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A REVIEW ON RECENT DEVELOPMENT OF PYRAZOLINE AS A PHARMOCOLOGICALLY ACTIVE MOLECULE

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ABSTRACT: Pyrazoline, among the various 5-membered heterocyclic compound derivatives has drawn attention towards it because of its various pharmacologically activities associated with it. Pyrazolines are a five membered heterocyclic having two adjacent nitrogen atoms within the ring with only one endocyclic double bond and is basic in nature. A lot of research work has been done on synthesis and biological activities of various pyrazoline derivatives over the years. Pyrazolines derivatives display tremendous biological activities such as antimicrobial, anti-inflammatory, analgesic, antipyretic, antidepressant, antitubercular, antiamoebic, anthelmintic, anticonvulsant, antihypertensive, antidiabetic, antitumor, anti-HIV, local anaesthetic, antioxidant, insecticidal, tranquilizing and receptor selective biological activity. The history of pyrazoline shows that it attracted many chemists to explore pyrazoline as a biologically active molecule. The study of biological evaluation of pyrazoline derivatives has been an interesting field of pharmaceutical chemistry. This review article focuses on the pharmacological profile of pyrazoline with various activities and examples in form of figures.

INTRODUCTION: 5-membered heterocyclic compound i.e. Pyrazoline with two adjacent nitrogen at 1-2 positions and three carbon atoms are well known and have been synthesized using various methods. The three partially reduced forms of the pyrazole are 1-Pyrazoline, 2-pyrazoline and 3-pyrazoline, all are having different positions of the double bonds. Pyrazoline derivatives are having one endocyclic double bond. These derivatives play an important role in heterocyclic compounds history and possess considerable biological activities, thus making it an important pharmacophore for carrying out further drug research.

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It was reported in the literature that different pyrazolines derivatives possess tremendous biological activities such as antimicrobial, anti-inflammatory, analgesic, antipyretic, antidepressant, antitubercular, antiamoebic, anthelmintic, anticonvulsant, antihypertensive, antidiabetic, antitumor, anti-HIV, local anaesthetic, antioxidant, insecticidal , tranquilizing and receptor selective biological activity.

This review emphasize on latest work done on various pharmacological activities associated with pyrazoline.

Pharmacological Activity:

1. **Antimicrobial activity:** Extensive work has been done describing the antimicrobial profile of pyrazoline. Development of resistance to antimicrobial agents amongst important bacterial pathogens occurs rapidly, so there is much need to explore new antimicrobial agents.

Shailesh H. Shah et al [1] synthesized Azetidin-2-One based Phenyl Sulfonyl Pyrazoline derivatives (1a) and investigated them for antimicrobial activity concluding that compound having methoxy-hydroxide type linkage has shown good activity against the bacterial strains.

Various pyrazoline derivatives (1b) were synthesized by Salman Ahmad Khan et al [2] under microwave irradiation and evaluated them against various bacterial strains.

A New series of 4-(4-Chloro phenyl)-3-chloro-1-{4-[5-(Substituted phenyl)-1-phenyl- 4,5-dihydro-pyrazol-3-yl]phenyl}azetidin-2-one (1c) were synthesized by Shailesh H. Shah et al [3] and were screened against antibacterial and antifungal strains.

B. Sharifzadeh et al [4] reported an efficient method for the regioselective synthesis of new thiazolyl-pyrazoline derivatives (1d) and examined the antibacterial activity of the selected products. [4]

P. R. Desai et al [5] synthesized acetyl pyrazoline derivatives (1e) and were evaluated for antimicrobial activity. They inferred that electronic effect seems to play an important role in increasing antimicrobial activity. [5]

Pyrazolines (1f) developed by Krishna *et al* [6] showed promising antimicrobial activity against all the tested microbes. Pinka patel et al [7] prepared a new series of pyrazolines based thiazolidin-4-one derivatives (1g) and revealed that amongst newly synthesized , compound having 4-chlorophenyl type linkage has shown good activity against the bacterial strains.

Some new chlorosubstituted 4-Aroylpyrazolines (1h) were synthesised by Shreya M. Rathore et al [8] and were assayed for their antimicrobial activity on *E.coli*, *S. aureus*, *P. aeruginosa*, *P. vulgaris*. Antimicrobial active Pyrazoline derivatives (1i) were efficiently synthesized by M.M. Kendre et al [9] reflecting moderate to good activity against different strains of bacteria and fungi.

B.F. Abdel-Wahab et al [10] synthesized some novel compounds based on 1,2,3-triazoles-linked pyrazolines (1j) with potential antimicrobial activity.

Satyender Kumar et al [11]investigated the antimicrobial profile of 1,3,5-trisubstituted pyrazolines derivatives (1k)and inferred that most of them showed good activity comparable with that of standard drugs ciprofloxacin and fluconazole. It was revealed that compounds containing methoxy group showed high antimicrobial activity.

2-pyrazoline derivatives (1l) synthesized by Dipankar et al [12] were found to have good antimicrobial activity in the range of 20-70 µg/ml. Green synthesis of 1-phenyl-3(5-bromothiophen-2-yl)-5-(substituted phenyl)-2-pyrazolines (1m) was done by Sasikala et al [13] and all synthesized pyrazoline derivatives showed moderate antimicrobial activities against bacterial and fungal strains.

Sailu B et al [14] found most of the new pyrazoline derivatives (1n) synthesized to be active compared to the standard drug ampicillin.

V. P. Vaidya et al [15] indicated that all the synthesized pyrazolines containing naphthofuryl substituents (1o) did not show any appreciable antimicrobial activity.

Hemant panwar et al [16] evaluated the synthesized pyrazolinyl-1, 3, 4-thiadiazino (6,5-b) indoles (1p) as antimicrobial agent and Compound 1q was found the most potent one with lesser toxicity in this series.

Sahoo et al [17] observed a significant level of activity of synthesized 3, 5-diphenyl substituted pyrazoline derivatives (1q) against different bacterial strains.

Different Pyrazoline derivatives (1r) were synthesized by Biresh K Sarkar et al [18] and were explored for antimicrobial activity against various bacterial and fungal strains.

Some novel pyrazolines (1s) prepared from piperazine chalcones are screened for antimicrobial studies by Baseer et al [19] and showed moderate to good activity.

The antimicrobial activity of Acetyl pyrazoline derivatives (1t) was assayed against varieties of bacterial strains by H.S. Joshi et al [20].

