RESEARCH ARTICLE

Biomedicus: J. Biol. Biomed. Front., 1: 39-49, 2026

BIOMEDICUS
Journal of Biological &
Biomedical Frontiers

TSSBR

Repositioning of FDA Approved NSAIDs for Potential STAT3 Inhibitors: A Molecular Docking Study

Zainab Ahsan[1], Erum Zafar[1], Ayesha Qasim[2], Aisha Jamshed[3], Mouzma Amjad[3] and Muhammad Khan[1]*

[1]Cancer Research Lab, Institute of Zoology, University of the Punjab, Quaid-e-Azam Campus, Lahore 54590, Pakistan
[2]Department of Zoology, University of Okara, Okara, Pakistan
[3]Department of Biological Sciences, Virtual University of Pakistan, 52200, Pakistan

Zainab Ahsan and Erum Zafar contributed equally to this study.

ABSTRACT

Signal transducer and activator of transcription 3 is a latent transcription factor involved in various cellular processes, cell proliferation, apoptosis, inflammation, immunity, angiogenesis, and metastasis. Controlled regulation of STAT3 activity is maintained in normal cells, but its sustained activation causes tumor growth and carcinogenesis. This computational study aims to elucidate the potential of FDA-approved non-steroidal anti-inflammatory drugs in inhibiting STAT3. Molecular Docking was performed using AutoDock and visualized through LigPlot+ and Biovia Discovery Studio Visualizer. The findings demonstrate that NSAIDs, including ibuprofen, naproxen, diclofenac, celecoxib, mefenamic acid, etoricoxib, indomethacin, and aspirin, exhibit substantial binding affinity with STAT3 monomers. The binding energies calculated are -5.6 to 7.5 kcal/mol, with inhibition constants from 7.5 to 3.03μM, respectively. Notably, key amino acid residues such as GLN326, HIS457, LYS244, PRO487, ARG335, ASP566, CYS468, PRO471, LYS383, LEU378, VAL323, THR456, LYS318, GLU455, ASP570, LYS573, CYS251, TRP474, PRO336, ASP334, SER403, ILE258, ARG325, LYS348, ARG350, and GLU324 are identified as pivotal in mediating the interaction between NSAIDs and STAT3. This study provides valuable insights into the molecular interactions between FDA-approved NSAIDs and STAT3, offering a foundation for further exploration of their potential as therapeutic agents in the context of STAT3-mediated diseases.

KEY WORDS: FDA-approved drugs, Molecular docking, NSAIDs, STAT3, Anticancer, Drug discovery

INTRODUCTION

Signal transducer and activator of transcription 3 (STAT3) is a member of the cytoplasmic transcription factor family known for signal transduction and activation of transcription, which includes seven members: STAT1, STAT2, STAT3, STAT4, STAT5a, STAT5b, and STAT6[1]. STAT1 has structural similarity to STAT3 and STAT5, and primarily functions as an oncogene[2]. Particularly, STAT3 is a DNA-binding protein that ultimately regulates the essential genes like cell proliferation, metastasis, differentiation, apoptosis, immune responses, angiogenesis, nephrogenesis, gliogenesis, inflammation, and hepatogenesis[3]. STAT3, being a pleiotropic protein, activates different gene sets in response to different stimuli like growth factors, cytokines (such as IL-6 and IL-12), and oncogenes[4].

STAT3 resides on chromosome 17q21, has structural similarity to other members of the STAT family. It consists of six domains: N-terminal (ND) with a coiled-coil domain (CCD), linker domain, SH2 domain, transcriptional activation domain (TAD), and DNA-binding domain (DBD). The CCD is essential for nuclear localization signals and protein interactions[5]. In resting cells, STAT3 is in an inactive state and is activated via many pathways, such as receptor tyrosine kinases (e.g., PDGFR, EGFR) and non-receptor tyrosine kinases (e.g., Abl, Src)[6]. The most crucial pathway that regulates STAT3 activity is the Janus kinase STAT pathway involving key regulators JAK1, JAK2, and Tyk2. This pathway is activated via extracellular ligand

*Corresponding author: mkhan.zool@pu.edu.pk
Received 14 December 2025; Revised 05 January 2026; Accepted 27 January 2026; Published 25 Junr 2026

interactions with transmembrane receptors, ultimately leading to various transcriptional mechanisms independent of second messengers[7]. STAT3 becomes activated through phosphorylation at a specific tyrosine residue (Tyr 705) in response to the attached stimuli involving the common signal-transducing subunit (gp130), which primes the activation of STAT3 and RAS/MAP kinase pathways[8]. The dimer STAT3 then moves into the nucleus, serving as a transcription activator for various target genes[9]. Usually, STAT3 deactivates within an hour due to the action of various cellular regulators, leading to dephosphorylation and translocation back into the cytoplasm[10].

Nonsteroidal anti-inflammatory drugs (NSAIDs) include a varied group of drugs that share a common mode of action. They are commonly recommended for fever, inflammation, and pain, and account for a noteworthy percentage of annual drug prescriptions among individuals aged 60 and above[11,12]. NSAIDs include widely used medications like naproxen, aspirin, paracetamol, indomethacin, mefenamic acid, ibuprofen, diclofenac, and celecoxib. Aspirin is often used in low doses for cardiovascular and cerebrovascular conditions[13]. NSAIDs are antipyretic and analgesic, used worldwide to lessen many pain conditions, from headaches to osteoarthritis. NSAIDs can be administered alone or in conjunction with opioids for severe pain management[14,15] (Fig. 1).

