Pyrazole as an anti-inflammatory scaffold: A comprehensive review

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Abstract---Inflammation is a common component behind pathophysiology of many chronic diseases like cardiovascular, arthritis, bowel disorders, cancer, chronic wounds, and lesions which are the most significant cause of death in the world, according to the World Health Organization. Chronic inflammation associated diseases are expected to increase persistently by the next 30 years as 3 of 5 people die daily due to chronic inflammatory diseases. So, the prerequisite of novel anti-inflammatory agents has been noteworthy increased than ever. Heterocyclic compounds are being developed at the large pace over the most recent couple of decades due to their intriguing pharmacological activities. The most remarkable and well-known heterocyclic nucleus is pyrazole which has pulled the consideration of numerous specialists to explore its wide potential. Pyrazole derivatives are considered as valuable class of compounds owing to their extremely noticeable anti-inflammatory activity. This review delivers a vast summary of pyrazole derivatives developed last decade for their action against inflammation along with docking studies with a hope that it will be useful for medicinal chemists working in anti-inflammatory drug development.

Keywords---inflammation, heterocyclic compounds, pyrazole, docking studies, binding affinity.
Introduction

Inflammation as a defense mechanism is essential for health which is the response of immune system against damaging stimuli (pathogens, toxic compounds, damaged cells, radiations) and initiate the healing process by eradicating harmful stimuli. Acute inflammation (uncontrolled) may grow into chronic, which can contribute to development of chronic inflammatory diseases later. Inflammation is involved as a common component behind pathophysiology of many chronic diseases like cardiovascular, arthritis, cancer, bowel diseases, chronic wounds and lesions (1) which are the most significant cause of death in the world, according to the World Health Organization. Chronic inflammation associated diseases are expected to increase persistently by the next 30 years as 3 of 5 people die daily due to chronic inflammatory diseases including stroke, heart disorders, chronic respiratory diseases, cancer, diabetes and obesity. (2)

Nonsteroidal anti-inflammatory drugs are the utmost prescribed agents for treating inflammatory diseases. These NSAIDs hinders arachidonic acid to prostaglandins conversion by inhibiting COX-1 and COX-2. COX-1 isoform is principally accountable for PGs synthesis to expend cytoprotective effect in the gastrointestinal tract and regulate renal function, while COX-2 selectively release PGs participating in the inflammation. Subsequently, prolonged use of COX-1 inhibitors cause serious side effects like gastrointestinal bleeding, lesions and nephrotoxicity. (3) Selective COX-2 inhibitors cause side effect such as cardiovascular disorders, but LOX inhibitors act by reducing side effects occasioned from both COX-1 and COX-2. Consequently, it is an objective to improve anti-inflammatory agents with less side effects which is possible with dual COX/5-LOX inhibition. (4)

Heterocyclic compounds are extremely beneficial and exclusive class of organic compounds demonstrating a wide range of biological properties. (5) These are abundant in nature and highly significant to life due to their presence in various natural products such as hormones, vitamins, alkaloids and in pharmaceuticals, dyes, herbicides, and several other compounds. They have been regarded as heart of modern drug discovery due to their ability to form hydrogen bonds between heteroatoms and receptors of the body to exhibit significant pharmacological activities. (6)

Nitrogen-containing heterocycles are considered as broad frameworks amongst heterocyclic compounds due to their striking structural characteristics. Pyrazole has grown up as highly valuable and significant due to its wide-ranging biological outlines amongst most potential nitrogen-containing families. Since it is frequently observed in commercially available medications, it has gained more attention. Pyrazomycin (anti-cancer), Deramaxx (NSAID), Floxan and Difenamizole (anti-inflammatory) are the perfect instances of renowned roles of pyrazole moiety. Pyrazolone (3-oxygenated derivative, additional keto-group), is the fundamental constituent of Metamizole sodium and Phenylbutazone (NSAIDs) and its benzo-fused derivative (tetrahydroindazole) is employed against cancer and inflammation. (7)
Ludwig Knorr provided the term Pyrazole in 1883. In 1959, first natural pyrazole named as 1-pyrazolyl-alanine was isolated from watermelon seeds. Chemically, pyrazole is the five membered ring containing two adjacent nitrogen atoms with molecular formula C$_3$H$_4$N$_2$ which has 6 π electrons. Pyrazole (aromatic) is closely correlated with its reduced or oxidized (non-aromatic) forms such as pyrazoline, pyrazolidine, and pyrazolone (Fig.1). Moreover, unsubstituted pyrazoles exist in three possible tautomers (Fig. 2). (8)

