Int. j. adv. multidisc. res. stud. 2025; 5(3):876-882

Received: 12-04-2025
Accepted: 22-05-2025

International Journal of Advanced Multidisciplinary Research and Studies

ISSN: 2583-049X

Molecular Docking Study of Ibuprofen Analogue for Anti-inflammatory and Analgesic Activity

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Abstract

Non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, are widely used for pain relief and inflammation management. However, their clinical utility is often limited by gastrointestinal side effects arising from non-selective inhibition of both COX-1 and COX-2 enzymes. To address this issue, the ibuprofen derivatives with structural modifications aimed at enhancing COX-2 and Prostaglandin E2 selectivity. The approach involved incorporating of 4-amino Pyrazole ring into the ibuprofen scaffold to modulate its binding affinity and selectivity for the COX-2 and prostaglandin active site. These modifications were guided by computational modeling, molecular docking tool that is Swiss Dock. The docking study of the novel ibuprofen derivative 4- Amino Pyrazole Ibuprofen had shown the selectivity towards Prostaglandin E2 that suggests it could bind to Cox-2 effectively and similar to ibuprofen. The ADME study of the derivative was also done through SwissADME tool and it showed less to no toxicity of the ibuprofen derivative.

Keywords: NSAIDs, Ibuprofen Derivative, Computational Modeling, Molecular Docking, SwissDock, 4-Amino Pyrazole, SwissADME

1. Introduction

Ibuprofen or 2-[4(2-methyl) propylphenyl] propionic acid is the derivative of propionic acid and associates to the paradigm of Non selective Cox inhibitors of a Non-Steroidal Anti-inflammatory Drug. It is a white crystalline powder with a molecular formula $C_{13}H_{18}O_2$ and molecular weight of 206.29g/mol [1]. It is frequently remunerations both in prescription and over the counter forms medication worldwide. The typical over the counter dosage for drugs is 200mg to 400mg every 4-6 hours with a maximum daily limit of 1200mg. For prescription strength higher doses may be recommended under medical Supervision. It is effectual for ambit of conditions including headache, muscle cramps, toothache, menstrual cramps, arthritis, minor injuries, fever reduction etc. Ibuprofen is available over-the-counter in many forms comprising tablets, capsules, liquid suspension and topical gels [2].

Ibuprofen was first discovered in the 1960s by a team of researchers at the Boots Company in the United Kingdom. It was initially marketed under the brand name Brufen and was later introduce in the United States under the brand Mortin and it was introduced in India in 1974 by Boots Pharmaceuticals under brand name Brufen [3]. Currently, it is widely available under various brand and is used to treat variety of conditions. Ibuprofen have remained a popular choice for pain and inflammation relief due to its effectiveness and availability.

Ibuprofen non-selectively inhibits both COX-1 and COX-2 enzymes. COX-1 is involved in the production of prostaglandins that protect the gastric mucosa, support kidney function, and regulate platelet aggregation. COX-2 is primarily induced during inflammation and produces prostaglandins that mediate pain and inflammatory responses. By inhibiting these enzymes, ibuprofen decreases the synthesis of prostaglandins, which are lipid compounds that play key roles in inflammation, pain signaling, and fever Regulations [4]. The decrease in prostaglandin levels leads to a reduction in sensitization of pain receptors (nociceptors), which results in diminished pain perception as well as lower levels of prostaglandins reduce vasodilation and the permeability of blood vessels, which decreases the influx of immune cells and fluid to the site of injury, thus mitigating inflammation. Ibuprofen acts on the hypothalamus to lower elevated body temperature. By inhibiting prostaglandin E2

synthesis, which is elevated during fever, ibuprofen helps restore normal thermoregulation [5]. The inhibition of COX-1 can also impact platelet aggregation since COX-1 is responsible for producing thromboxane A2, a promoter of platelet aggregation. This can lead to a temporary anti-platelet effect [6].

2. Material and Methods

2.1 Chemical sketch tool

The molecular design of the ibuprofen analogue was created using a Chemical SketchTool, a specialized software application used for drawing, editing, and visualizing molecular structures [7]. This tool enables researchers to construct complex molecular frameworks, perform basic molecular modeling, and generate SMILES (Simplified Molecular InputLine Entry System) notation for further computational analyses [8].

The advancedutilizition of sketching software such as ChemSketch,orChemDraw, the chemical structure was refined to maintain steric stability and ensure proper functional group positioning. The final SMILES format was generated, allowing seamless incorporation into computational tools for target prediction, docking simulations, and ADME profiling [9, 10].

