IPS Journal of Advanced and Applied Biochemistry
IPS J. Adv. Appl. Biochem., 1(2): 38-50 (2025)
DOI: https://doi.org/10.54117/ijaab.v1i2.67

Computational Screening of High-Affinity Natural Product-Derived Inhibitors Targeting NF-κB Protein: A Molecular Docking Approach toward Anti-Inflammatory and Anticancer Therapeutics

Chukwuebuka Egbuna[1*], Kingsley C. Patrick-Iwuanyanwu[1], Eugene N. Onyeike[1], Colin B. Lukong[2], Cecilia Chika Unegbu[3,4], Chukwuemeke D. Edward[5], Chukwudi J. Chikwendu[6], Chijioke C. Ilechukwu[6], Michael C. Olisah[7], Anthony O. Ekesiobi[8], Jonathan C. Ifemeje[6] and Ikechukwu H. Iheukwumere[9]

[1]African Centre of Excellence for Public Health and Toxicological Research, University of Port Harcourt, Rivers State, Nigeria.
[2]Department of Biochemistry, Faculty of Sciences, Madonna University, Elele Campus, Rivers State, Nigeria.
[3]Natural Sciences Department, Bowie State University, 14000 Jericho Park Rd., Bowie MD 20715, United States.
[4]Chemistry/Biochemistry Department, Federal Polytechnic, Nekede, Imo State, Nigeria.
[5]Department of Science Laboratory Technology, School of Applied Science, Delta State Polytechnic, Ogwashi-Uku.
[6]Department of Biochemistry, Faculty of Natural Sciences, Chukwuemeka Odumegwu Ojukwu University, Anambra State Nigeria.
[7]Department of Medical Biochemistry, Faculty of Basic Medical Sciences, Chukwuemeka Odumegwu Ojukwu University, Uli, Anambra State 431124, Nigeria.
[8]Department of Biological Sciences, Chukwuemeka Odumegwu Ojukwu University, Uli Campus, Anambra State.
[9]Department of Microbiology, Faculty of Natural Sciences, Chukwuemeka Odumegwu Ojukwu University, Anambra State, Nigeria.
*Corresponding authors e-mail: egbunachukwuebuka@gmail.com: +2347039618485

Abstract

Nuclear factor kappa B (NF-κB) is a pivotal transcription factor involved in inflammation, immune responses, and cancer progression. In the quest for safer and more effective therapeutic agents, this study employed molecular docking to screen 313 bioactive phytochemicals against NF-κB, aiming to identify potential natural inhibitors. Ligands were curated from literature and public databases and prepared using ChemDraw, VConf, and Open Babel, while the NF-κB protein (PDB ID: 1SVC) was retrieved from the RCSB Protein Data Bank and refined using BIOVIA Discovery Studio. Binding site prediction was achieved via PrankWeb and literature data. Docking was conducted with PyRx 0.8 using AutoDock Vina, and binding interactions were analyzed in Discovery Studio. Results revealed that hypericin and withanolide exhibited the strongest binding affinities (-8.4 kcal/mol), surpassing standard NF-κB inhibitors such as olmesartan (-6.3 kcal/mol) and disulfiram (-3.5 kcal/mol). Other top-performing compounds included diosmin (-8.3 kcal/mol), tomatidine, tubeimoside-I, and solanine (all -8.0 kcal/mol), each interacting with key NF-κB residues through hydrogen bonding and hydrophobic interactions. These phytochemicals, available from diverse medicinal plants, showed superior binding profiles, highlighting their therapeutic potential. Overall, the study underscores the promise of natural compounds in modulating NF-κB activity and supports their further investigation through molecular dynamics simulations and experimental validation. These findings provide a foundation for the development of phytochemical-based NF-κB inhibitors with potential applications in inflammation and cancer therapy.