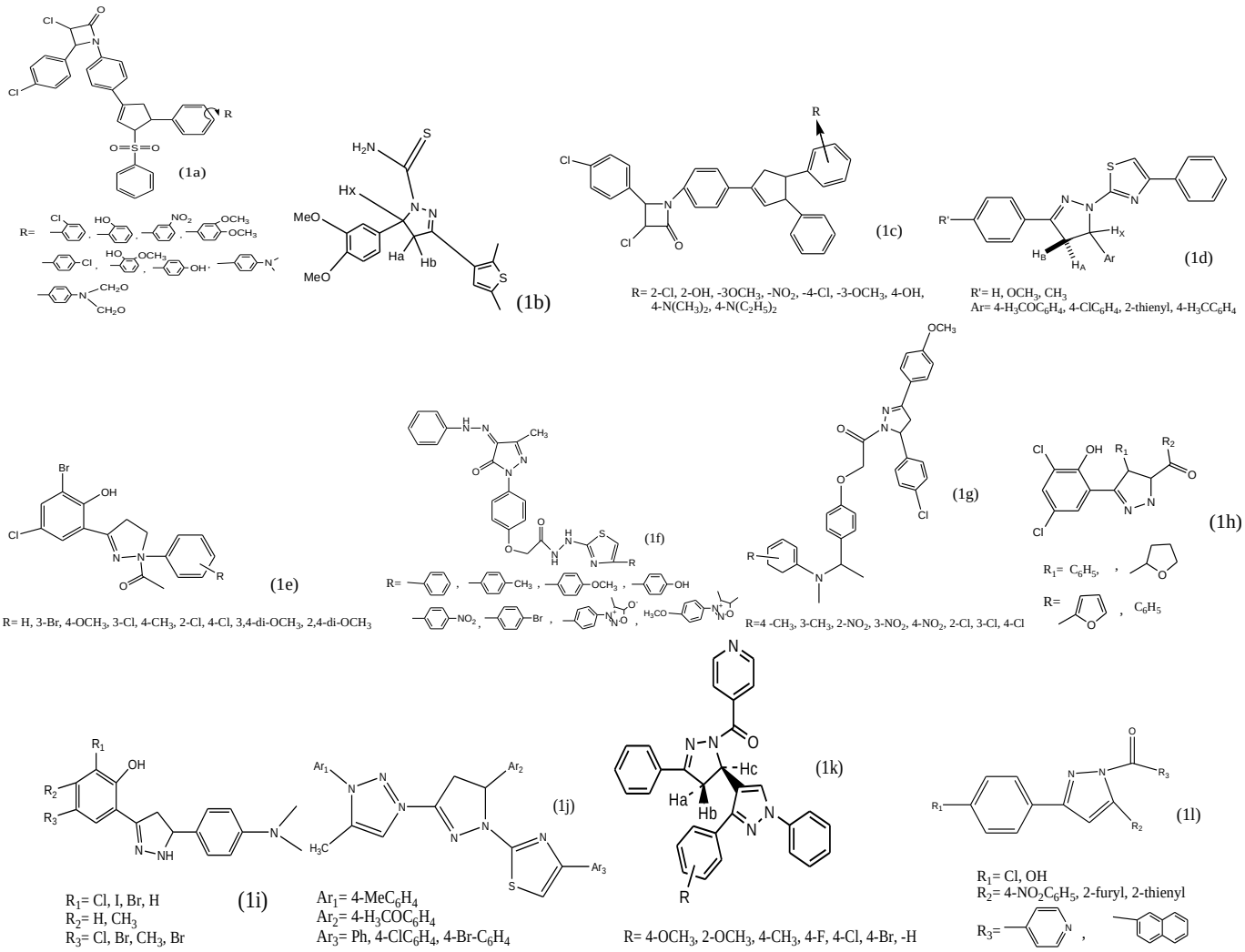
Hassan et al [21] synthesized a new series of anthracenylpyrazolines (1u) and found potency of these agents about 50% in comparison to standard.
B.S. Dawane et al [22]synthesize some new series of 1-(4-(4'-chlorophenyl)-2-thiazolyl)-3-aryl- 5 - (2-butyl-4-chloro-1H-imidazol-5yl) – 2 - pyrazolines (1v)and their antimicrobial profile was studied.
Potential anti-bacterial activities of C-12 pyrazolinyl spiro ketolide derivatives (1w) were reported by L. Hu et al [23].

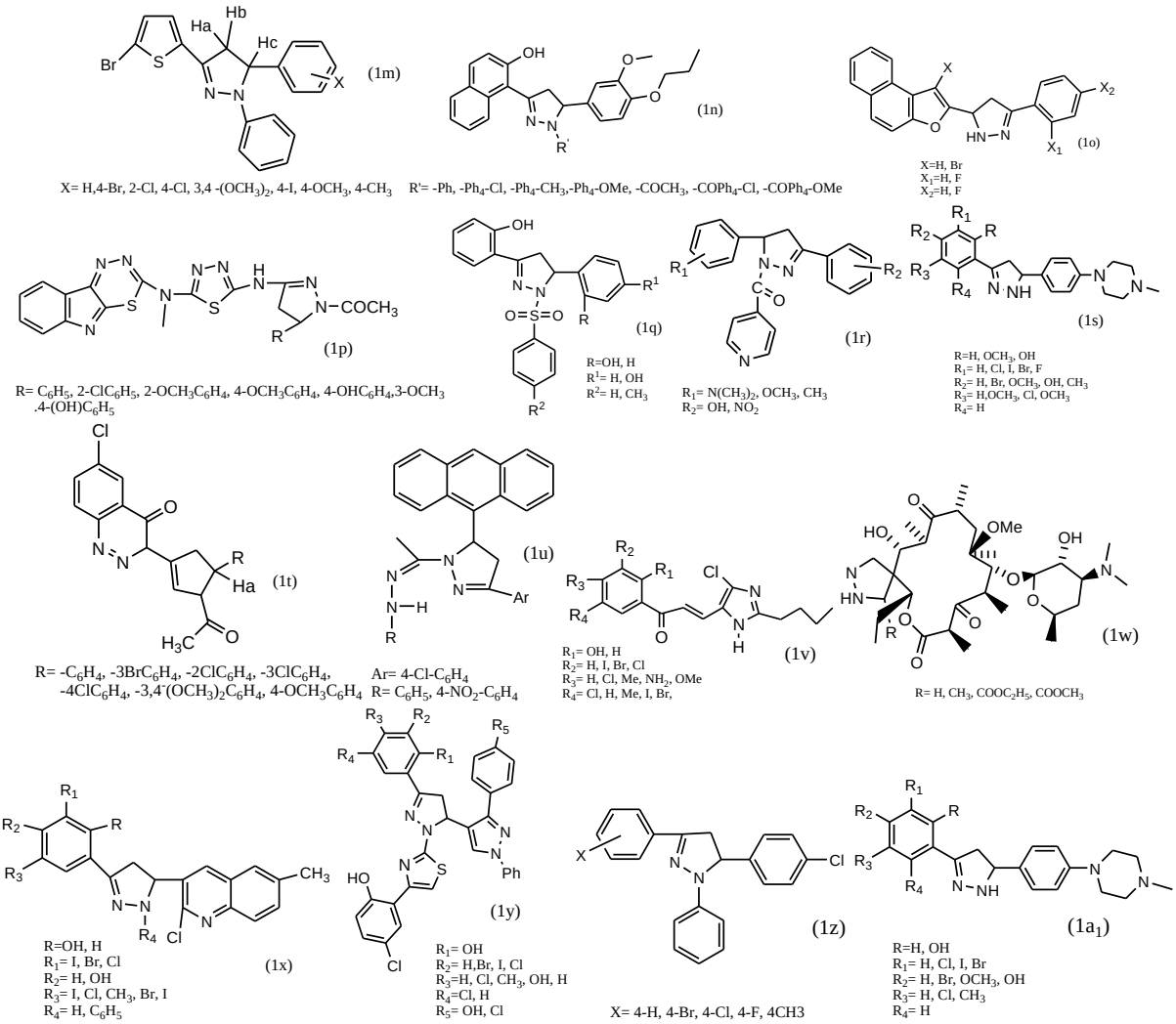
Shyam S. Mokle et al [24] found that among the screened 2-pyrazolines (1x) most of the compounds showed good bacterial inhibition almost equivalent to that of standard.

