International Journal of ChemTech Research
CODEN (USA): IJCRGG, ISSN: 0974-4290, ISSN(Online):2455-9555
Vol.10 No.13, pp 225-229, 2017

"Invitro Anticancer Screening of Substituted 3-(Phenyl Sulfanyl)-5-(Pyridin-3-Yl)-4h-[1, 2, 4] Triazol-4-Amine Derivatives"

S. R. Kane[1], S. K. Mohite[2], S. V. Jawarkar*[3]

[1,2]Rajarmabapu College of Pharmacy, Kasegaon. 415404, India
[3]S. D. Patil institute of Pharmacy, Islampur. 415409, India

Abstract : Heterocyclic nucleus played a vital role in the development of different medicinal agents and in the field of agrochemicals. This nucleus is present in many products such as drugs, vitamins, food, flavorings, plant dyes, adhesives and herbicides. It is seen from the current literature that pyridine congeners are associated with different biological properties like pesticide, insecticides and fungicidal activity. These reports encouraged us to plan for modification of 1, 2, 4-triazole into various bioactive structures and their subsequent evaluation for biological activity. In present investigation we have focused on synthesis and invitro study of anticancer activity.
Keyword : 1, 2, 4-triazole, MTT, 5-flurouracil, invitro anticancer activity.

Introduction-

Organic chemistry is a chemistry involving the scientific study of the structure, properties, and reactions of organic compounds and organic materials, i.e., matter in its various forms that contain carbon atoms.[1] Study of structure includes many physical and chemical methods to determine the chemical composition and the chemical constitution of organic compounds and materials[2,3]. Study of properties includes both physical properties and chemical properties and uses similar methods as well as methods to evaluate chemical reactivity[4], with the aim to understand the behavior of the organic matter in its pure form (when possible), but also in solutions, mixtures, and fabricated forms.The study of organic reactions includes probing their scope through use in preparation of target compounds (e.g., natural products, drugs, polymers, etc.) by chemical synthesis as well as the focused study of the reactivates of individual organic molecules, both in the laboratory and via in-silico study[5,6].

Materials and Methods:

Material:-

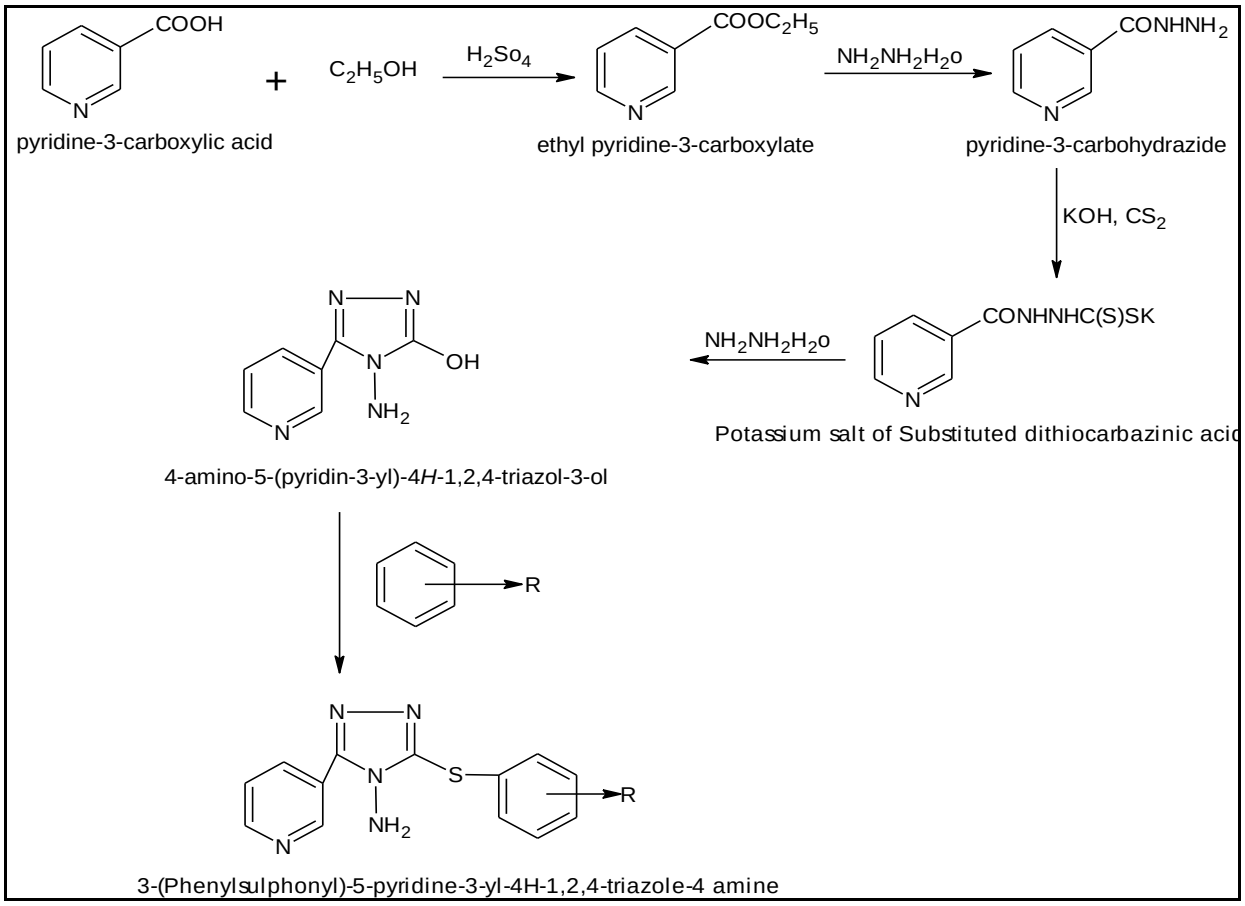
All chemicals and solvents are of Merk and procured from commercial sources. The reagents were purchased from Research lab, Mumbai. Catalyst microwave system model CATA-R System.

Methods-By Conventional Method and Microwave Technique (Catalyst).

The synthesis of compounds comprises 5 successive steps which will proceed as follows [7,8]

Step 1st: Synthesis of ethyl pyridine-3-carboxylate (compound 1).
Step 2nd: Synthesis of pyridine-3-carbohydrazide (compound 2).
Step 3rd: Synthesis of potassium salt of substituted dithiocarbazinic acid (compound 3).
Step 4th: Synthesis of 4- amino-5-(pyridin3yl)-4H-1, 2, 4 triazol-3-thiol (Compound 4).
Step 5th: Synthesis of 3-(phenyl sulfanyl)-5-(pyridin-3-yl)-4H -1, 2 ,4triazol -4-amine

Reaction Scheme:-



Where, R-(5a1-5a8) are different aryl groups

5a1=p-Bromo
5a2=o-Nitro
5a3=m-Nitro
5a4=p-Nitro
5a5=m-dichloro
5a6=chlorobenzene
5a7=p-chlorotolune
5a8=p-dichloro

Table No1-Physicochemical data of compounds 5a1-5a3

Compound	R	Molecular formula	MW	MP(^{0}C)	% Yield	Rf Value	Mobile Phase
1.	p-bromotolune	$C_{14}H_{12}N_5SBr$	361.9	240^{0}C - 242^{0}C	52.22%	0.76	E:A:E(1:9)
2.	o-nitro	$C_{13}H_{10}N_6So_2$	314	140^{0}C-142^{0}C	60.45%	0.68	E:A:E(1:9)
3.	m-nitro	$C_{13}H_{10}N_6So_2$	314	146^{0}C-148^{0}C	54.23%	0.64	E:A:E(1:9)
4.	p-nitro	$C_{13}H_{10}N_6So_2$	314	142^{0}C-144^{0}C	62.52%	0.76	E:A:E(1:9)
5.	m-dichloro	$C_{13}H_{10}N_5SCl$	303.45	260^{0}C-262^{0}C	56.23%	0.59	E:A:E(1:9)
6.	Chlorobenzene	$C_{13}H_{10}N_5S$	269	264^{0}C-266^{0}C	65.51%	0.7	E:A:E(1:9)
7.	p-chlorotolune	$C_{14}H_{12}N_5SCl$	317.45	252^{0}C-254^{0}C	54.74%	0.8	E:A:E(1:9)
8.	p-dichloro	$C_{13}H_{10}N_5SCl$	303.45	255^{0}C-257^{0}C	57.23%	0.71	E:A:E(1:9)