2.2 Molecular target prediction

The identification of a biological target was conducted using Swiss Target Prediction, a free and widely used online web server. This tool predicts potential protein receptors based on ligand similarity analysis, evaluating molecular fingerprints against a database of known active compounds.

2.3 Molecular docking

Molecular docking was performed to determine binding affinity and stability between the designed ibuprofen analogue and the selected protein target [11, 12]. The docking simulation was conducted using SwissDock, a freely accessible computational docking server.

Docking Workflow:

Protein Target Selection:

- The 3D crystal structure of the selected target protein was retrieved from the Protein Data Bank (PDB).

Ligand Preparation:

- The SMILES notation of the ibuprofen analogue was converted into PDB format using RCSB PDB, ensuring proper conformational representation [13,14].

2.4 ADMEstudy

To assess the drug-likeness, pharmacokinetics, and toxicity of the designed ibuprofen analogue, an Absorption, Distribution, Metabolism, and Excretion (ADME) study was conducted using SwissADME, a specialized web server for evaluating pharmaceutical properties.

Parameters Evaluated in the ADME Study [15, 16, 17, 18]:

Physicochemical Properties:

- Molecular weight, polarity, and hydrogen bonding capacity.

Lipophilicity & Solubility:

- LogP values were calculated to evaluate hydrophobic interactions and bioavailability.

Drug Toxicity & Metabolism Predictions:

- Possible metabolic pathways, hepatic metabolism, and potential toxicological risks were determined.

Bioavailability & Pharmacokinetics:

- Intestinal absorption, blood-brain barrier permeability, and plasma protein binding were analyzed to predict biological distribution.

This study validated the pharmacological feasibility of the ibuprofen analogue, ensuring its suitability for anti-inflammatory and analgesic applications.

3. Result and Dicussion

3.1 Chemical Structure of Ibuprofen analogue

The newly designed ibuprofen analogue contain chemical structure in the format of Smiles: CC(C)CN1C=C(N)C(=N1)C(C)C(O)=O was drawn. The structure of ibuprofen analogue was designed with the help of Chemical Sketch Tool and Chemically known as4-amino,1-iso-butyl-3-propionic acid.

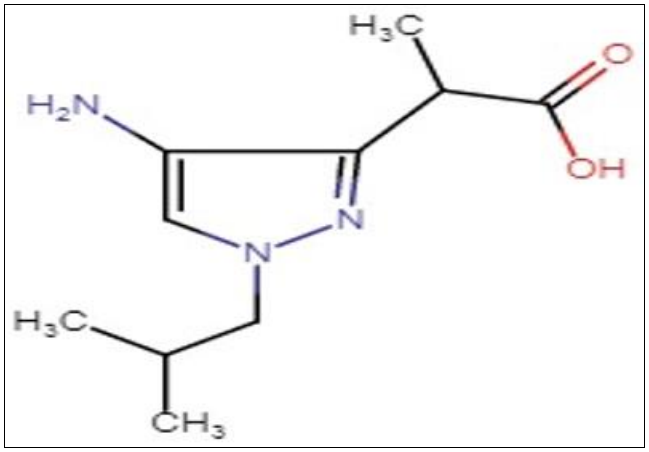

Fig 3.1: Ibuprofen Analogue

3.2 Molecular SwissADME Study

The Swiss ADME tool suggest that the ibuprofen has improved physiochemical properties and binding affinity to the COX-2 enzyme compared to ibuprofen.

Table 3.1: SwissADME Reading

Property	Entry 1
Molecule	Molecule 1
Canonical SMILES	CC(Cn1cc(c(n1)C(C(=O)O)C)N)C
Formula	C10H17N3O2
MW	211.26
#Heavy atoms	15
#Aromatic heavy atoms	5
Fraction Csp3	0.6
#Rotatable bonds	4
#H-bond acceptors	3
#H-bond donors	2
MR	58.67
TPSA	81.14
iLOGP	1.1
XLOGP3	0.89
WLOGP	1.32
MLOGP	0.46
Silicos-IT Log P	0.37
Consensus Log P	0.83
ESOL Log S	-1.69
ESOL Solubility (mg/ml)	4.28
ESOL Solubility (mol/l)	0.0203
ESOL Class	Very soluble
Ali Log S	-2.18
Ali Solubility (mg/ml)	1.4
Ali Solubility (mol/l)	0.00663