Some 1-thiazolyl-2-pyrazoline derivatives (1y) were synthesized by Bhaskar S. Dawane et al [25]and evaluated as antimicrobial agents by applying the principles of green chemistry. Most of the compounds showed very good antibacterial and antifungal activity.

Ragini Gupta (1z) et al [26] synthesized pyrazolines under ultrasonic irradiation and synthesized compounds were screened for their antimicrobial activity. Some of the compounds showed significant antimicrobial activity. [26]

M.A. Baseer et al [27] concluded that some novel pyrazolines ($1a_1$) synthesized using piperazine chalcones and phenyl hydrazine possess moderate to good antimicrobial activity.





Anti-Inflammatory and Analgesic Agents:

An ample of work has been done to study the anti-inflammatory and analgesic effect of pyrazolines. Neethu et al [28] demonstrated the anti inflammatory activity of the synthesized Pyrazoline analogues of Vanillin by cyclooxygenase assay. The synthesized compounds (2a) showed significant anti inflammatory effect.

A new series of fluoro substituted pyrazoline derivatives were synthesized by by S. Y. Jadhav et al [29] and screened for their in vivo antiinflammatory and analgesic activity and showed that two compounds (2b) and (2c) exhibit excellent activity.

5-trifluoromethyl-D2-pyrazolines derivatives (2d) synthesized by Ranjana Aggarwal et al [30] exhibited significant anti-inflammatory activity as compared to indomethacin (78%).

Suhas S. Awati et al [31] concluded that the modified pyrazoline deivatives (2e) showed remarkable anti-inflammatory action.

Pyrazoline derivatives (2f) by S. Sridhar et al [32] have been found to possess an interesting profile of analgesic activity.

B. Dipankar et al [33] revealed from the study that D8 (2g) was found to be the most effective compound among all the synthesized 2-pyrazoline derivatives with respect to their analgesic and anti-inflammatory activity as well as it is less ulcerogenic in comparison to standard drug diclofenac.

Pyrazolines (2h) by Jainey PJ et al [34] with electron withdrawing group on aromatic ring favours anti-inflammatory activity. Velmurgan et al [35] demonstrated the analgesic activity of 3, 5-Disubstituted pyrazoline derivatives (2i) by tail-

flick method and acetic acid induced writhing method. Carradori [36] showed the anti-inflammatory potential of some thiazole based pyrazolines.

Jyothi M V et al [37] synthesized pyrazolines (2j) and studied for their anti-inflammatory activity. Compounds possess some degree of anti-inflammatory activity and were free from toxicity Khalil et al [38] inferred the compound (2k) of 3, 5-Diaryl-2-Pyrazoline Derivatives as most potent, which has shown higher percentage of inhibition of edema than the standard drug indomethacin.

Balakrishna Kalluraya et al [39] synthesized a series of acetyl/propyl pyrazolines carrying 5-aryloxypyrazole moiety (2l) and investigated them for their anti-inflammatory and analgesic activity showing that presence of aryloxy group in the 5th position will decreased the anti-inflammatory and analgesic activity when compared with that of 5-chloro derivatives.

Ghaneya Sayed Hassan et al [40] studied the anti-inflammatory and analgesic activities of new Diarylpyrazoline derivative (2m) using dextran-induced rat paw edema, formaldehyde arthritis test and paw pressure test. The synthesized compounds showed significant activity as anti-inflammatory and analgesic agents.

Srinath N et al [41] screened the 1, 3, 5-Trisubstituted-2-Pyrazolines (2n) and screened them for their analgesic profile indicating the favorable effect of electron releasing substituents on the analgesic activity of the 2-pyrazolines.

3,5-diaryl substituted 2-pyrazolines (2o) synthesized by Pankaj malhotra et al [42] were examined for anti-inflammatory activity and reported that all the derivatives except a few have shown significant activity.

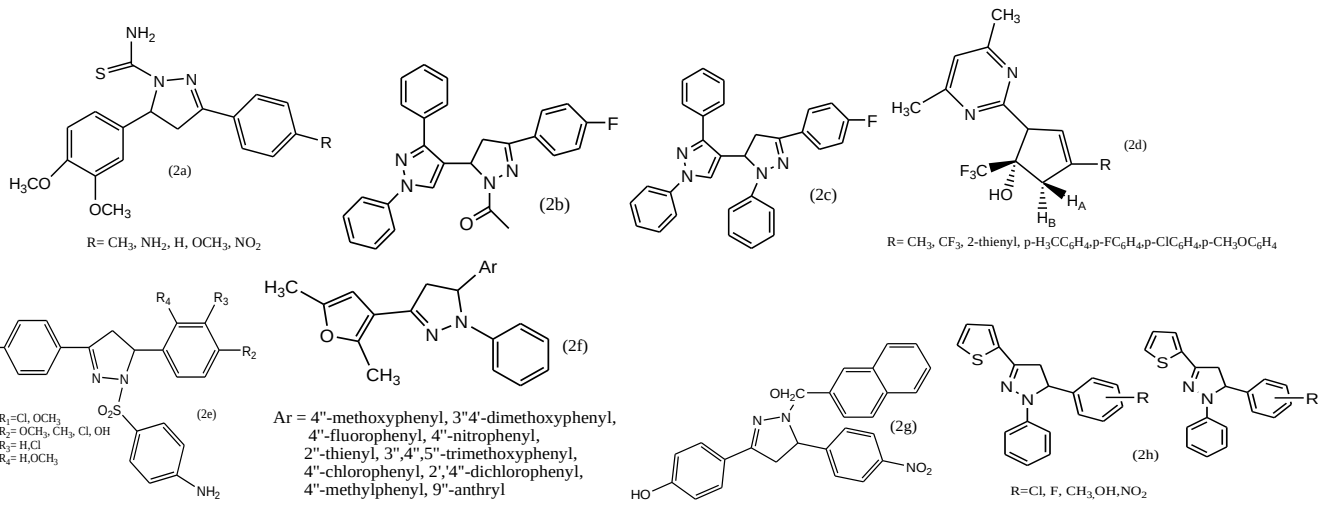
Setaraman venkataraman et al [43] synthesized pyrazolines (2p) significantly reduce the inflammation when compared with the control. R. S. Joshi et al [44] investigated a series of morpholine bearing pyrazolines(2q) as analgesic and anti-inflammatory agent and revealed that some compounds showed good analgesic and anti-inflammatory inhibition almost equivalent to the standard.