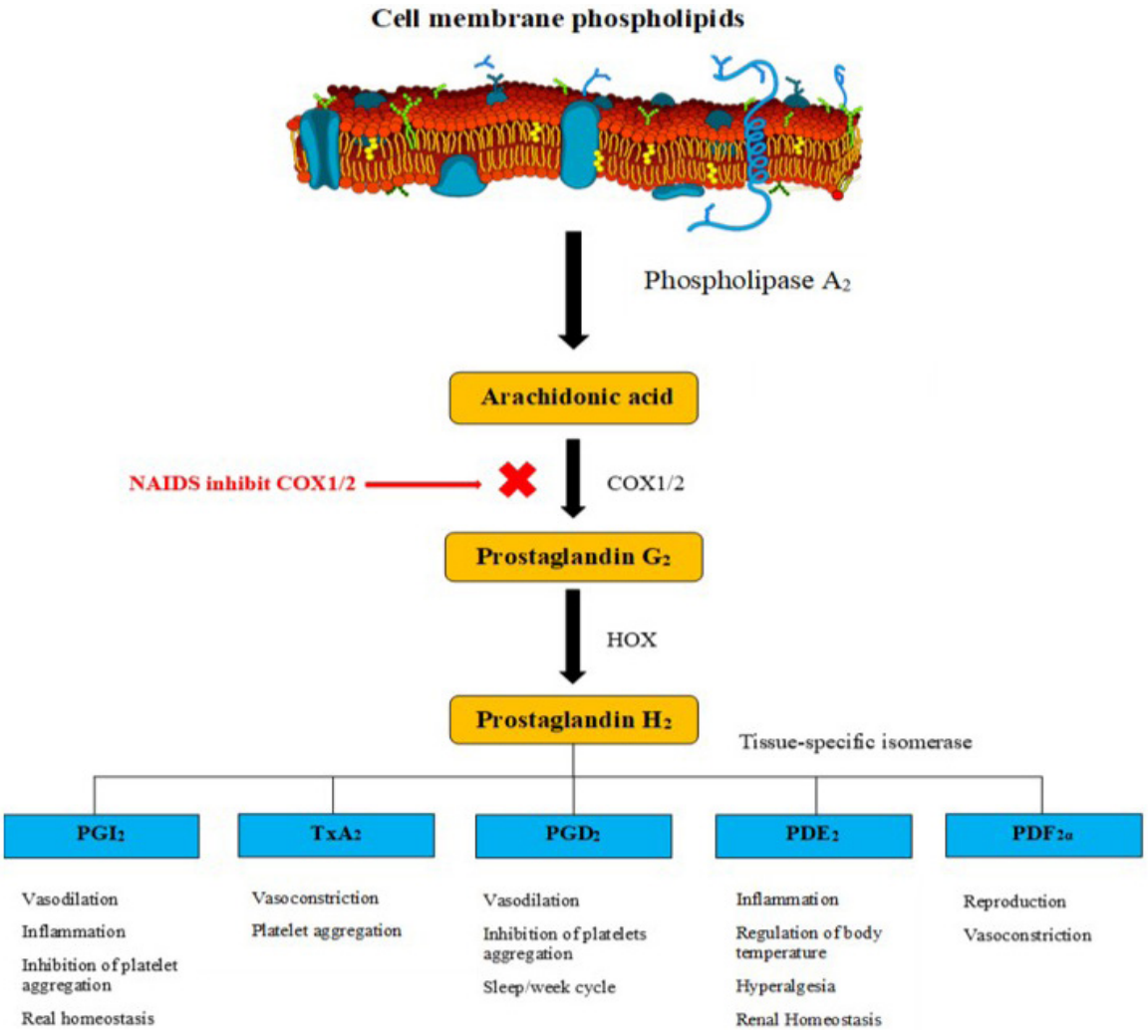

Fig. 1. Mechanism of action of NSAIDs. Arachidonic acid is released from cell membrane phospholipids by phospholipase A_2. It is then converted by cyclooxygenase enzymes (COX-1 and/or COX-2) to the unstable intermediate prostaglandin H_2 (PGH_2) via prostaglandin G_2. PGH_2 serves as the common precursor for tissue-specific prostanoids.

Molecular docking is an advanced technique used to place three-dimensional small ligands at receptor active sites in different orientations. It relies on the concept of induced fit, where successful binding is contingent on the complementary shapes and matching energy profiles of ligands and proteins[16]. In this current computational investigation, our main objective is to undertake the repurposing of nonsteroidal anti-inflammatory drugs (NSAIDs) as potential inhibitors of STAT3.

MATERIALS AND METHODS

In this study, a molecular docking tool was used for analyzing the interactions between STAT-3 and FDA-approved NSAIDs. The software tools used included Auto-Dock MGL Tools (https://ccsb.scripps.edu/mgltools/downloads/), Auto-Dock vina (https://ccsb.scripps.edu/mgltools/downloads/), PyMOL (https://www.pymol.org/), Discovery Studio Visualizer 2.5 (https://discover.3ds.com/discovery-studio-visualizer-download), and Ligplot+ 4.5.3 (https://www.ebi.ac.uk/thornton-srv/software/LigPlus/download.html).

Protein preparation

STAT3β/DNA complex (PDB code 1BG1) crystalline structure was taken from the Protein Data Bank (PDB) under Research Collaboratory for Structural Bioinformatics (RCSB). Pre-existing ligands and molecules of water were detached, and then polar hydrogens and Kollman charges were added using the tool AutoDock Vina. CASTp server (http://sts.bioe.uic.edu/) is a tool to predict the catalytic site, and it was used for STAT-3 protein's binding pockets and cavities predictions[17].

Ligand preparation

Eight FDA-approved three-dimensional structures of studied NSAIDs were taken from the online PubChem database in the format of a structure-data file (SDF). These .sdf format of the ligands were then converted to PDB format using PyMOL and then to PDBQT format using Auto-Dock MGL tools. Discovery Studio Visualizer (DSV) was used to visualize the PDBQT format of these structures.

Docking and visualization

For the grid box and docking parameter file formation, AutoDock Vina was used. Docking analysis viewed all ligand bonds as rotatable and the protein molecule as rigid. A grid box of 40 × 40 × 40Å was used with center at the coordinates of 115.415, 87.292, and 31.356 for X, Y, and Z. The binding site of 1BG1 was docked with each ligand, and for ligand nine, poses were generated, and the finest pose with the lowest binding energy was taken for further analysis. DSV was used to visualize the docking results, and for complexes with the lowest binding energy, Ligplot diagrams were generated.

Estimation of drug likeness

SwissADME server (http://www.swissadme.ch/) assessed the pharmacokinetics, including absorption, distribution, metabolism, and excretion of ligands[18]. With the help of the candidate drug's canonical SMILES drug-likeness were evaluated based on Lipinski's Rule of Five, Egan, Ghose, Muegge's and Veber rules. For further ADMET predictions, the ADMETsar server (http://lmmd.ecust.edu.cn/admetsar2) was also used.