Ali Class	Soluble
Silicos-IT LogSw	-1.09
Silicos-IT Solubility (mg/ml)	17
Silicos-IT Solubility (mol/l)	0.0804
Silicos-IT class	Soluble
GI absorption	High
BBB permeant	No
Pgp substrate	No
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	No
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
log Kp (cm/s)	-6.96
Lipinski #violations	0
Ghose #violations	0
Veber #violations	0
Egan #violations	0
Muegge #violations	0
Bioavailability Score	0.56
PAINS #alerts	0
Brenk #alerts	0
Leadlikeness #violations	1
Synthetic Accessibility	2.86

The given information in the above have been plotted in the graph known as Egg boiled Plot. The yellow spot on the egg plot shows BBB permeation, the white portion shows high absorption and the small pink dot shows the metabolism by PGP [19, 20, 21].

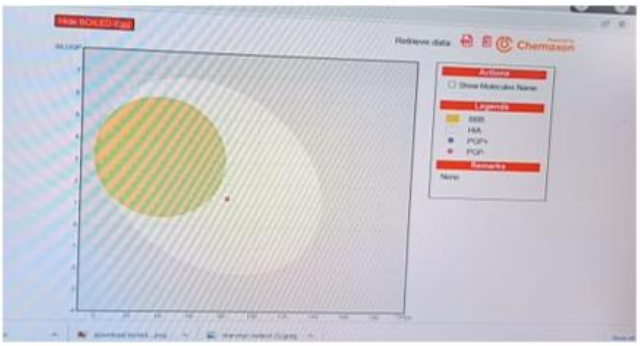

Fig 3.2: Egg Boiled Plot Graph

3.3 Molecular Docking

This ligand binds favorably with the target, given strong negative AC scores.

The best docking pose is in Cluster 0 with -49.18 kcal/mol, indicating a potentially stable binding conformation. Ibuprofen primarily inhibits COX-2 and COX-1 enzymes (cyclooxygenases), which are involved in inflammation and pain [22, 23, 24].

The docking target: 4yk5.pdb — this is COX-2 enzyme crystal structure.

Docking score: The ligand that is ibuprofen analogue binds strongly (AC Score: -49.18 kcal/mol)— this suggests it could bind to COX-2 effectively and similar to ibuprofen, indicating it likely has similar

action — i.e., COX-2 inhibition — based on docking.

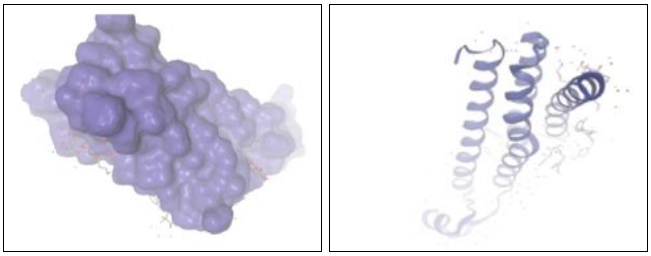

Fig 3.3: Molecular docking of ligand with ibuprofen Analogue

Table 3.2: Molecular Docking Reading

Cluster Number	Cluster Member	AC Score	SwissParam Score
0	1	-49.179713	-6.1374
1	1	-48.417977	-5.9442
2	1	-46.48387	-5.8039
3	1	-46.318288	-5.8918
4	1	-45.552381	-5.7535
5	1	-45.501437	-5.715
6	1	-44.614507	-5.5673
7	1	-44.513546	-5.7119
8	1	-44.365733	-6.0092
9	1	-44.189822	-5.7706
10	1	-43.913579	-5.597
11	1	-43.913014	-5.5921
12	1	-43.845946	-5.7995
13	1	-43.688575	-5.6151
14	1	-43.436508	-5.4537
15	1	-43.289696	-5.4421
16	1	-43.144749	-5.4107
17	1	-43.115971	-5.6022
18	1	-42.402098	-5.573
19	1	-42.366128	-5.6435
20	1	-42.23073	-5.5195
21	1	-42.059693	-5.4155
22	1	-41.991886	-5.4318
23	1	-41.921926	-5.5922
24	1	-41.833661	-5.5192
25	1	-41.653241	-5.4659
26	1	-41.567252	-5.5569
27	1	-41.365256	-5.754
28	1	-41.187652	-5.5337
29	1	-41.079586	-5.3959
30	1	-40.951013	-5.4254
31	1	-40.763235	-5.429
32	1	-40.587545	-5.2757
33	1	-40.3945	-5.2006
34	1	-39.951913	-5.3591
35	1	-39.770608	-5.4033
36	1	-39.687038	-5.1237
37	1	-39.49699	-5.3765
38	1	-39.12549	-5.3755
39	1	-39.002681	-5.4804
40	1	-39.002622	-5.2608
41	1	-38.441447	-5.2959
42	1	-38.375825	-5.2997
43	1	-38.372575	-5.1397
44	1	-38.314981	-5.0448
45	1	-38.219043	-5.2292
46	1	-37.903385	-5.1137
47	1	-37.545763	-5.1194
48	1	-37.29522	-4.8215
49	1	-37.169806	-5.2122