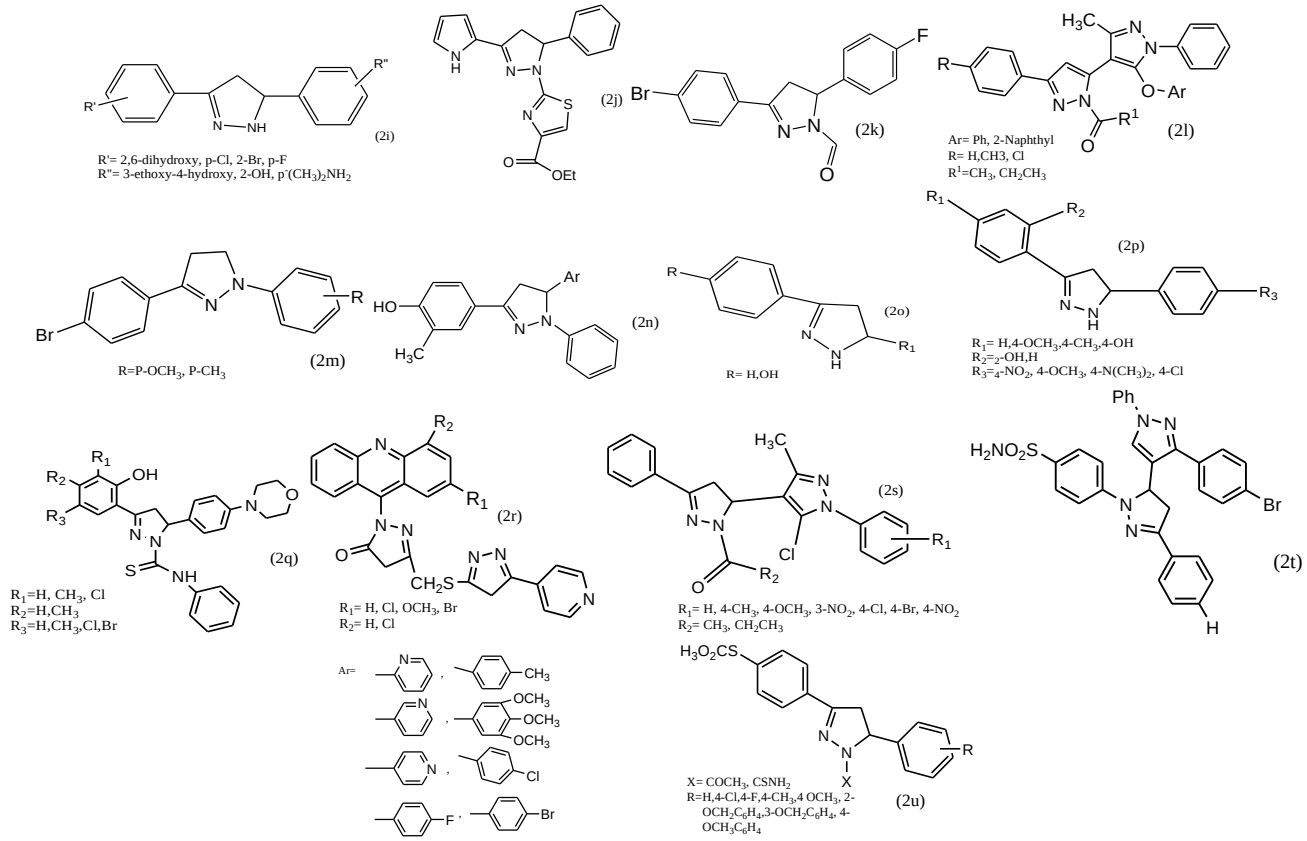
Newly synthesized acridinyl pyrazoline derivatives (2r) were screened by T. Chandra et al [45] for anti-inflammatory and analgesic activities

K.S. Girisha et al [46] prepared a series of acetyl/propyl pyrazolines (2s) carrying a pyrazole moiety reporting that compounds bearing electron withdrawing nitro group in the arylmoiety showed the highest analgesic activity.

P.K. Sharma et al [47] investigate the anti-inflammatory and antimicrobial profile of a new series of pyrazolylpyrazolines. Compound (2t) was identified as the most biologically active member.

R. Fioravanti et al [48] explored the N-substituted-3,5-diphenyl-2-pyrazoline derivatives (2u) as cyclooxygenase (COX-2) inhibitors . Some of the compound showed good activity against COX-2.





Antidepressant Activity:

Depression is one of the central nervous system disorder. Pyrazolines have been found to possess antidepressant potential.

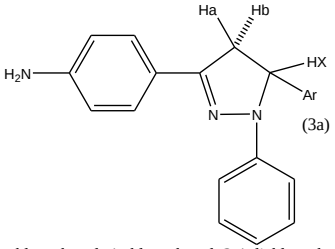
Some New 1,3,5-trisubstituted-2-pyrazolines (3a) were synthesized by Atla Srinivasa Rao et al [49] and evaluated for their antidepressant profile. Compound 3a showed antidepressant activity similar to standard, tranylcypromine. It was revealed that the presence of electron releasing group on phenyl ring system attached at C-5 position of 2-pyrazoline is important for their activity.

Bijo Mathew et al [50] synthesized thiophene containing pyrazoline carbothioamides (3b) with promising antidepressant action. It was revealed that they exhibit a typical reduction in immobility in the forced swim test by increasing the swimming behaviour.

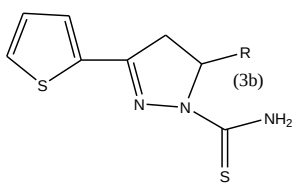
B. K. Kaymakcıoğlu [51] demonstrated the antidepressant activity of a series of 2-pyrazoline derivatives (3c) and two compounds showed promising antidepressant activity.

3,5-Diaryl pyrazolines analogs (3d) were developed as selective and reversible MAO-A inhibitors by M. Karuppasamy et al [52]. The docking studies were performed to gain further structural insights of the binding mode and possible interactions with the active site of MAO-A.

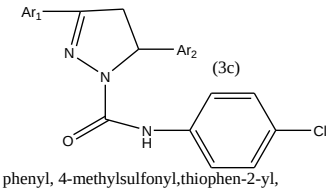
Kaplancikli et al [53] studied the antidepressant activity of synthesized triazolopyrazolines(3e).