Prediction of toxicity

For the prediction of toxicity, the canonical SMILES of NSAIDs were retrieved from PubChem, and then using the pkCSM server (http://biosig.unimelb.edu.au/pkcsm/prediction), different levels of toxicity were predicted, such as cytochrome inhibition, skin sensitivity, and hepatotoxicity[19].

RESULTS

In the proliferation of cells, apoptosis, and response of the immune system, STAT3 plays a very important role. The prepared protein and ligand was docked and pharmacokinetics were assessed via online tools (Fig. 2).

The STAT3 (PDB ID: 1BG1) 3D structure contains 296 amino acids. In STAT3, 88 binding pockets are identified by CASTp, being a key target, pocket 2 which contains 22 residues, i.e. MET331, HIS332, PRO333, ASP334, ARG335, ILE467, CYS468, MET470, PRO471, ASN472, TRP474, THR515, VAL563, ASP566, ASN567, ILE569, ASP570, LYS573, LYS574, LYS615, GLU616, LYS642 (Fig. 3). The binding energies, inhibition constants, along binding interactions of all the complexes are given in Table I.

Binding energies and interactions

Both Ibuprofen and Aspirin efficiently bind with STAT3, with -5.6 kcal/mol binding energies and 7.5μM inhibition constants. Ibuprofen forms hydrogen bonding with GLU455 and different hydrophobic interactions with LEU378, HIS437, and LEU438. Aspirin forms hydrogen bonds with ARG335, ASP566, and LYS573, along with hydrophobic interactions with ILE467 and PRO471 (Fig. 4).

Naproxen in complex with 1BG1 showed -6.8 kcal/mol binding energy and 3.82μM inhibition constant. It forms hydrogen bonding with PHE321, LYS244, and hydrophobic interactions with PRO487 and LEU459 (Table I). Diclofenac, mefenamic acid, and etoricoxib all exhibit -6.8 kcal/mol binding energies and 3.82μM inhibition constants (Fig. 4). Diclofenac forms hydrogen bonding with HIS332 and hydrophobic interactions with ILE467 and MET470.

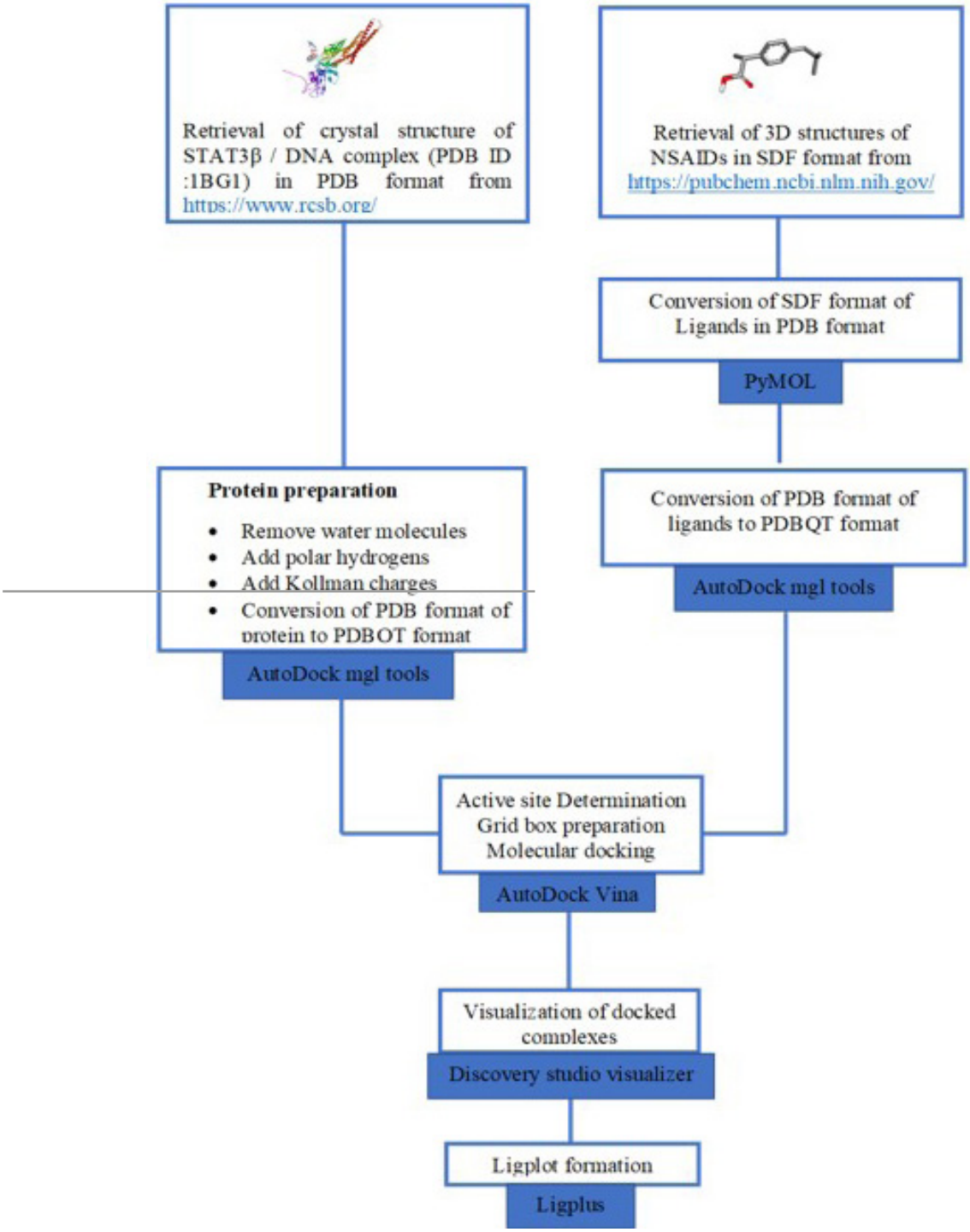

Fig. 2. Summary of docking analysis. Protein (STAT3β/DNA complex, PDB: 1BG1) and ligand preparation and conversion to PDBQT format was performed using AutoDock tools and PyMOL. Docking performed with AutoDock Vina; complexes visualized in Discovery Studio Visualizer and interactions plotted using LigPlot+.