3.4 Molecular target Prediction

The target prediction study of Ibuprofen Analogue (4-amino,1-iso-butyl-3-propionic acid) was done to know its bestest target site by Molecular Docking Study tool s i.e, Swiss Target Prediction. The outcome of the analogue shows an average probability with cyclooxygenase target of oxidoreductase target class [21, 22, 23, 24].

Table 3.3: Molecular Target Prediction Result

SwissTargetPrediction	Unnamed: 1	Unnamed: 2	Unnamed: 3	Unnamed: 4	Unnamed: 5	Unnamed: 6
Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Solute carrier family 22 member 12	SLC22A12	Q96S37	CHEMBL6120	Electrochemical transporter	0.0626219668353	72/43
Aldose reductase	AKR1B1	P15121	CHEMBL1900	Enzyme	0.0535560755162	186/54
Cytochrome P450 19A1	CYP19A1	P11511	CHEMBL1978	Cytochrome P450	0.0535560755162	1/0
Thromboxane A2 receptor	TBXA2R	P21731	CHEMBL2069	Family A G protein-coupled receptor	0.0535560755162	118/0
Cyclooxygenase-1	PTGS1	P23219	CHEMBL221	Oxidoreductase	0.0535560755162	43/0
Cyclooxygenase-2	PTGS2	P35354	CHEMBL230	Oxidoreductase	0.0535560755162	111/0
Interleukin-8	CXCL8	P10145	CHEMBL2157	Secreted protein	0.0535560755162	12/0
Solute carrier family 22 member 6 (by homology)	SLC22A6	Q4U2R8	CHEMBL1641347	Electrochemical transporter	0.0535560755162	2/0
Fatty acid binding protein adipocyte	FABP4	P15090	CHEMBL2083	Fatty acid binding protein family	0.0535560755162	44/0
Fatty acid binding protein epidermal	FABP5	Q01469	CHEMBL3674	Fatty acid binding protein family	0.0535560755162	4/0
Transthyretin	TTR	P02766	CHEMBL3194	Secreted protein	0.0535560755162	8/0
Fatty acid binding protein muscle	FABP3	P05413	CHEMBL3344	Fatty acid binding protein family	0.0535560755162	11/0
Fatty acid-binding protein, liver (by homology)	FABP1	P07148	CHEMBL5421	Fatty acid binding protein family	0.0535560755162	4/0
Branched-chain-amino-acid aminotransferase, mitochondrial	BCAT2	O15382	CHEMBL3616354	Transferase	0.0535560755162	2/0
Peroxisome proliferator-activated receptor alpha	PPARA	Q07869	CHEMBL239	Nuclear receptor	0.0535560755162	84/0
Thromboxane-A synthase	TBXAS1	P24557	CHEMBL1835	Cytochrome P450	0.0535560755162	146/0
Aldo-keto-reductase family 1 member C3	AKR1C3	P42330	CHEMBL4681	Enzyme	0.0535560755162	134/0
Thyroid hormone receptor alpha	THRA	P10827	CHEMBL1860	Nuclear receptor	0.0535560755162	13/0
Thyroid hormone receptor beta-1	THRB	P10828	CHEMBL1947	Nuclear receptor	0.0535560755162	16/0
11-beta-hydroxysteroid dehydrogenase 1	HSD11B1	P28845	CHEMBL4235	Enzyme	0.0535560755162	35/0
Neprilysin (by homology)	MME	P08473	CHEMBL1944	Protease	0.0535560755162	138/0
Prostanoid EP2 receptor	PTGER2	P43116	CHEMBL1881	Family A G protein-coupled receptor	0.0535560755162	22/0
Glutathione reductase	GSR	P00390	CHEMBL2755	Oxidoreductase	0.0535560755162	2/0
Kynurenine 3-monooxygenase (by homology)	KMO	O15229	CHEMBL2145	Oxidoreductase	0.0535560755162	13/0
Aldo-keto reductase family 1 member B10 (by homology)	AKR1B10	O60218	CHEMBL5983	Enzyme	0.0535560755162	15/0
Gamma-amino-N-butyrate transaminase (by homology)	ABAT	P80404	CHEMBL2044	Transferase	0.0535560755162	4/0
Steroid 5-alpha-reductase 1	SRD5A1	P18405	CHEMBL1787	Oxidoreductase	0.0535560755162	9/0
Steroid 5-alpha-reductase 2	SRD5A2	P31213	CHEMBL1856	Oxidoreductase	0.0535560755162	14/0
Angiotensin-converting enzyme (by homology)	ACE	P12821	CHEMBL1808	Protease	0.0535560755162	186/0
Macrophage migration inhibitory factor	MIF	P14174	CHEMBL2085	Enzyme	0.0535560755162	2/0
Casein kinase II alpha	CSNK2A1	P68400	CHEMBL3629	Kinase	0.0535560755162	51/0
Casein kinase II alpha (prime)	CSNK2A2	P19784	CHEMBL4070	Kinase	0.0535560755162	7/0
Endothelin receptor ET-A (by homology)	EDNRA	P25101	CHEMBL252	Family A G protein-coupled receptor	0.0535560755162	72/0
Free fatty acid receptor 1	FFAR1	O14842	CHEMBL4422	Family A G protein-coupled receptor	0.0535560755162	56/0
Androgen Receptor	AR	P10275	CHEMBL1871	Nuclear receptor	0.0535560755162	2/0