Keywords: *NF-κB inhibition; Phytochemicals; Molecular docking; Inflammation; Natural products*

Article History
Received: 05 Jan 2025
Accepted: 25 Jan 2025
Published: 27 Jan 2025

Scan QR code to view•

How to cite this paper: Egbuna, C., Patrick-Iwuanyanwu, K. C., Onyeike, E. N., Lukong, C. B., Unegbu, C. C., Edward, C. D., Chikwendu, C. J., Ilechukwu, C. C., Olisah, M. C., Ekesiobi, A. O., & Ifemeje, J. C. (2025). Computational Screening of High-Affinity Natural Product-Derived Inhibitors Targeting NF-κB Protein: A Molecular Docking Approach toward Anti-Inflammatory and Anticancer Therapeutics. *IPS Journal of Advanced and Applied Biochemistry*, *1*(2), 38–50. https://doi.org/10.54117/ijaab.v1i2.67

Introduction

The nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) protein complex plays a critical role in the regulation of various biological processes, including DNA transcription, cytokine production, immune responses, and cell survival (Liu *et al*., 2017). This protein complex is essential for maintaining normal cellular function and is actively involved in the modulation of cell differentiation, proliferation, and immunological defense mechanisms (Egbuna *et al*., 2022). NF-κB functions primarily as a

transcription factor, orchestrating the expression of genes associated with inflammation, immune responses, cell adhesion, growth, and apoptosis. Because of its pivotal role in these processes, NF-κB is a central regulator of both physiological and pathological cellular responses.

However, dysregulation of the NF-κB pathway—whether through aberrant activation, overexpression, or persistent signaling—has been strongly associated with the onset and progression of numerous pathological conditions (Jayab *et al*., 2024). Its activation is tightly controlled under normal physiological conditions but can become dysregulated in response to chronic stimulation or mutations within upstream regulators. This dysregulation often results in sustained NF-κB activity, contributing to a pro-inflammatory microenvironment that supports disease development and progression.

Specifically, abnormal NF-κB activity has been implicated in a wide range of diseases, including various cancers, inflammatory bowel disease, autoimmune disorders, chronic inflammation, gastritis, atherosclerosis, septic shock, viral infections, rheumatoid arthritis, and asthma (Vlahopoulos, 2017; de Gregorio *et al*., 2020; Adetuyi *et al*., 2022). The broad involvement of NF-κB in these conditions is partly due to its ubiquitous presence in nearly all animal cell types and its complex interactions with numerous signaling pathways. These pathways are triggered by a variety of stimuli such as proinflammatory cytokines, reactive oxygen species (ROS), physical and chemical stress, ultraviolet (UV) radiation, heavy metals, oxidized low-density lipoprotein (LDL), and microbial or viral antigens (Adetuyi *et al*., 2022). These environmental and endogenous stimuli activate upstream kinases, leading to the phosphorylation and subsequent degradation of the inhibitor IκB, which allows NF-κB to translocate to the nucleus and activate target gene expression.

Furthermore, constitutive activation of NF-κB has been shown to promote the transcription of anti-apoptotic and prosurvival genes, such as *Bcl-2* and *Bcl-XL*, thereby contributing to tumor cell resistance to apoptosis and chemotherapeutic agents (Godwin *et al*., 2013; Mehta *et al*., 2013). This phenomenon is particularly evident in hematological malignancies such as acute myeloid leukemia (AML), where more than 50% of patients exhibit constitutively active NF-κB, which enables leukemic cells to evade programmed cell death and supports their uncontrolled proliferation (Darwish *et al*., 2019). In a study involving 103 AML patients, Darwish *et al*. (2019) used quantitative real-time polymerase chain reaction (RT-PCR) to evaluate NF-κB expression in bone marrow samples. Their findings revealed that 80.5% of the patients (83 out of 103) had elevated NF-κB expression levels compared to the control group, suggesting a strong correlation between NF-κB overexpression and AML pathogenesis. These findings underscore the critical role of NF-κB in cancer biology and the need for effective strategies to target this pathway.