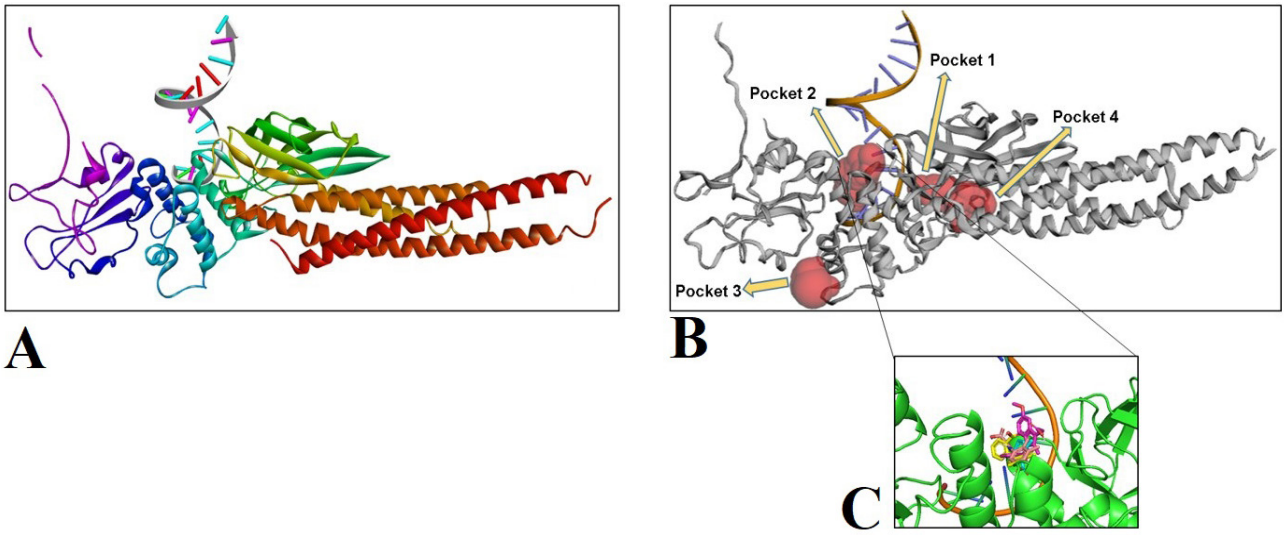

Fig. 3. Structure of STAT3 (1BG1). (A) 3-D geometry obtained using DSV software and online CASTp. (B) It showed the binding cavities and domains within pocket number 1, 2, 3, and 4 are expressed in red color. (C) All the studied ligands showed binding to the binding pocket number 2.

Table I. NSAIDs in complex with STAT3 showed different hydrogen or hydrophobic interactions as well as halogen bonding visualized via DSV.

NSAIDs	Binding affinity (kcal/mol)	Inhibition constant (μM)	Interacting amino acid residues (Bond Distance)		
			H-bonds	Hydrophobic interaction (Bond Distance)	Halogen
Ibuprofen	-5.6	7.5	GLU455(2.82Å)	LEU378(3.57Å), LEU438(4.08Å), HIS437(4.56Å)	
Naproxen	-6.8	3.82	PHE321(2.36Å), LYS244(3.50Å)	PRO487(3.97Å), LEU459 (3.97Å), LYS244(4.24Å)	
Diclofenac	-6.8	3.82	HIS332 (3.14Å)	ILE467(4.83Å), MET470(4.55Å), LYS573(3.52Å), ARG335(4.59Å)	
Celecoxib	-7.4	3.57	GLN247 (2.64Å), GLN326 (2.19Å), CYS251 (3.40Å), SER514 (2.73Å), ASP334 (2.02Å), GLY253 (3.28Å)	ILE258(5.12Å), PRO336(5.36Å) PRO333(4.77Å), CYST251(5.10Å), CYS328(5.80Å)	GLU324(3.52Å) GLN247 (2.87Å)
Mefenamic acid	-6.8	3.82	ASP570(1.98Å)	MET470(5.23Å), ILE467(5.15Å), PRO471(5.26Å), ARG335(3.99Å), LYS573(4.70Å)	
Etoricoxib	-6.8	3.82	ASP570(1.96Å)	ASP570 (3.66Å), LYS573(4.44Å), ARG335(3.48Å)	
Indomethacin	-7.5	3.03	ARG335 (2.61Å), ASP334 (2.31Å), LYS573 (2.30Å), HIS332 (2.82Å)	PRO471(4.01Å), HIS332(4.97Å), LYS573 (3.98Å), ASP566(4.09Å), MET470(5.21Å)	
Aspirin	-5.6	7.5	ARG335 (2.15Å), ASP566 (1.92Å), LYS573 (3.56Å)	ILE467(5.00Å), PRO471 (5.46Å), MET470 (4.05Å)	