Mineralocorticoid receptor	NR3C2	P08235	CHEMBL1994	Nuclear receptor	0.0535560755162	1/0
Progesterone receptor	PGR	P06401	CHEMBL208	Nuclear receptor	0.0535560755162	3/0
Dual specificity protein phosphatase 3	DUSP3	P51452	CHEMBL2635	Phosphatase	0.0535560755162	4/0
3-phosphoinositide dependent protein kinase-1	PDPK1	O15530	CHEMBL2534	Kinase	0.0535560755162	3/0
Prostanoid EP1 receptor	PTGER1	P34995	CHEMBL1811	Family A G protein-coupled receptor	0.0535560755162	214/0
Inosine-5'-monophosphate dehydrogenase 2	IMPDH2	P12268	CHEMBL2002	Oxidoreductase	0.0535560755162	12/0
Plasma retinol-binding protein	RBP4	P02753	CHEMBL3100	Secreted protein	0.0535560755162	19/0
Integrin alpha2/beta1	ITGB1 ITGA2	P05556 P17301	CHEMBL3137268	Unclassified protein	0.0535560755162	28/0
Intercellular adhesion molecule (ICAM-1), Integrin alpha-L/beta-2	ITGAL ICAM1 ITGB2	P20701 P05362 P05107	CHEMBL2096661	Membrane receptor	0.0535560755162	24/0
Nuclear receptor subfamily 4 group A member 1	NR4A1	P22736	CHEMBL1293229	Nuclear receptor	0.0535560755162	7/0
Heat shock 70 kDa protein 1	HSPA1A	P0DMV8	CHEMBL5460	Other cytosolic protein	0.0535560755162	8/0
Aldo-keto reductase family 1 member C1	AKR1C1	Q04828	CHEMBL5905	Enzyme	0.0535560755162	10/0
Lysosomal protective protein	CTSA	P10619	CHEMBL6115	Protease	0.0535560755162	84/0
D-amino-acid oxidase	DAO	P14920	CHEMBL5485	Enzyme	0.0535560755162	16/0
Aldo-keto reductase family 1 member C2	AKR1C2	P52895	CHEMBL5847	Enzyme	0.0535560755162	46/0
Prostanoid EP4 receptor	PTGER4	P35408	CHEMBL1836	Family A G protein-coupled receptor	0.0535560755162	21/0
Prostanoid EP3 receptor	PTGER3	P43115	CHEMBL3710	Family A G protein-coupled receptor	0.0535560755162	12/0
Serine/threonine protein phosphatase PP1-alpha catalytic subunit	PPP1CA	P62136	CHEMBL2164	Phosphatase	0.0535560755162	6/0
DNA topoisomerase I	TOP1	P11387	CHEMBL1781	Isomerase	0.0535560755162	2/0
Prostanoid IP receptor	PTGIR	P43119	CHEMBL1995	Family A G protein-coupled receptor	0.0535560755162	2/0
Replication protein A 70 kDa DNA-binding subunit	RPA1	P27694	CHEMBL1764940	Unclassified protein	0.0535560755162	12/0
G-protein coupled receptor kinase 2	GRK2	P25098	CHEMBL4079	Kinase	0.0535560755162	2/0
Muscarinic acetylcholine receptor M1	CHRM1	P11229	CHEMBL216	Family A G protein-coupled receptor	0.0535560755162	4/0
Heat shock protein HSP 90-alpha	HSP90AA1	P07900	CHEMBL3880	Other cytosolic protein	0.0535560755162	3/0
Neurotensin receptor 1	NTSR1	P30989	CHEMBL4123	Family A G protein-coupled receptor	0.0535560755162	2/0
Induced myeloid leukemia cell differentiation protein Mcl-1	MCL1	Q07820	CHEMBL4361	Other cytosolic protein	0.0535560755162	28/0
C-C chemokine receptor type 2	CCR2	P41597	CHEMBL4015	Family A G protein-coupled receptor	0.0535560755162	48/0
Estrogen receptor beta	ESR2	Q92731	CHEMBL242	Nuclear receptor	0.0535560755162	7/0
Matrix metalloproteinase 2	MMP2	P08253	CHEMBL333	Protease	0.0535560755162	21/0
p53-binding protein Mdm-2	MDM2	Q00987	CHEMBL5023	Other nuclear protein	0.0535560755162	30/0
Lysine-specific demethylase 4C	KDM4C	Q9H3R0	CHEMBL6175	Eraser	0.0535560755162	29/0
Angiotensin II receptor	AGTR2	P50052	CHEMBL4607	Family A G protein-coupled receptor	0.0535560755162	4/0
c-Jun N-terminal kinase 3	MAPK10	P53779	CHEMBL2637	Kinase	0.0535560755162	2/0
Phosphodiesterase 10A	PDE10A	Q9Y233	CHEMBL4409	Phosphodiesterase	0.0535560755162	2/0
Carbonic anhydrase II	CA2	P00918	CHEMBL205	Lyase	0.0535560755162	36/0
Carbonic anhydrase I	CA1	P00915	CHEMBL261	Lyase	0.0535560755162	31/0
Carbonic anhydrase XII	CA12	O43570	CHEMBL3242	Lyase	0.0535560755162	19/0
Carbonic anhydrase IX	CA9	Q16790	CHEMBL3594	Lyase	0.0535560755162	20/0
Receptor-type tyrosine-protein phosphatase gamma	PTPRG	P23470	CHEMBL4905	Phosphatase	0.0535560755162	3/0
Aminoacyl-tRNA synthetase	EPRS	P07814	CHEMBL3873	Enzyme	0.0535560755162	1/0
Lysine-specific demethylase	KDM5A	P29375	CHEMBL2424504	Eraser	0.0535560755162	6/0