![Fig. 1: Structures of Pyrazole and its reduced and oxidized forms](image)

![Fig 2: Tautomers of unsubstituted pyrazoles](image)

Pyrazole is a colorless solid having 69-70°C melting point, 186-188°C boiling point (due to intermolecular hydrogen bonding). Its first nitrogen atom is “pyrrole-like” and electron pair is in conjugation with the aromatic system, but second nitrogen atom is like pyridine as lone pair of electrons are not contributing to delocalization, as in case of pyridine. Pyrazoles, due to its nitrogen atom’s different nature, react with both acid and base. Subsequent protonation destabilizes π-bonds which make pyrazole a weaker base (pKa= 2.52). It also behaves as a weak acid (pKa=14.21). Acidity can be increased after introducing electron withdrawing groups. (9)

Individual atom in pyrazole ring system affects its chemical reactivity. The N2-atom (with two electrons) is basic and reacts with electrophiles while The N1-atom non-reactive and release its proton in the presence of base. These two N-atoms properties reduce the electron density at C3 and C5 and offer C4 for electrophilic attack. In the presence of strong base, deprotonation at C3 cause ring opening reactions. Protonation of pyrazoles forms parazonium cations which make C4 unavailable for electrophilic attack while facilitate C3 for the same. The pyrazole anion remains unreactive toward nucleophiles, but electrophiles can easily attach those. (10)

The pyrazole compounds are usually synthesized by reacting hydrazine’s with 1,3-diketones. Typical methods involve condensation of 1,3-dicarbonyl compounds or 1,3-dielectrophiles with hydrazines (Knorr synthesis) (Fig. 3) and cycloadditions [3+2] comprising diazomethane (1,3-dipole compound) and alkynes (Pechmann synthesis) (Fig. 4). (11)
In medicinal chemistry, numerous compounds comprising pyrazole rings are exhibiting biological activities for instance anti-microbial, leishmanicidal, antifungal, anti-viral, pesticidal, anti-hyperglycemic, anti-inflammatory, and antitumoral activities. (11) This review outlines pyrazole derivatives developed last decade for their action against inflammation along with docking studies with a hope that it will be useful for medicinal chemists working in anti-inflammatory drug development.

**Anti-Inflammatory Activity: Review**

Jadhav *et al* synthesized fluorinated pyrazoles chalcones and assessed for anti-inflammatory activity using carrageenan paw edema method and Molecular docking study was accomplished by AutoDock software. Compound 1a (3-NO$_2$) was the most active with 67% inhibition which was similar to the reference standard Diclofenac sodium (% inhibition = 57%). The SAR study revealed that 2-hydroxy 4-fluoro phenyl substituted pyrazole chalcones showed better activity. The nitro group (electron withdrawing) considerably increased the activity. (12)

Abdellatif *et al* developed amino/methanesulphonyl group containing pyrazole derivatives as COX-2 pharmacophore for *in vitro* and *in vivo* anti-inflammatory activities. Compounds 2a-2f showed good Selectivity index (246.8–353.8) for COX-2 in contrast to Celecoxib (SI= 326.7). These derivatives revealed good edema inhibition of 83–96% relative to Celecoxib (82.8%) and were less ulcerogenic (ulcer indexes= 0.7–2.0) than Indomethacin and Celecoxib (ulcer index= 21.3 and 1.3). MOE version 2008.10 modeling software was utilized to demonstrate binding
conformations with receptor. Sulfonyl moiety proved its significance for COX-2 selectivity. (13)