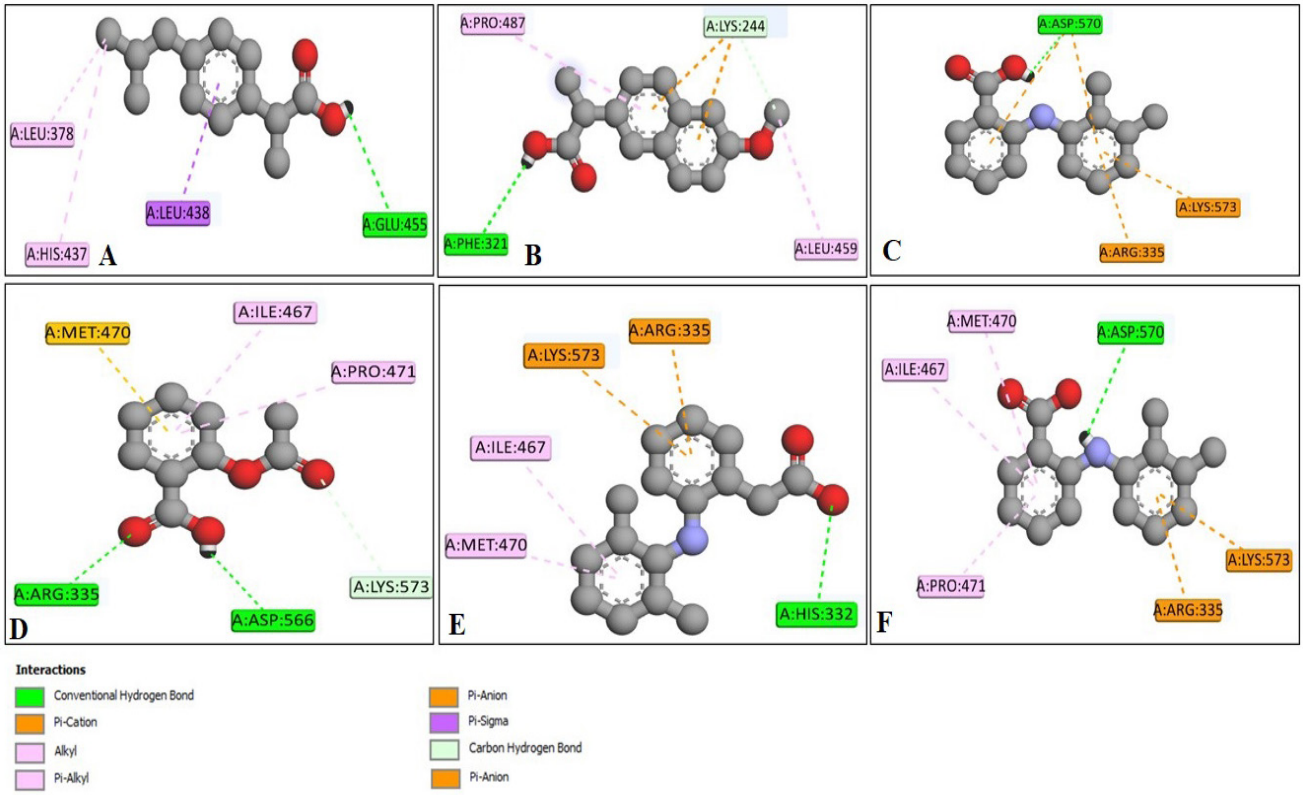

Fig. 4. 2D diagrams visualized via DSV showed binding interactions between 1BG1 and FDA-approved NSAIDS Ibuprofen (A), Naproxen (B), Etoricoxib (C), Aspirin (D), Diclofenac (E), Mefenamic Acid (F). Different types of interactions are shown by different colors as indicated in the Legends.

Table II. Physico-chemical Characteristics of FDA-approved NSAIDs predicted via pkCSM and ADMETsar.

ADMET	Parameters	Coelicoxib	Indomethacin	Etoricoxib
Absorbance	Water solubility (log S) mol/L	-4.45	-3.84	-4.145
	Intestinal absorption (%age absorbed)	92.995	98.649	97.946
	P-glycoprotein I/II inhibitor	Yes	No	No
Distribution	log VDss (L/Kg)	-0.273	-1.633	0.05
Metabolism	CYP2D6 substrate/Inhibitor	No	No	No
	CYP3A4 substrate/Inhibitor	Yes/No	No	Yes
Excretion	Total clearance (Log ml/min/kg)	0.435	0.088	0.174
	Renal OCT2 substrate	No	No	Yes
Toxicity	AMES Toxicity	No	No	No
	Max. tolerable dose (log mg/kg/day)	0.178	1.109	0.064
	Hepatotoxicity	Yes	Yes	Yes

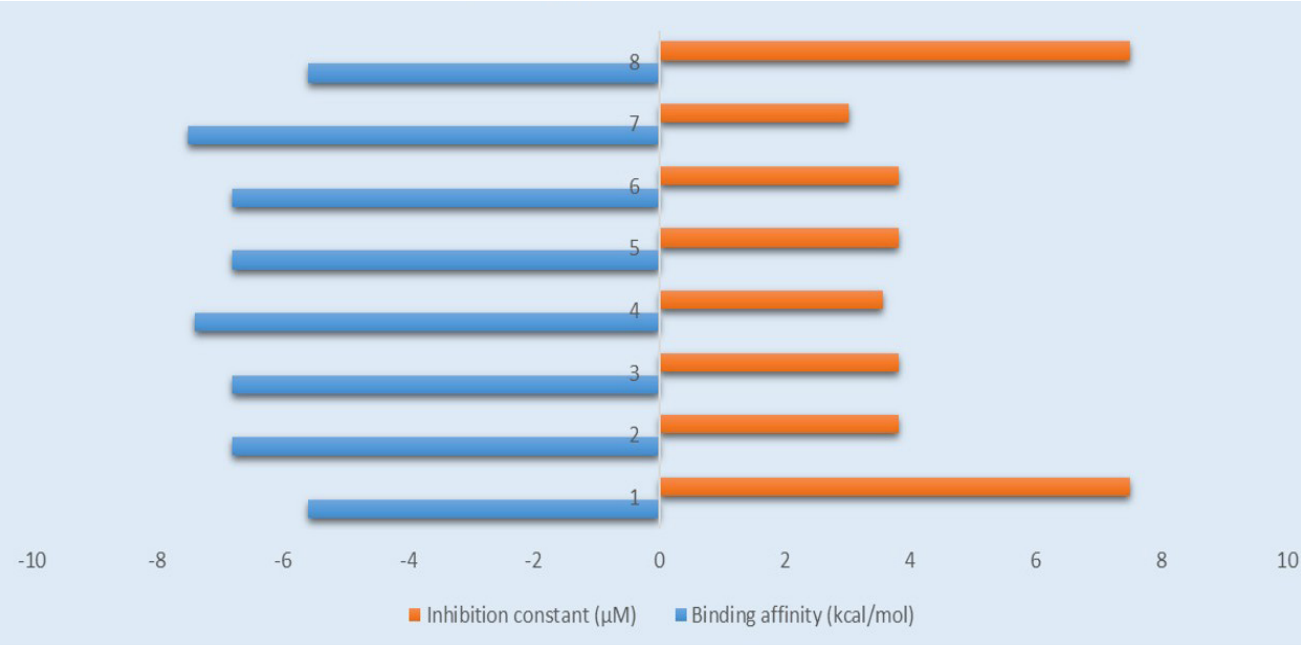

Fig. 5. Graphical Representation of binding energies and predicted inhibition constants (μM) for studied FDA-approved NSAIDs. As indicated clearly, the complex with high binding affinity has the lowest inhibition constant and vice versa.