Table No 2-Physicochemical data of compound 5a1-5a5 by microwave method

Compound	R	Time (min)	Molecular formula	MW	MP (^{0}C)	% Yield	Rf Value	Mobile Phase
1.	p-bromotolune	5	$C_{14}H_{12}N_5SBr$	361.9	240^{0}C -242^{0}C	52.22%	0.76	E:A:E(1:9)
2.	o-nitro	5	$C_{13}H_{10}N_6So_2$	314	140^{0}C-142^{0}C	60.45%	0.68	E:A:E(1:9)
3.	m-nitro	5	$C_{13}H_{10}N_6So_2$	314	146^{0}C-148^{0}C	54.23%	0.64	E:A:E(1:9)
4.	p-nitro	5	$C_{13}H_{10}N_6So_2$	314	142^{0}C-144^{0}C	62.52%	0.76	E:A:E(1:9)
5.	m-dichloro	5	$C_{13}H_{10}N_5SCl$	303.45	260^{0}C-262^{0}C	56.23%	0.59	E:A:E(1:9)
6.	Chlorobenzene	5	$C_{13}H_{10}N_5S$	269	264^{0}C-266^{0}C	65.51%	0.7	E:A:E(1:9)
7.	p-chlorotolune	5	$C_{14}H_{12}N_5SCl$	317.45	252^{0}C-254^{0}C	54.74%	0.8	E:A:E(1:9)
8.	p-dichloro	5	$C_{13}H_{10}N_5SCl$	303.45	255^{0}C-257^{0}C	57.23%	0.71	E:A:E(1:9)

Cytotoxic assay of compound on MCF-7 cancer cell line[9]:-

The **MCf-7** cell line was maintained in DMEM medium supplemented with 10 % fetal bovine serum. The cells were plated at a density of 1 × 104 cells per well in a 96-well plate, and cultured for 24 h at 37°C. The cells were subsequently exposed to 01 mM . The plates were incubated for 24 h, and cell proliferation was measured by adding 10 µL of MTT (thiazolyl blue tetrazolium bromide) dye (5 mg/ml in phosphate-buffered saline) per well. The plates were incubated for a further 4 h at 37°C in a humidified chamber containing 5% CO2. Formazan crystals formed due to reduction of dye by viable cells in each well were dissolved in 200 µl DMSO, and absorbance was read at 490 nm. The results were compared with the standard drug inhibitors 5-flurouracil. (20µg/ml).Percent cytotoxicity of the compounds was calculated by using following formula.

Percent of inhibition = Reading of control - Reading of treated cells / Reading of control X 100

Result:-

Anticancer activity of synthesized compound against MCF-7 Cancer cell line.

Sr.No	Absorbance	% of Inhibition
Negative Control	0.538	-
Positive Control	0.103	80.85
5a1=p-Bromo	0.156	71.00
5a2=o-Nitro	0.031	94.23
5a3=m-Nitro	0.046	91.44
5a4=p-Nitro	0.202	62.45
5a5=m-dichloro	0.290	46.09
5a6=chlorobenzene	0.130	75.83
5a7=p-chlorotolune	0.275	48.88
5a8=p-dichloro	0.101	81.22

Standard: 5-flurouracil (20 µg/ml of DMSO)

In-vitroanticancer activity-

The anticancer activities of synthesized compounds were screened against MCF-7 Cancer cell line by cytotoxic assay method using standard 5 Fluorouracil.