Gedawy et al explored pyrazole sulfonamide derivatives possessing dual COX/5-LOX inhibitory activity which is a better approach for a broader spectrum with less side-effects and. The compound 3a (2-chlorothienyl) and 3b (benzothiophen-2-yl) showed higher activity than Celecoxib and Indomethacin. The compound 3b inhibited COX-1 with IC\textsubscript{50} of 5.40 while COX-2 and 5-LOX with IC\textsubscript{50} of 0.01 and 1.78 µM respectively. It was selectively active towards COX-2 over COX-1 which was confirmed from its selectivity index 344.56. Molecular docking was accomplished using Open Eye package. In COX-1, access of sulfonamide was restricted to the side pocket was restricted by larger Ile523 leading to selectivity towards COX-2 over COX-1. (14)

Abdellatif et al developed pyrazole derivatives comprising vicinal diaryl system and evaluated their COX inhibition. Four compounds (4b, 4c, 4d and 4e) exhibited COX-2 selectivity index of 8.69-9.26 which was comparable to Celecoxib (8.60). Compound 4e (thiazolidinone series) was the potent COX-2 active derivative with IC\textsubscript{50} value 0.62 µM and selectivity index of 9.15. Docking studies were performed using the Open Eye Modeling software. Thiazolidindione series involving methylene linker displayed similar pose as of Celecoxib while the series of thiazolidinone involving methylene hydrazone linker unveiled different pose. The compound 4a and 4b overlaid same pose with IC\textsubscript{50} of 0.48 and 0.63 µM respectively. (15)

Abdellatif et al designed schiff and chalcone substituted pyrazoles and showed considerable edema inhibition (13–93%) when compared with Celecoxib (58–93%). Compound 5d showed the best screening results (% inhibition = 93.62, SI = 215.44, ulcer index = 7.25) as compared to Celecoxib as standard (% inhibition = 93.51%, SI = 308.16, ulcer index = 8). The designed analogs were docked utilizing AutoDock 4.1. Compounds 5a, 5b, 5c and 5d exhibited four hydrogen interations with COX-2 active site of but no hydrogen bond with COX-1 which described their selectivity and ulcer safety profiles. (16)
Abdellatif et al designed pyrazole derivatives having SO₂Me group and evaluated their COX inhibition, ulcerogenic accountability and in vivo anti-inflammatory activity. Most of the derivatives were selective towards COX-2 isozyme with less ulcerogenic liability ranges 2.64–3.87 compared to Ibuprofen and Celecoxib with ulcer index of 20.25 and 2.99 respectively. Structural data revealed that the methoxy substituted derivatives (6a, 6b, 6c, 6d, 6e and 6f) displayed higher activity than the derivatives without substitution. Para substituted methoxy also improved binding with COX-2. (17)

Bharathi et al explained synthesis of pyrazole benzonitriles for their evaluation as anti-inflammatory agent. Compound 7d exhibited 85.45 % inhibition when compared to Diclofenac sodium standard drug. The compound 7b with chloro substituent increased the activity and methyl substituted compound 7a showed significant activity. The compound 7f (nitro substituted) revealed 83.47 % inhibition which was greater than Diclofenac sodium. Hydorxyl group substitution in compound 7c reduced its activity. The compound 7a-7g displayed hydrogen, hydophobic and π-alkyl interactions with active site of enzyme. (18)

Dennis Bilavendran et al synthesized analogues of thiophene containing pyrazoles and assessed for anti-inflammatory activity. Pyrazolo-pyridines have shown % inhibition of 96.42% with least binding score of -12.45 to -14.27 kcal/mol. The hydroxy group in compound 8a and nitro in compound 8b showed a comparable activity comparative to standard drugs. Autodock 4.2.6 was used for in silico molecular docking studies. (19)