Table III. Lipinski's Rule of Five for FDA-approved NSAIDs via SwissADME.

Lipinski's rule of five (RO5)	Compounds							
	Ibuprofen	**Naproxen**	**Diclofenac**	**Celecoxib**	**Mefenamic acid**	**Etoricoxib**	**Indomethacin**	**Aspirin**
Molecular weight < 500kDa	206.28	230.26	296.15	381.37	241.29	358.84	357.79	180.16
Log P (< 5)	3.07	3.04	4.36	5.75	3.75	5.26	3.93	1.31
H- bond donor (5)	1	1	2	1	2	0	1	1
H – bond acceptor (<10)	2	3	2	7	2	4	4	4
Violation	0	0	0	1	0	1	0	0

Mefenamic acid forms hydrogen bonding with ASP570 and different hydrophobic interactions with MET470, ILE467, and PRO471. Etoricoxib forms hydrogen bonding with ASP570 and different hydrophobic interactions with LYS573 and ARG335 (Fig. 5).

Indomethacin exhibits the lowest binding energy, i.e., -7.5 kcal/mol, and inhibition constant of 3.03 μM. It forms hydrogen bonding with ARG335, ASP334, and LYS573, and hydrophobic interactions with PRO471 and HIS332. While Celecoxib shows the second lowest binding energy, i.e., -7.4 kcal/mol and an inhibition constant of 3.57μM. And forms multiple hydrogen bonds with GLN247, CYS251, and different hydrophobic interactions with ILE258, PRO336, and PRO333 (Fig. 6).

Drug likeness and ADMET properties

Pharmacokinetics for absorption, distribution, metabolism, and excretion (ADME) are essential to interpret the pharmacodynamics. The different parameters were analyzed via online tools pkCSM and ADMETsar (Table II). Table III. Lipinski's Rule of Five for FDA-approved NSAIDs via SwissADME.

As per Lipinski's rule, the ligands with two or fewer violations have a low toxicity level and have a good absorption value. All the ligands showed no or zero violations, further confirming their bioactive availability (Table III).

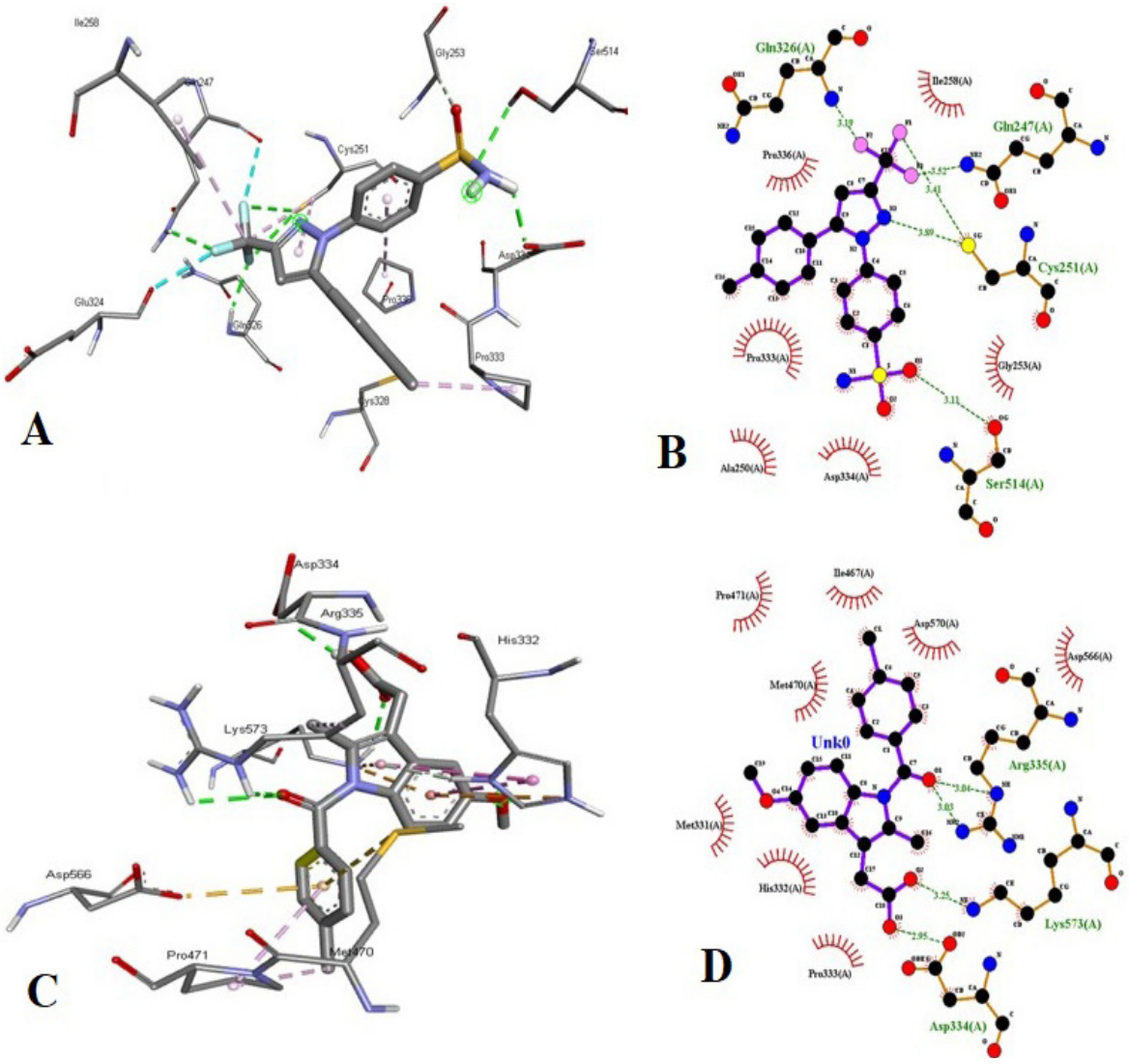

Fig. 6. (A) Three-dimensional (3D) representation of Coelicoxib. (B) Ligplot representation of the complex, green dotted lines show the hydrogen bonds, while the spoked arcs in red show the hydrophobic interactions between Coelicoxib and IBG1. (C) Three-dimensional (3D) representation of Indomethacin. (D) Ligplot representation of the complex, green dotted lines show the hydrogen bonds, while the spoked arcs in red show the hydrophobic interactions between Indomethacin and IBG1.

