drug exhibits anti-inflammatory, analgesic, and ulcer genic activities compared to that of standards indomethacin and acetylsalicylic acid, respectively[13].



Srikanth Jupudi et al; (2013) Synthesized 1,3 Thiazine Derivatives by reacting acetanilide derivatives with substituted aryl aldehydes to get chalcones (A&E) .This chalcones are then cyclized by reacting with thiosemicarbazide to give 2-hydrazinyl 1,3 –thiazine derivatives (B&F) .this derivatives were treated with substituted aryl aldehydes or ketones to get 2-arylidiene hydrazinyl 1,3 thiazine derivatives(C&G) these compounds were refluxed with glycine in ethanol or vilsmear-Hack reagent (DMF-$POCl_3$) giving 2-substituted imidazolidine -4-0ne 1,3 thiazine derivatives(D_{1-4}) and 2-substituted pyrazolyl1,3 thiazine derivatives (H_{1-4}).and all the synthesized compounds were screened against antihelmintic activity. From the data we get an idea that the D_1 have maximum anti-inflammatory activity than the rest compounds[14].



CONCLUSION

The above informational data got from the literature gives an idea that thiazines are an important class of heterocyclic and their significances are challenging in disease of various infections .A survey of thiazine revealed that the moiety have possess a great deal of interest to the medicinal chemist and biochemist and can be taken as a lead molecule for designing potential bioactive compounds and thiazine derivatives have various pharmacological activities

This review gives an idea to the researchers in determining the best and most productive, economical suggestive and clinically important compounds of thiazines.
I hope that my brief review will help all those are interested to research in this class of heterocyclic compounds to develop potent pharmacologically active drugs in the field of medicinal chemistry.

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