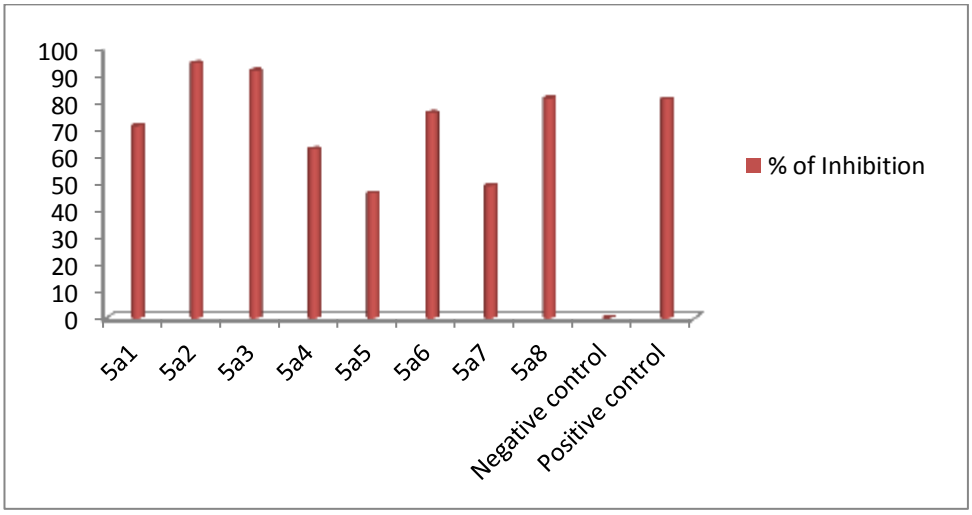


Fig. no.1 :*In-vitro* anticancer activity of synthesized compounds (5a1-5a8)

Discussion:-

The compound 5a2, 5a3, and 5a8 were observed significant *in-vitro* anticancer activity having percentage of inhibition to the extent 94.23%, 91.44%, 81.22% respectively compared with 5- fluorouracil percentage inhibition of 80.85%. The prepared synthesized compounds displayed inhibition activities against MCF-7 Cancer cell line. The present study indicated that the compound 5a2, 5a3, and 5a8 shown maximum inhibition as compared to the positive control 5- fluorouracil

References:-

1. Morrison and Boyd Organic Chemistry, Publication by Pearson education (Singapore) Pvt. Ltd. Indian branch, 482 F.T.E, Pratapganj Delhi 110 092,India 6th edition 2004,1-2.
2. Burger A. In, Burgers Medical Chemistry and drug discovery, Wolff. M.E(Ed), 5th edition, Vol-1, John Wiely and Sons, New York, 1995, 3-4.
3. J. A. Joule and K. Mills, Heterocyclic chemistry, Blackwell Publisher, Germany, 4th edition; 2000, 504-510.

4. Raj K. Bansal, heterocyclic chemistry, New Age International Publishers, New Delhi,4th edition; 2005, 1-3.
5. Ram Janam Singh and Dharmendra Kumar Singh,Synthesis and Biological activity of some 3,5 diaryl-4H-1,2,4 Triazole derivatives., 1(2), 2010,1-6.
6. S.Ravichandran and E.Karthikeyan,Microwave Synthesis-A Potential tool for Green chemistry,International Journal of Chem tech Research,3(1),2011,466-470.
7. SomaniR,R.ShindeG.K,ShirodkarP.Y.andSanapG.J,Synthesis of some novel 1,2,4 triazole analogue as potential Anti-tubercular agent ,Indian Drugs, 51(01), 2014,41-47.
8. KhosrowZamani, Khalil Faghihi,M. Reza Sangi and JavadZolgharnein, Synthesis of Some New Substituted 1,2,4-Triazole and1,3,4-Thiadiazole and Their Derivatives,Turk J Chem., 27,2003, 119 - 125.
9. P.Senthilraja,K. Kathiresan,In vitro cytotoxicity MTT assay in Vero, HepG2 and MCF -7 cell lines study of Marine Yeast, Journal of Applied Pharmaceutical Science, 5(03),80-84,2015.

*****