El-Shoukrofy et al designed pyrazole hybrids possessing thiophene and evaluated their in vitro COX inhibition and in vivo anti-inflammatory activity. These hybrids have shown more selectivity towards COX-2 than COX-1. Compounds 9a was the most potent and gastrointestinal safe compared to Diclofenac sodium, Indomethacin and Celecoxib. Compounds 9a and 9b (EI% = 68% and 70%) were more superior than Diclofenac sodium (EI% = 56%) and Celecoxib (EI% = 60%). The compound 9d exhibited the highest COX-2 selectivity index. Molecular docking studies were achieved by accessing Molecular Operating Environment. Compounds 9a, 9b, 9c and 9d interacted with COX-2 active site and exhibited excellent binding interactions like arene–arene, arene-cation interaction. (20)
Hassan et al assessed pyrazole derivatives for their *in vitro* COX-1/COX-2 inhibition and *in vivo* anti-inflammatory activity. Most of the derivatives displayed selective COX-2 inhibition. Compound 10a, 10b, 10c, 10d and 10e exhibited IC$_{50}$ of 19.87-61.24 nM towards COX-2. Compound 10d and 10e (fluoro and the methoxy derivatives) displayed selectivity index of 17.47 and 13.10, respectively. Docking studies were achieved with the aid of Autodock. Analysis revealed that derivatives adopted similar interactions with enzyme as that of SC-558 which is extremely selective COX-2 inhibitor. (21)

Macarini et al synthesized six derivatives of pyrazole after ADME studies and virtual screening for COX-1 and COX-2 inhibition. The compound 11a exhibited the greatest activity for COX-2 inhibition with IC$_{50}$ value of 0.73 μM whereas the control Celecoxib displayed IC$_{50}$ value of 0.88 μM. The compounds with the 3,5-dimethylpyrazole ring interact with the enzyme through H-bonds due to presence of polar groups. AutoDock Vina was assessed for molecular docking studies. The C=O group of the chalcone moiety showed hydrogen bond with enzyme which was not possessed by Celecoxib. This provides a reason of its higher selectivity. (22)

Song et al discovered pyrazole-4-carboxaldehydes hydrazone derivatives which were evaluated for their anti-inflammatory activity by expending LPS-induced TNF-α model and xylene-induced ear-edema method. Compounds 12a and 12b exhibited TNF-α inhibitory ability with 5.56 and 3.69 μM IC$_{50}$ values. The compound 12b inhibited the ear edema by 49.59 % as compared to Dexamethasone (50.49 % inhibition) as reference drug. Discovery Studio was
utilized for molecular docking results which indicated that phenyl and hydrazide group of side chain displayed a noteworthy interaction with TNF-α target site. (23)

Taher et al designed and synthesized pyrazole and pyrazoline derivatives as anti-inflammatory drugs. The study presents that lengthening of carbon chain in derivatives possessing amine moieties as in compound 13a and 13b presented higher activities when compared to others. Docking studies were initiated by using Molecular Operating Environment 2019.0101 software which illustrated compounds 13a and 13b as the most potent with docking scores comparable to Indomethacin. Compound 13a via carbonyl group revealed maximum binding affinity with active site. (24)

Tageldin et al developed pyrazolo pyrimidinone and pyrazolo triazolo pyrimidinone derivatives for their evaluation using in vitro COX-1/2 inhibition and in vivo anti-inflammatory testing. Compounds 14a, 14b, 14c, 14d and 14e indicated excellent selectivity towards COX-2 inhibition which was comparable to Celecoxib. Compound 14a and 14c exhibited 43.4 and 46.9 % inhibition superior to Celecoxib and Diclofenac sodium with % inhibition of 8.6 and 36.1 respectively. Molecular docking studies were carried out by utilizing Molecular Operating Environment. It was observed that compounds had not displayed specific binding with COX-1 binding site due to its much smaller volume than COX-2. (25)
Zabiulla et al described benzophenones possessing sulphur bridged oxadiazole pyrazole system as anti-inflammatory agents. The compound 15a with fluoro group (electron withdrawing) revealed as highly active showing 52.17% edema inhibition which was more than Diclofenac (23.07%). SAR suggested that substituents type and position on benzoyl ring were able to decide activity level. Autodock 4.2.6 was assessed for molecular docking analysis. The binding energy of the derivatives on COX-1 was more as compared to COX-2 which leads to higher selectivity towards COX-2. (26)