DISCUSSION

STAT3 is generally known for involvement in the regulation of various important cellular functions like cell proliferation, apoptosis, and the response of the immune system. The continuous activation of STAT3 causes various types of cancers that including breast, liver, colorectal, and pancreatic cancers[20]. Although STAT3 is an important target of cancer but there is no specific therapy approved by the FDA that specifically targets its activation, which is a major challenge in the treatment of cancer. As STAT3 plays very important roles in multiple pathways of cells so it's difficult to target it for selective inhibition[7,8].

Nonsteroidal anti-inflammatory drugs (NSAIDs) are being recognized as potential anticancer agents. They inhibit tumors through mechanisms such as promoting apoptosis and COX-2 inhibition[21]. This study investigated the potential of eight FDA-approved NSAIDs, Aspirin, Celecoxib,

Diclofenac, Etoricoxib, Ibuprofen, Indomethacin, Mefenamic Acid, and Naproxen, as inhibitors of STAT3 (Table I).

Among these drugs, celecoxib exhibited the highest binding affinity, with -7.4 kcal/mol binding energy and 3.57 μM inhibition constant. In STAT3, it formed multiple hydrophobic and hydrogen bonds with key residues that indicate celecoxib could be a highly stable inhibitor (Fig. 4). Previous studies have shown that celecoxib is very effective in reducing polyp formation in familial adenomatous polyposis (FAP), which further supports its anticancer properties[3,22].

In comparison, ibuprofen exhibited the lowest binding affinity, with -5.6 kcal/mol binding energy and 7.5 μM inhibition constant. Even though it had weaker interaction with STAT3, the earlier studies show that it might lower the risk of cancer through other mechanisms beyond inhibition of STAT3, especially in colorectal cancer[23].

Other NSAIDs, including diclofenac, etoricoxib, and naproxen, exhibited intermediate binding energies and formed multiple hydrophobic and hydrogen interactions with STAT3. Naproxen, with -6.8 kcal/mol binding energy, created multiple hydrogen bonds, indicating that it is a potential inhibitor of STAT3. Indomethacin also exhibited strong interactions, with -7.5 kcal/mol binding energy, which highlights its applicability in the treatment of cancer. Comprehensively, our docking study supports existing literature, indicating that NSAIDs can be repurposed as potential anticancer agents, specifically focusing on STAT3[23-25]. Aspirin and ibuprofen are drugs with all the necessary safety profiles that make them candidates for repurposing in cancer treatment. Specifically, aspirin has shown significant potential in reducing the risk of breast, colorectal, and prostate cancers[23]. Drug discovery and its feasibility are assessed through toxicity and drug likeness. Evaluating the pharmacokinetic profiling of compounds is essential to ensure their efficiency and safety of use. The ADMET properties of all studied ligands were found to be within acceptable limits, as shown in Table II.

STAT3β is already in the active or DNA-bound conformation, so the analysis is restricted to only its active state. However, it restricts our ability to explore alternative conformations such as the unbound or inactive state. Because STAT3 proteins undergo substantial conformational changes once bound to DNA, focusing on just the DNA-bound structure may mask important aspects of how STAT3β modulates interconversion between states, such as activation, dimerization, or interaction with other cofactors.

This computational study provides strong *in silico* demonstrations, but further experimental validation is crucial. Both preclinical and clinical studies are necessary for assessing the safety and efficacy of NSAIDs in cancer patients.

CONCLUSION

This study highlights the promising role of FDA-approved NSAIDs as potential inhibitors of STAT3, offering a novel approach to cancer treatment. The repurposing of these drugs, with their known safety profiles, could expedite the development of targeted therapies for cancer. Further research on preclinical and clinical evaluations is required to confirm these results in inhibiting STAT3-mediated oncogenesis.

DECLARATIONS

Acknowledgement

The authors would like to thank the University of the Punjab for institutional support.

Authors' contribution

MK conceived and supervised the study. ZA and EF contributed equally to the molecular docking analysis, data interpretation, and wrote the manuscript. AQ contributed to ligand preparation and pharmacokinetic analysis. AJ and MA contributed to data collection and literature review. All authors read and approved the final manuscript.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethics statement

No human participants, identifiable personal data, or live animals were involved. Therefore, institutional ethics approval was not required.

Generative AI and AI-assisted technology statement

The authors declare that they have not used generative AI or AI-assisted technologies in this manuscript.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, and those of publishers, the editor and the reviewers. Any product that may be evaluated in this article, or claim that may be made by this manufacturer, is not gaurenteed or endorsed by the publisher.

Statement of conflict of interest

The authors have declared no financial or personal conflicts of interest.

REFERENCES

1. Verhoeven, Y., Tilborghs, S., Jacobs, J., De Waele, J., Quatannens, D., Deben, C., Prenen, H., Pauwels, P., Trinh, X.B., Wouters, A. and Smits, E.L., 2020. The potential and controversy of targeting STAT family