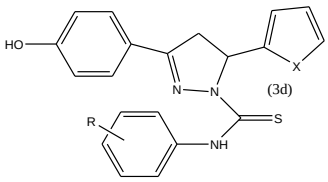
Ar= 2-chlorophenyl, 4-chlorophenyl, 2,4-dichlorophenyl, 4-bromiophenyl, 4-methoxyphenyl, 3,4-dimethoxyphenyl, 2,4-dimethoxyphenyl, 4-methylphenyl, 3,4,5-timethoxyphenyl, 9-anthracenyl, 3-pyridinyl, 4-pyridinyl



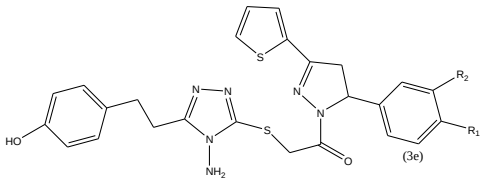
R= Phenyl, 4-chlorophenyl, 4-methoxyphenyl, 3-nitrophenyl, 2-hydroxyphenyl, 4-hydroxyphenyl, 4-N,N-dimehylphenyl



Ar_1= phenyl, 4-methylsulfonyl,thiophen-2-yl, 5-chlorothiophen-2-yl, 5-bromothiophen-2-yl
Ar_2= 2,6-dichlorophenyl



R= H, 4-methoxy, 3-methoxy, 2-methoxy, 2-methyl, 3-methyl



R_1= H, F, Cl, CH_3, $N(CH_3)_2$, O-CH_2-O
R_2=H

Anticancer Activity:

Various chemists have designed pyrazolines to examine their influence on cancer. P. Rathore et al [54] synthesized pyrazoline substituted benzenesulfonylureas and screened them for potential antiproliferative agents. The compound (4a) displayed remarkable antiproliferative activity.

Neera Raghav et al [55] prepared cyclized derivatives, pyrazolines (4b) and evaluated them for inhibitors of mammalian cathepsin B and cathepsin H as cancer therapeutics.

Two groups of novel coumarin pyrazoline hybrids endowed with phenylsulfonyl moiety (4c) were synthesized by K.M. Amin et al [56] and demonstrated the antitumor potency of the screened compounds.

The *in vitro* cytotoxic activity against four human tumor cell lines of isosteviol derivatives containing pyrazoline heterocyclic fragments (4d) were evaluated by S.-L. Zhu et al [57]. It was revealed that introduction of pyrazoline heterocyclic fragments to isosteviol were beneficial to the cytotoxic activities.

N.J. Fan et al [58] synthesized certain steroidal C-17 pyrazolinyl derivatives (4e) and tested for their cytotoxic activity against brine shrimp and three human cancer cell lines (NCI-H460, HeLa, and HepG2). Some of these synthetic compounds exhibited significant cytotoxic activity.

F.M. 274 Awadallah et al [59] synthesized pyrazolinyl-dihydropyrimidine derivatives and were investigated for their antiproliferative activity against A 549 (lung), HT 29 (colon), MCF 7and MDA-MB 231 (breast) cell lines. Compounds 4f and 4g, showed high activity against three of the cell lines. Derivatives with scaffolds of 1,3,5-tri-substituted pyrazoline and 1,3,4,5-tetra-substituted pyrazoline (4h) were synthesized and tested for their inhibitory effects on human tumor cell lines by M. Abdel-Halim et al [60].

Alexander Ciupa et al [61] synthesized some 3-(pyrid-2-yl)-pyrazolines (4i) and reported the antiproliferative activity in two cancer cell lines.

A series of 1,3-thiazolone derivatives bearing pyrazoline moiety (4j) were synthesized by Nadia A Khalil et al [62] and screened for their in vitro antitumor activity against human breast adenocarcinoma cell line (MCF-7). It was found that five of the tested compounds exhibited good antitumor activity in comparison to the reference drug, doxorubicin.

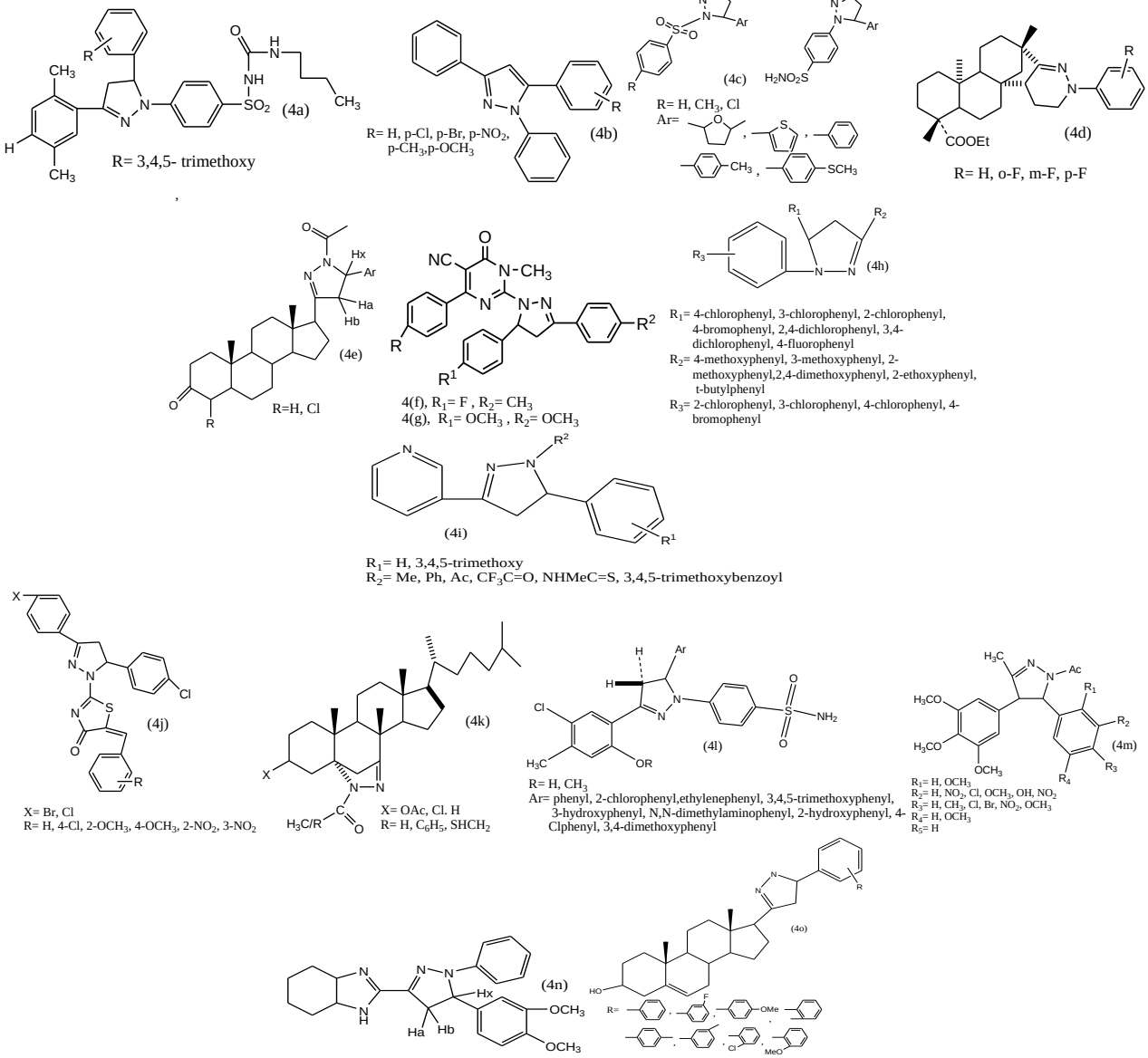
Steroidal derivatives containing pharmacologically attractive pyrazoline moieties (4k) are synthesized by Shamsuzzaman et al [63] and screened for in vitro anticancer evaluation. The compounds displayed moderate to good cytotoxicity on cervical and leukemia cancer cell 32 lines. All the compounds were found to be non toxic to normal cell lines.