Abdelgawad et al evaluated 4-aryl-hydrazonopyrazolones for their in vitro COXs/5-LOX enzyme inhibition and in vivo anti-inflammatory activities. The compounds 16a-16d proved excellent % edema inhibition of 72.72-54.54% with great ED$_{50}$ values of 0.044–0.104 mmol/kg as compared to Celecoxib bearing ED$_{50}$ value of 0.032 mmol/kg. Compounds 16c, 16d and 16e were observed as the most potent with COX-2 selectivity index values ranging from 5.29–5.69 towards COX-2 when compared to Celecoxib (SI = 3.52). Binding conformations were investigated by MOE modeling software. (27)

Abdellatif et al evaluated Lonazolac analogs such as pyrazole derivatives with 1,3,4-trisubstitution for their evaluation as anti-inflammatory agents. The compounds 17a-c (bisaminosulphonyl derivatives) were the most selective towards COX-2 with good anti-inflammatory potency bearing ED$_{50}$ value of 50.43 µmol/kg in comparison with Celecoxib (ED$_{50}$= 82.2 µmol/kg). These were less ulcerogenic means gastrointestinal safer than Ibuprofen. Docking was performed
by using Open Eye software. Compound 17c exhibited similar binding pattern like Celecoxib via hydrogen-bond interactions. Chloro substitution was superior than NO\textsubscript{2} and Br substitution. (28)

Kulkarni \textit{et al} developed quinoline-2-carboxamides containing pyrazole and assessed for their anti-inflammatory activity using protein denaturation method. Compound 18a (benzo substituted) and 18b (methyl substituted) exhibited promising percent inhibition of 82.52\% and 74.77\% which was comparable to the standard Diclofenac Sodium (87.88\%). Compounds were docked by expending SurfFlex-Dock algorithm. Compounds 18a and 18b showed interaction with three and two amino acids of the active site respectively. (29)

Abd El Razik \textit{et al} designed hybrids of benzodioxole–pyrazole and investigated for \textit{in vitro} COXs/5-LOX inhibition along with \textit{in vivo} anti-inflammatory action. Compound 19a–19c displayed significant anti-inflammatory. Compound 19c displayed higher selectivity towards COX-2 with 52.75 \% inhibition as compared to standard. MOE version 2014.09 was utilized for docking evaluation. Compound 19a–19c showed similar binding pattern like Celecoxib and Meclofenamic acid with COX-2 and 5-LOX. The sulfonamide moiety help in recognition of active compounds via H-bond interactions. (30)

Abdelgawad \textit{et al} synthesized pyrazole-hydrazone derivatives for COXs/5-LOX inhibition and investigated for anti-inflammatory activity. Compound 20a and 20b with IC\textsubscript{50} value of 0.67 and 0.58 \textmu M presented superior COX-2 inhibition than Celecoxib (IC\textsubscript{50} = 0.87 \textmu M) and showed outstanding 5-LOX inhibition with IC\textsubscript{50} of 1.92 \textmu M greater than Zileuton drug (IC\textsubscript{50} = 2.43 \textmu M). The compound 20b (chloro derivative) revealed as the most active against COX-2 while compound 20a (p-tolyl analogue) displayed more potency against 5-LOX inhibition. The compound 20c (carboxylic acid derivative) displayed maximum activity with 20 \% inhibition relative to Celecoxib (% inhibition= 17.5\%). MOE program was utilized for Molecular docking studies and revealed two to four H-bonds with enzyme. (4)
Lokeshwari et al. established 2-pyrazolines synthesis and screened for their in vitro anti-inflammatory activity. The compound 21a-21c showed considerable phospholipase A2 inhibition with IC$_{50}$ values ranging 10.2-11.9µM. The docking was attempted with SWISS-DOCK. The top most poses of compound 21c showed binding energies in the range of -7.6 to -6.9 kcal/mol. (31)