members in cancer. In: *Seminars in cancer biology*. *Acad. Press*, **60**: 41-56. https://doi.org/10.1016/j.semcancer.2019.10.002
2. Yu, H., Pardoll, D. and Jove, R., 2009. STATs in cancer inflammation and immunity: A leading role for STAT3. *Nat. Rev. Cancer*, **9**:798-809.
3. Xiong, A., Yang, Z., Shen, Y., Zhou, J. and Shen, Q., 2023. Transcription factor STAT3 as a novel molecular target for cancer prevention. *Cancers* (Basel), **15**: 1057-1072.
4. Khan, I., Chen, X., Khan, Y., Muhammad, R., Hu, X., Zou, M. and Zhao, Y., 2021. STAT3: Key regulator in oncogenic pathways and emerging therapeutic target. *Cell Mol. Biol. Lett*., **26**: 12.
5. Pan, L., Chen, X., Fu, S., Yu, W., Li, C., Wang, T., Lo, H.W. and Lin, J., 2020. LLY17, a novel small molecule STAT3 inhibitor induces apoptosis and suppresses cell migration and tumor growth in triple-negative breast cancer. *Breast Cancer Res. Treatment*, **181**:31-41.
6. Lee, H., Jeong, A.J. and Ye, S.K., 2019. Highlighted STAT3 as a potential drug target for cancer therapy. *BMB Rep*., **52**: 415. https://doi.org/10.5483/BMBRep.2019.52.7.152
7. Jin, W., 2020. Role of JAK/STAT3 signaling in the regulation of metastasis, the transition of cancer stem cells, and chemoresistance of cancer by epithelial–mesenchymal transition. *Cells*, **9**: 217. https://doi.org/10.3390/cells9010217
8. Xiong, A., Yang, Z., Shen, Y., Zhou, J. and Shen, Q., 2024. Transcription factor STAT3 as a novel molecular target for cancer prevention. *Cancers* (Basel), **16**: 1-10.
9. Chen, L., Liu, Y. and Liu, H., 2022. Involvement of STAT3 in cancer and inflammation: Mechanisms and therapeutic strategies. *Cell Death Dis*., **13**: 869.
10. Yang, J., Liao, X. and Agarwal, P., 2024. STAT3, a master regulator of stem cell differentiation and cancer progression. *Cell Signal*, **94**: 110309.
11. Wehling, M., 2014. Non-steroidal anti-inflammatory drug use in chronic pain conditions with special emphasis on the elderly and patients with relevant comorbidities: management and mitigation of risks and adverse effects. *Euro. J. Clin. Pharmacol.*, **70**:1159-1172.
12. Abdu, N., Mosazghi, A., Teweldemedhin, S., Asfaha, L., Teshale, M., Kibreab, M., Anand, I.S., Tesfamariam, E.H. and Russom, M., 2020. Non-steroidal anti-inflammatory drugs (NSAIDs): Usage and co-prescription with other potentially interacting drugs in the elderly: A cross-sectional study. *PLoS One*, **15**: e0238868. https://doi.org/10.1371/journal.pone.0238868
13. Pham, T.T., Miller, M.J., Harrison, D.L., Lloyd, A.E., Crosby, K.M. and Johnson, J.L., 2013. Cardiovascular disease and non-steroidal anti-inflammatory drug prescribing in the midst of evolving guidelines. *J. Eval. Clin. Pract.*, **19**: 1026-1034.
14. Singgih, M.F., Achmad, H., Sukmana, B.I., Carmelita, A.B., Putra, A.P., Ramadhany, S., Putri, A.P., 2020. A review of nonsteroidal anti-inflammatory drugs (NSAIDs) medications in dentistry: Uses and side effects. *Sys. Rev. Pharm*., **11**: 293-298. https://doi.org/10.31838/srp.2020.5.43
15. Kushner, P., McCarberg, B.H., Wright, W.L., Aldoori, W., Gao, P., Iqbal, A. and Petruschke, R., 2024. Ibuprofen/acetaminophen fixed-dose combination as an alternative to opioids in management of common pain types. *Postgrad. Med*., **29**: 1-9.
16. Jakhar, R., Dangi, M., Khichi, A. and Chhillar, A.K., 2020 Relevance of molecular docking studies in drug designing. *Curr. Bioinf*., **15**: 270-278. https://doi.org/10.2174/1574893615666191219094216
17. Ye, B., Tian, W., Wang, B. and Liang, J., 2024. CASTpFold: Computed atlas of surface topography of the universe of protein folds. *Nucl. Acids Res*., 52(W1):W194-W199. https://doi.org/10.1101/2024.05.04.592496
18. Bakchi, B., Krishna, A.D., Sreecharan, E., Ganesh, V.B.J., Niharika, M., Maharshi, S., Puttagunta, S.B., Sigalapalli, D.K., Bhandare, R.R. and Shaik, A.B., 2022. An overview of applications of the SwissADME web tool in the design and development of anticancer, antitubercular, and antimicrobial agents: A medicinal chemist's perspective. *J. mol. Struct*., **1259**: 132712. https://doi.org/10.1016/j.molstruc.2022.132712
19. Azzam, K.A., 2023 SwissADME and pkCSM webservers predictors: An integrated online platform for accurate and comprehensive predictions for in silico ADME/T properties of artemisinin and its derivatives. *Kompleksnoe Ispolzovanie Mineralnogo Syra Complex Use Mineral Resour*., **325**: 14-21. https://doi.org/10.31643/2023/6445.13
20. Ma, J.H., Qin, L. and Li, X., 2020. Role of STAT3 signaling pathway in breast cancer. *Cell Commun. Signal*., **18**: 1-3. https://doi.org/10.1186/s12964-020-0527-z
21. Sousa, S.M., Xavier, C.P., Vasconcelos, M.H. and Palmeira, A., 2023. Repurposing some of the well-known non-steroid anti-inflammatory drugs (NSAIDs) for cancer treatment. *Curr. Topic. Med. Chem*., **23**: 1171-1195. https://doi.org/10.2174/1568026623666230130150029
22. Ahmadi, M., Bekeschus, S., Weltmann, K.D., von Woedtke, T. and Wende, K., 2022. Non-steroidal anti-inflammatory drugs: Recent advances in the use of synthetic COX-2 inhibitors. *RSC Med. Chem*., **13**: 471-496. https://doi.org/10.1039/D1MD00280E

23. Chudy-Onwugaje, K., Huang, W.Y., Su, L.J., Purdue, M.P., Johnson, C.C., Wang, L., Katki, H.A., Barry, K.H. and Berndt, S.I., 2021. Aspirin, ibuprofen, and reduced risk of advanced colorectal adenoma incidence and recurrence, and colorectal cancer in the PLCO cancer screening trial. *Cancer*, **127**: 3145-3155. https://doi.org/10.1002/cncr.33623
24. Kolawole, O.R. and Kashfi, K., 2022. NSAIDs and cancer resolution: New paradigms beyond cyclooxygenase. *Int. J. mol. Sci.*, **23**: 1432. https://doi.org/10.3390/ijms23031432
25. Ozleyen, A., Yilmaz, Y.B., Donmez, S., Atalay, H.N., Antika, G. and Tumer, T.B., 2023. Looking at NSAIDs from a historical perspective and their current status in drug repurposing for cancer treatment and prevention. *J. Cancer Res. Clin. Oncol.*, **149**: 2095-20113. https://doi.org/10.1007/s00432-022-04187-8