1,3,5-trisubstituted pyrazolines bearing benzene sulfonamide (4l) were synthesized by R. Bashir et al [64] and evaluated for antitumor activity. Compounds exhibited considerable antitumor activities against the entire tested tumor cell lines.

M. Lee et al [65] synthesized methylpyrazoline analogs (4m) of combretastatin A-4 were tested to determine their cytotoxicity against the growth of cancer cells in culture using an invitro 72 h continuous exposure-MTT assay.

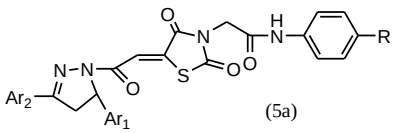
Pyrazoline bearing benzimidazoles were synthesized by M. Shaharyar et al [66] and evaluated for anticancer activity. Compounds (4n) was found to be the most active candidate of the series. A.H. Banday et al [67] reported the synthesis of 17-pyrazolinyl derivatives of pregnenolone (4o) and their evaluation as potential anticancer agents

against various human cancer cell lines. Various compounds showed significant cytotoxic activity against HT-29, HCT-15, 502713 cell lines.

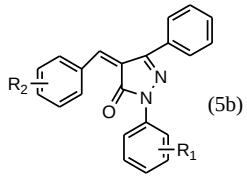


Antiviral Activity:

Pyrazolines was explored by chemists for antiviral activity. Thiazolidinonepyrazoline hybrids (5a) were synthesized by D Havrylyuk et al [68] and antiviral activity of synthesized compounds was determined. The compounds showed insignificant activities against the four strains of influenza virus. Ramajayam et al [69] demonstrated the potency of synthesized pyrazolines (5b) as protease inhibitor of SARS virus.



Ar_1= 4-Cl-C_6H_5, 4-OMe-C_6H_5
Ar_2= Ph, naphthalen-2-yl
R= Me, OMe, Cl



R_1= H, 4-Cl, 4-OCH_3, 4-$CH(CH_3)_2$, 4-$C(CH_3)_3$, 4-CN, 4-OCF_3, 4-Cl, 3,4-Cl_2, 4-F, 3-NO_2
R_2= H, 3-OCH_3, 3-NO_2, H, 4-Cl, 4-COOH, 4-OCH_3, 4-OH, 4-COOH

2.

Antitubercular Activity:

Tuberculosis arise from infection with Mycobacterium Tuberculosis. Pyrazolines was explored for its antitubercular activity many of times.

S.C. Karad et al [70] investigated in vitro antituberculosis activity of novel pyrazolylpyrazolines (6a) at 250 mg/mL against M.tuberculosis H37Rv stain. Some of the compounds possessed brilliant activity.

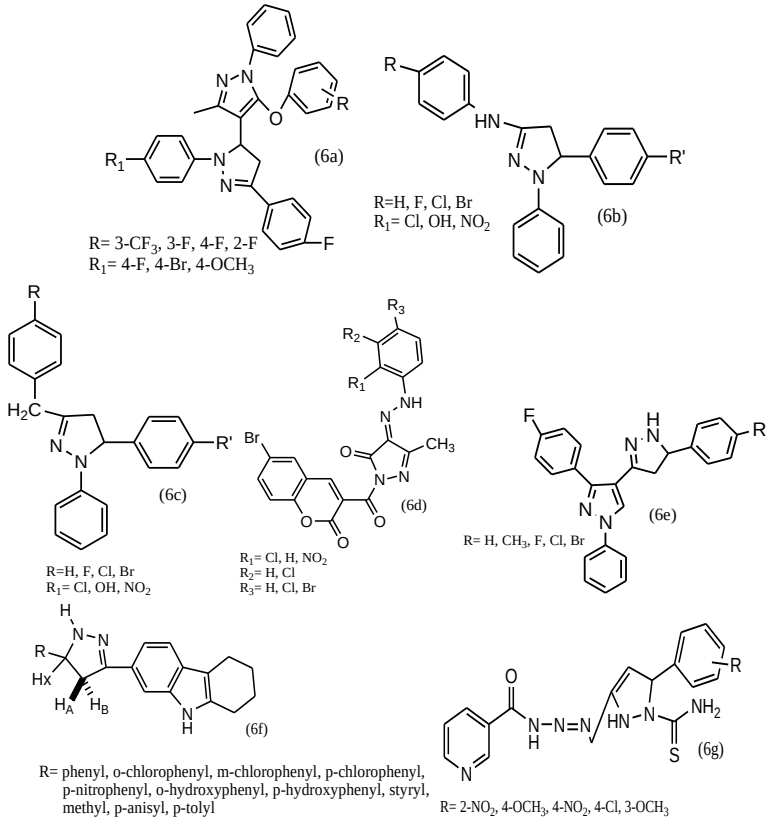
A series of 2‑pyrazoline compounds (6b) were synthesized by Hipparagi and Bhanushali et al [71] and were screened for anti‑tubercular activity against isoniazid resistance mycobacterium tuberculosis, using Microplate Alamar Blue assay method. None of the compound was found to be equipotent with standard isoniazid.

The anti-tubercular screening of all synthesized pyrazoline derivatives (6c) was carried outby Bhanushali & Shivkumar [72] against Mycobacterium tuberculosis of H37Rv strain.

Hariraj N et al [73] synthesized and evaluated pyrazolin-5-one derivatives of 6-bromo Coumarins (6d) as antitubercular agents. All the synthesized Pyrazoline-5-one derivatives showed promising Anti-TB activity against M tuberculosis.

A new series of fluorinated pyrazoles (6e) were synthesized from the corresponding chalcones, by ultrasonic irradiation by S. N. Shelke et al [74]. The newly synthesized compounds were investigated for their anti-tubercular activities against Mycobacterium tuberculosis H37Rv.

Taj et al [75] synthesized new pyrazoline derivatised carbazoles (6f) and screened for their antitubercular activity against the standard atreptomycin and pyrazinamide. Kasabe et al [76] observed good antitubercular activity of synthesized pyrazolines(6g).



Antioxidant Activity:

Antioxidants are substances that may protect cells from the damage caused by unstable molecules known as free radicals.