Nossier et al. developed pyrazole-substituted heterocyclic ring systems and explored for their anti-inflammatory activity by utilizing carrageenan-induced paw edema method. Compound 22a displayed 85.78% edema inhibition which was higher than Celebrex and Indomethacin (72.99% and 83.76%). It was further docked using MOE 2008.10 software. (32)

Abdellatif et al. designed triaryl-pyrazole series for anti-inflammatory action. Most of the derivatives displayed COX-2 selectivity. The compound 23a-23d (trimethoxy derivatives) were the most active derivatives with ED$_{50}$ range of 53.99-69.20 µmol/kg comparable to Celecoxib (ED$_{50}$= 82.15 µmol/kg). These compounds also displayed less ulceration effect such as 1.20- 2.68 which was comparable to Celecoxib with 2.90 ulcer index. MOE version 2008.10 was utilized for Molecular docking studies. Compound 23a, 23b and 23d showed three and 23a, 23b and 23d displayed two hydrogen bonding interactions. (33)
Abdel-sayed et al designed pyrazolines with 1,3,5-trisubstitution and reported their in vivo anti-inflammatory evaluation. Compounds 24a-24c indicated more potency than the Celecoxib. Molecular modeling studies with the help of MOE 2008.10 revealed similar binding interactions of derivatives with COX-2 as that of SC-558. The fragments with p-nitrophenyl were selectively fitted in COX-2 enzyme and revealed hydrogen bond with active site of enzyme. (34)

Alam et al synthesized hybrid pyrazole analogues and evaluated for their anti-inflammatory activity. The compounds 25a (p-methylaniline) and 25b (2-chloroaniline) exhibited 78.09% and 76.56% inhibition when compared to Ibuprofen (79.23% inhibition). These compounds were more selective towards COX-2 bearing selectivity index values of 72.73 and 65.75 which was comparable to 78.06 selective index value of Celecoxib. Molecular docking studies using Glide 7.0 XP Maestro 10.1 was performed to determine possible interactions. The SO$_2$NH$_2$ had defined their selectivity via hydrogen-bond interaction. The methylene amino group between the pyrazole and aryl ring improves flexibility and accommodated more favorably by COX-2 binding pocket. (35)

El-Feky et al reported quinoline involving pyrazole derivatives for their evaluation as anti-inflammatory agent. Compound 26 demonstrated the highest anti-inflammatory activity with less ulcerogenic liabilities. The derivative with 4-bromophenyl substituent was more active than chloro substitution owing to its higher lipophilicity. Bulky methyl group were less potent and selective towards inhibition. Substitution with lipophilic and electron withdrawing groups were able to decide selectivity towards COX-2. Molecular Operating Environment was assessed for Molecular modeling studies. Compound 26 (chloro substituted) interacted with enzyme via hydrophobic interactions and hydrogen interactions. (36)
Kamble et al synthesized thiazoles bearing pyrazoles for assessing their anti-inflammatory activity. Compound 27a-27c exhibited significant COX-II inhibition with % inhibition ranging from 66.99-78.91%. SAR revealed that COX-2 inhibition potential was enhanced by introducing electron donating substituent. Molecular docking investigation had been attempted using AutoDock 4.2. Compound 27c displayed one of the best binding energy of -11.62 kcal/mol as compare to standard Celecoxib. (37)

Somakala et al described pyrazole acetamide derivatives and assessed their in vitro and in vivo anti-inflammatory evaluation using BSA anti-denaturation and carrageenan induced rat paw edema method respectively. The most active compound 28a displayed 83.1 % inhibition which was higher than Diclofenac sodium (81.6 %) and was safe on gastric mucosa. Chloro, fluoro, and bromo groups containing derivatives were more active in comparison to standard. GLIDE version 9.8 was used for docking assessment. These compounds revealed strong interaction with the enzyme. (38)