5A						
Matrix metalloproteinase 13	MMP13	P45452	CHEMBL280	Protease	0.0535560755162	13/0
Matrix metalloproteinase 9	MMP9	P14780	CHEMBL321	Protease	0.0535560755162	16/0
Squalene synthetase (by homology)	FDFT1	P37268	CHEMBL3338	Enzyme	0.0535560755162	9/0
Lysine-specific demethylase 5B	KDM5B	Q9UGL1	CHEMBL3774295	Eraser	0.0535560755162	6/0
Matrix metalloproteinase 8	MMP8	P22894	CHEMBL4588	Protease	0.0535560755162	14/0
Endothelin-converting enzyme 1	ECE1	P42892	CHEMBL4791	Protease	0.0535560755162	11/0
AMP deaminase 3	AMPD3	Q01432	CHEMBL2912	Enzyme	0.0535560755162	1/0
PI3-kinase p110-alpha subunit	PIK3CA	P42336	CHEMBL4005	Enzyme	0.0535560755162	10/0
Hydroxycarboxylic acid receptor 2	HCAR2	Q8TDS4	CHEMBL3785	Family A G protein-coupled receptor	0	13/0
Matrix metalloproteinase 12	MMP12	P39900	CHEMBL4393	Protease	0	10/0
Intercellular adhesion molecule-1	ICAM1	P05362	CHEMBL3070	Adhesion	0	1/0
Selectin E	SELE	P16581	CHEMBL3890	Adhesion	0	1/0
Hydroxyacid oxidase 1	HAO1	Q9UJM8	CHEMBL4229	Enzyme	0	5/0
Vitronectin receptor alpha	ITGAV	P06756	CHEMBL3660	Membrane receptor	0	21/0
Serine/threonine-protein phosphatase	PPP5C	Q9BPW0	CHEMBL1293265	Phosphatase	0	2/0
Glutamate carboxypeptidase II	FOLH1	Q04609	CHEMBL1892	Protease	0	13/0
Cytochrome P450 26B1	CYP26B1	Q9NR63	CHEMBL3713687	Cytochrome P450	0	2/0
Cytochrome P450 26A1	CYP26A1	O43174	CHEMBL5141	Cytochrome P450	0	6/0
Leukotriene B4 receptor 1	LTB4R	Q15722	CHEMBL3911	Family A G protein-coupled receptor	0	3/0
Peptidyl-prolyl cis-trans isomerase NIMA-interacting 1	PIN1	Q13526	CHEMBL2288	Enzyme	0	22/0
Hematopoietic cell protein-tyrosine phosphatase 70Z-PEP	PTPN22	Q9Y2R2	CHEMBL2889	Phosphatase	0	1/0
G protein-coupled receptor 44	PTGDR2	Q9Y5Y4	CHEMBL5071	Family A G protein-coupled receptor	0	527/7