A Kumar et al [77]synthesized 3,5-disubstituted-2-pyrazolines (7a)and were screened for antioxidant activity using DPPH radical scavenging method, NO scavenging assay, superoxide radical

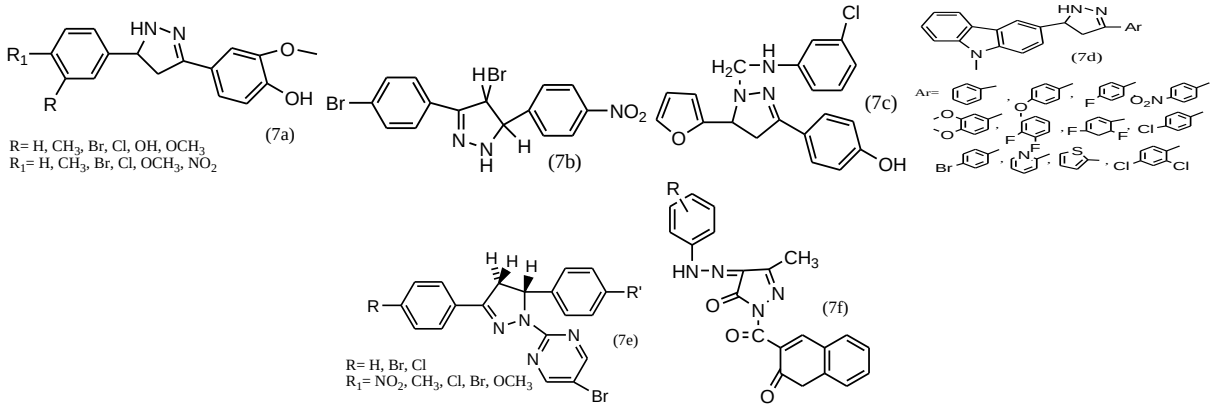
scavenging assay and hydrogen peroxide radical scavenging assay. All the compounds showed good free radical scavenging activity which is comparable to that of the standard ascorbic acid.

Anjan Kumar et al [78] 4-bromo-3(substituted phenyl)-5(substituted phenyl)-1-phenyl-2-pyrazoline were screened for anti-oxidant and anti-inflammatory activity. The antioxidant activity of compound (7b) was found to be the strongest.

Mannich base of pyrazolines (7c) was synthesized by P. C. Jagadish [79] compounds were subsequently evaluated for the antioxidant activity compound 3e having p-hydroxyl substitution showed best antioxidant activity as compared to ascorbic acid and rutin. A novel series of 3-(substituted)-aryl-5-(9-methyl-3-carbazole)-1H-2-pyrazolines (7d) was synthesized by B. P. Bandgar et al [80] and evaluated for antioxidant activity. Most of the compounds exhibited good DPPH and superoxide radical scavenging activity.

4,5-dihydropyrazolines carrying pyrimidine moiety (7e) were prepared by A. Adhikari et al [81] under conventional heating as well as microwave reaction condition. Newly synthesized pyrazolines were screened for their free radical scavenging activity by DPPH method.

A new series of Coumarin fused pyrazoline-5-one derivatives (7f) were developed P. Venkatesh et al [82] and examined for antioxidant activity by DPPH and Nitric oxide methods. Compound 2 possess good antioxidant activity in both methods.

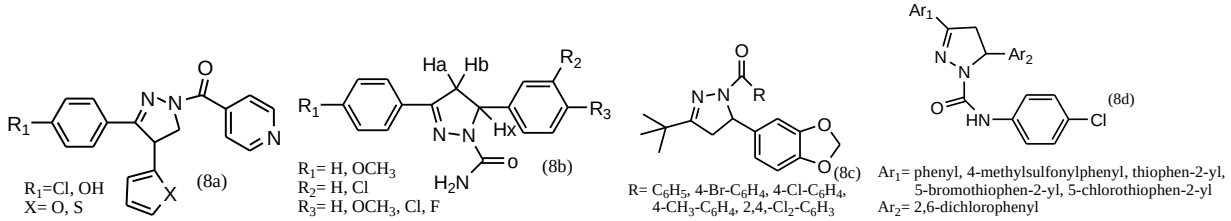


Anticonvulsant Activity:

Maruthi rao B et al [83] synthesized new 2-pyrazoline derivatives (8a) and evaluated them for anti-epileptic activity. The compounds showed good antiepileptic activity when compared to standards.

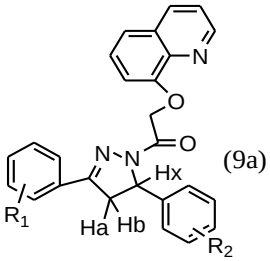
Ravinesh Mishra et al [84] synthesized 3,5-diphenyl-2-pyrazoline-1-carboxamide derivatives (8b) were and were screened for anticonvulsant activity by the maximal electroshock seizure (MES) method. The neurotoxicity was determined by rotorod toxicity test on male albino mice. It was shown that all of the tested compounds were protective against MES at 100-300 mg/kg dose levels.

M.N. Aboul-Enein et al [85] synthesized stiripentol (STP) derived analogues (8c) as anticonvulsant candidates. Screening of the compounds was done using PTZ and MES method. N. Beyhan et al [86] synthesized a series of 2-pyrazoline derivatives (8d) and screened for their anticonvulsant activity. It was indicated that among the tested compounds, 2-pyrazoline-1-carboxamide derivatives carrying 5-bromothiophen, 5-chlorothiophen and 2,6-dichlorophenyl groups exhibited noteworthy activity in PTZ test.



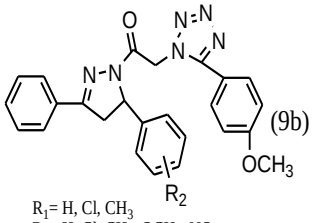
Antiamoebic Activity:

Pyrazoline derivatives (9a) were synthesized by F. Hayat et al [87]and evaluated for in vitro antiamoebic activity against HM1: IMSS strain of *E. Histolytica*. Compound showed promising antiamoebic activity. M.Y. Wani et al [88] reported novel tetrazole embedded 1,3,5-trisubstituted pyrazoline derivatives (9b) as *Entamoeba histolytica* growth inhibitors.



(9a)

R_1= 4-Br, 4-Cl, H
R_2= 4-OCH_3, H, 4-CH_3, 2-Cl, 3-Cl



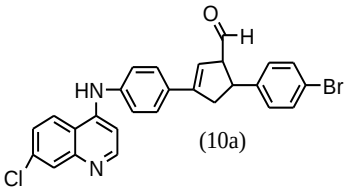
(9b)

R_1= H, Cl, CH_3
R_2= H, Cl, CH_3, OCH_3, NO_2

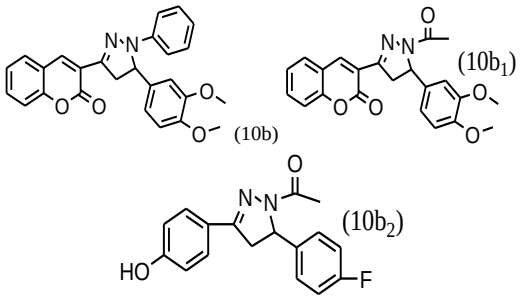
Antimalarial:

B. Insuasty et al [89] prepared a new series of N-acetyl and N-formyl-pyrazoline derivatives and demonstrated their antimalarial activity. Compound (10a) showed remarkable antimalarial activity.