Bansal et al prepared oxadiazoles containing pyrazole for anti-inflammatory activity with selective COX-2 inhibition. Compound 29a (NO2 derivative) was the most active COX-2 inhibitor with IC50 value of 0.31 µM. AutoDock tools 1.5.4 were utilized for molecular docking studies which revealed excellent binding affinity towards COX-2 instead of COX-1. Nitro group portrayed a critical role in COX-2 inhibition via hydrogen bonding. (39)

El-Moghazy et al developed pyrazoles containing benzenesulfonamides and were evaluated for in vivo anti-inflammatory activity. The highly active agents 30a, 30d,
and 30e were less ulcerogenic as compared to Indomethacin and Celecoxib. Electron-withdrawing group (NO$_2$) substitution at phenyl ring showed 62.67% edema inhibition, appears more promising anti-inflammatory agent than the electron-donating groups (CH$_3$, OCH$_3$) containing derivatives like 30b and 30c. Compound 30e containing 1,3,4-thiadiazole exhibited 64.93% edema inhibition. Computer-assisted docking analysis was carried out by utilizing Molecular Operating Environment software. (40)

Table 1: Summary of PDB codes, standard drugs, Docking score and SAR of reviewed derivatives

<table>
<thead>
<tr>
<th>Derivatives</th>
<th>PDB code (enzyme)</th>
<th>Functional group</th>
<th>Docking score Kcal/mol (Most active derivative)</th>
<th>Standard Drug</th>
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<tbody>
<tr>
<td>1</td>
<td>3LN1 (COX-2)</td>
<td>NO$_2$</td>
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<tr>
<td>2</td>
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<td>3</td>
<td>5WBE (COX-1)</td>
<td>Aryl, COOH, benzene sulfonamide</td>
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<tr>
<td>4</td>
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<td>Celecoxib</td>
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<tr>
<td>5</td>
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<td>OCH$_3$, Cl</td>
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<td>13</td>
<td>4Z0L (COX-2)</td>
<td>Lengthening of carbon chain, N-substitution</td>
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<td>Mofezolac (COX-1) Celecoxib</td>
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Table: 

<table>
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<tr>
<th></th>
<th>Compound</th>
<th>Structure</th>
<th>Activity</th>
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<td>SC-558 Celecoxib</td>
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<td>3LN1 (COX-2)</td>
<td>Trimethoxy derivatives with Cl, Br, CH_3, NH_2</td>
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<td>Celecoxib</td>
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<td>p-NO_2 phenyl with F</td>
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<td>SC-558</td>
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<tr>
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<td>3KK6 (COX-1) 1CVU (COX-2)</td>
<td>SO_2NH_2 with CH_3 and Cl</td>
<td>-12.907</td>
<td>Celecoxib</td>
</tr>
<tr>
<td>26</td>
<td>6COX (COX-2)</td>
<td>Cl</td>
<td>-10.26</td>
<td>Celecoxib</td>
</tr>
<tr>
<td>27</td>
<td>3NT1 (COX-2)</td>
<td>Cl, OCH_3</td>
<td>-11.62</td>
<td>Celecoxib</td>
</tr>
<tr>
<td>28</td>
<td>3D83 (p38a MAP kinase)</td>
<td>SO_2NH_-, Cl</td>
<td>-10.058</td>
<td>SB 203580</td>
</tr>
<tr>
<td>29</td>
<td>1Q4G (COX-1) 1CX2 (COX-2)</td>
<td>NO_2</td>
<td>-10.15 (COX-2)</td>
<td>Celecoxib</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-5.96 (COX-1)</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>1CX2 (COX-2)</td>
<td>NO_2</td>
<td>-10.16</td>
<td>Indomethacin Celecoxib</td>
</tr>
</tbody>
</table>

**Conclusion**

Pyrazole is an exclusive moiety accountable for anti-inflammatory activity. This article featured research efforts of numerous researchers stated in literature for anti-inflammatory compounds along with docking studies. To assess additional properties of pyrazole for inflammation, these investigations can be compared furthermore to obtain more research ideas about active derivatives against most prevalent inflammation associated diseases.

**References**