4. Future Aspects

In future we are Looking for Development of scheme and the synthesis of the 4-Amino Pyrazole ibuprofen analogue and will have further structural characterization and biological study

5. Conclusion

The 4-Amino Pyrazole-Ibuprofen, a novel ibuprofen analogue, was designed to retain the anti-inflammatory and analgesic properties of ibuprofen while potentially exhibiting improved pharmacokinetic and pharmacodynamic profiles. The introduction of a pyrazole ring in place of the benzene ring in ibuprofen provides a new scaffold for anti-inflammatory activity. The presence of an amino group at the 4-position of the pyrazole ring may enhance the compound's ability to interact with biological targets. The ibuprofen moiety, including the propionic acid group, is retained in the analogue, ensuring that the compound maintains its anti-inflammatory and analgesic properties.

The modified pyrazole ring and amino group may enhance the compound's ability to inhibit inflammatory mediators. The retained ibuprofen moiety and modified pyrazole ring may contribute to improved analgesic activity. The introduction of the pyrazole ring and amino group may improve the compound's solubility, permeability, and bioavailability.

The compound will further be evaluated in various *in vitro* and *in vivo* models to assess its anti-inflammatory and analgesic activities. SAR studies will be conducted to optimize the compound's structure and improve its pharmacological properties.The compound can be developed further through preclinical and clinical trials to assess its safety, efficacy, and potential as a therapeutic agent.The pyrazole ring in 4-Amino Pyrazole-Ibuprofen may contribute to COX-2 selectivity, as it provides a unique binding interaction with the prostaglandin enzyme.The amino group at the 4-position of the pyrazole ring may also play a role in COX-2 selectivity, as it may participate in hydrogen bonding interactions with the prostaglandin enzyme. The newely ibuprofen analogue i.e, 4-Amino Pyrazole-Ibuprofen will be effective in treating inflammatory diseases such as arthritis, rheumatism, and other conditions.The compound will be useful in managing pain associated with inflammation, injury, or surgery. The anti-inflammatory and analgesic properties of 4-Amino Pyrazole-Ibuprofen may make it a useful adjunct in cancer treatment. It will have a better safety profile compared to existing NSAIDs, with reduced risk of gastrointestinal side effects and may exhibit improved anti-inflammatory and analgesic efficacy compared to existing NSAIDs. 4-Amino Pyrazole-Ibuprofen may be more potent than existing NSAIDs, requiring lower doses to achieve therapeutic effects.

6. Acknowledgement

The authors thankful to Rungta Institute of Pharmaceutical Sciences and Research, Bhilai, Chhattisgarh and Rungta

Institute of Pharmaceutical Science, Bhilai, Chhattisgarh for providing necessary facilities and database

7. Conflict of Interest

The authors declare that no conflict of interest of any financial or other issues.

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