G. Wanare et al [90] synthesized pyrazoline analogs (10b-b_2) and evaluated for antimalarial activity against both chloroquine sensitive strain (3D7) and chloroquine resistant field isolate (RKL9) of P. Falciparum. All the tested compounds showed promising antimalarial activity. A series of 1,3,5-trisubstituted pyrazolines (10c) were synthesized by B.N. Acharya et al [91] and evaluated for in vitro antimalarial efficacy against chloroquine sensitive (MRC-02) as well as chloroquine resistant (RKL9) strains of Plasmodium falciparum and obtained promising results.



(10a)

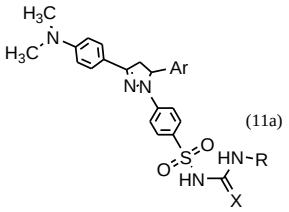


(10b) (10b_1) (10b_2)

Antidiabetic Activity:

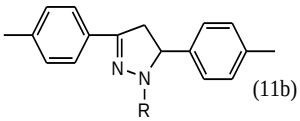
Syed Ovais et al [92] synthesized new pyrazoline substituted benzenesulfonylurea / thiourea derivatives. Compounds showed moderate to good anti-hyperglycaemic activity in glucose fed hyperglycaemic normal rats at the dose of 0.05 mM/kg b.w.

N. Santhi et al [93] synthesized 1,3,5-triaryl-2-pyrazolines and investigated their antidiabetic activity and were found to be better hypoglycemic agent compare with standard drug insulin in reducing the blood glucose level.



(11a)

Ar=phenyl, 4-methoxyphenyl, 2-chlorophenyl, 3,4,5-trimethoxyphenyl, 4-chlorophenyl, 4-methylphenyl
X= O, S
R= C_6H_5-CH_2, -C_4H_9

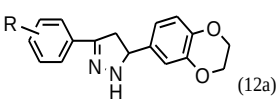


(11b)

R= $CONH_2$, $CSNH_2$, C_6H_4, SO_2, COC_6H_5

Antihepatotoxic Activity:

Habibullah Khalilullah et al [94] prepared some novel pyrazoline derivatives containing 1,4-dioxane ring system . Some of the synthesized compounds were evaluated for antihepatotoxic activity against CCl4-induced hepatotoxicity in rats. Compounds showed significant activity comparable to standard drug silymarin.

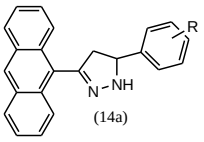


(12a)

R= H, 2-hydroxy, 4-hydroxy, 2,4-dihydroxy, 2-chloro, 4-chloro, 4-fluoro, 3,4-dimethoxy, 2-methyl, 3-methyl, 4-methyl, 4-nitro

Acetylcholinestrase Inhibitory Activity:

Nibha Mishra et al [95] studied the acetyl cholinesterase inhibitory property of diaryl pyrazoline derivatives (14a).



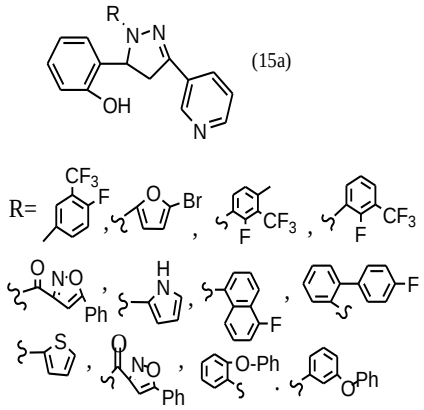
(14a)

R= 4-NO_2, 4-OH, 4-Cl, 4-CH_3, -H, 2-OH, 2,4-Di-OH, 3-NO_2, 4-OCH_3

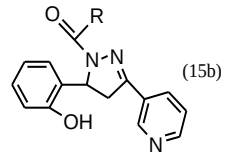
Raf Kinase Inhibition:

Omprakash Tanwar et al [96] had done the 3D-QSAR study for amino-substituted N-acyl and N-aroylpyrazolines (15a) as B-Raf kinase inhibitors using a common five-point pharmacophore model.

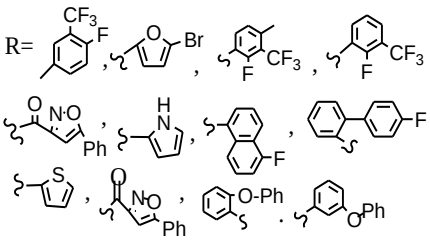
C. Blackburn et al [97] studied the B-Raf inhibitory activity of selected compounds from a diverse screening library of N-acyl and N-aroylpyrazolines (15b).



(15a)

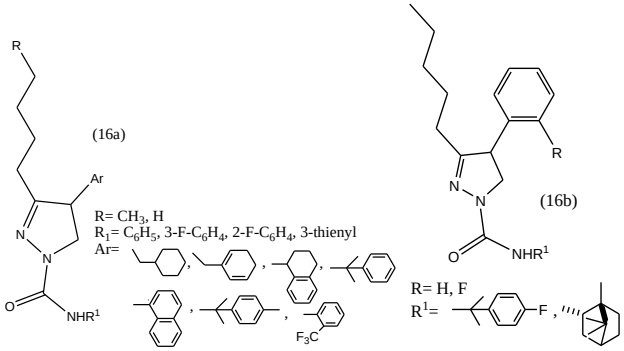


(15b)



Cannabinoid Receptor Antagonist:

J. H. M. Lange et al [98] synthesized two structurally related pyrazoline classes (16a, 16b) and were evaluated for their action on cannabinoid receptor. The tested compounds showed high affinities to the CB1 and CB2 receptor and were found to act as CB1 receptor agonists.



(16a)

R= CH_3, H
R_1= C_6H_5, 3-F-C_6H_4, 2-F-C_6H_4, 3-thienyl
Ar=

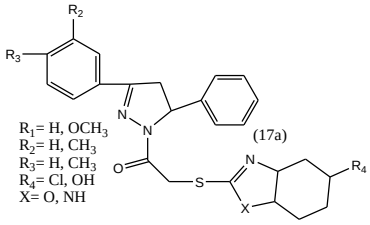
(16b)

R= H, F
R^1=

Antinociceptive Activiy:

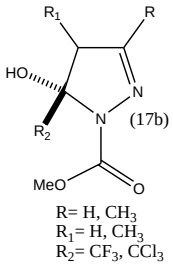
Z.A. Kaplancikli et al [99] demonstrated the antinociceptive activitiy of 1 [(Benzoxazole/ benzimidazole-2-yl)thioacetyl] pyrazoline derivatives All of the tested compounds exhibited significant antinociceptive activities in both hot plate and acetic acid-induced writhing tests.

J. Milano et al [100] evaluated the antinociceptive effect of four novel pyrazoline methyl esters against hot-plate and formalin tests of nociception.



(17a)

R_1= H, OCH_3
R_2= H, CH_3
R_3= H, CH_3
R_4= Cl, OH
X= O, NH



(17b)

R= H, CH_3
R_1= H, CH_3
R_2= CF_3, CCl_3

CONCLUSION: Pyrazoline is a biologically important compound and thus, it attracts various medicinal chemists. In this review, pharmacological profiles of various pyrazoline derivatives has been done.

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