Given its central role in disease mechanisms, NF-κB has emerged as a promising molecular target for therapeutic intervention. Notably, several herbal and dietary plant extracts have demonstrated potential *in vitro* for inhibiting NF-κB activity (Paur *et al*., 2010). Among these, the citrus flavonoid nobiletin has been reported to suppress NF-κB signaling in experimental mouse models, highlighting the potential of natural products in modulating this critical pathway (Lin *et al*., 2019). Natural compounds are of particular interest due to their structural diversity, multi-targeting capacity, and lower cytotoxicity compared to many synthetic drugs.

Natural products studies have long served as a foundation for drug discovery, with many of today's pharmaceutical agents either derived from or inspired by research on bioactive compounds found in nature (Ekesiobi *et al*., 2017; Anameze *et al*., 2023; Abiodun *et al*., 2024a; Abiodun *et al*., 2024b; Abiodun *et al*., 2024c; Ekesiobi *et al*., 2024; Ekesiobi & Onebunne, 2025). Their importance in modern therapeutic development is underscored by the fact that more than 60% of approved drugs are either natural products or derived from them (Egbuna *et al*., 2021; Ifemeje *et al*., 2021; Adetuyi *et al*., 2022; Egbuna *et al*., 2022; Singla *et al*., 2022; Aldosari *et al*., 2023; Egbuna *et al*., 2023; Egbuna *et al*., 2025).

Compounds, including alkaloids, terpenoids, flavonoids, and polyphenols, are known to possess a wide range of biological activities such as anti-inflammatory, antioxidant, immunomodulatory, and anticancer effects (Ekesiobi, 2025; Ekesiobi *et al*., 2025a; Ekesiobi *et al*., 2025b; Ekesiobi *et al*., 2025c; Iheukwumere *et al*., 2025a; Iheukwumere *et al*., 2025b; Ilechukwu *et al* 2025a; Ilechukwu *et al* 2025b). In the context of NF-κB inhibition, natural products offer a promising avenue for therapeutic development because they are often capable of modulating upstream and downstream effectors of the NF-κB signaling cascade. For instance, curcumin (from *Curcuma longa*), resveratrol (from grapes), epigallocatechin gallate (from green tea), and parthenolide (from feverfew) have all demonstrated NF-κB inhibitory activity in preclinical studies. The application of natural products in other facets of science was d

One of the key advantages of using natural products is their potential to act synergistically with conventional therapies (Egbuna *et al*., 2020). They can enhance the efficacy of chemotherapeutic agents or sensitize resistant tumor cells to apoptosis while minimizing side effects. Additionally, natural products can influence gene expression, epigenetic modifications, and cellular redox balance—factors that are crucial in NF-κB-mediated pathologies. Despite these promising attributes, many natural compounds suffer from issues such as low bioavailability, poor solubility, or rapid metabolism, which limit their clinical application. Nevertheless, advances in drug delivery systems and structural modifications are helping to overcome these barriers, revitalizing interest in natural product-based therapies.

The aim of this study is to conduct an *in silico* assessment of NF-κB protein inhibitors through molecular docking studies. By computationally evaluating the binding affinity and interaction profiles of selected compounds with the NF-κB protein, this study seeks to identify potential lead molecules that could serve as effective inhibitors of NF-κB activity. This approach offers a cost-effective and time-efficient strategy for the preliminary screening of therapeutic candidates prior to experimental validation. Such computational methodologies not only accelerate the drug discovery pipeline but also allow for the rational design of inhibitors with improved specificity

and efficacy. Given the therapeutic potential of natural products, their inclusion in *in silico* screening platforms enhances the likelihood of identifying novel, bioactive, and clinically translatable NF-κB inhibitors.

Materials and Methods

In silico study (Computational study)

Ligand Curation and Preparation

An extensive review of the literature was carried out to identify phytochemicals previously documented to exhibit anticancer activity. Key sources referenced included *Phytochemistry: An In Silico and In Vitro Update* (Kumar & Egbuna, 2018), *Phytochemicals as Lead Compounds for New Drug Discovery* (Egbuna et al., 2019), and *Drug Development for Cancer and Diabetes: A Path to 2030* (Saravanan et al., 2019). Based on this review, 313 phytochemicals (Appendix I) and a selection of established anticancer drugs (Appendix II) were chosen for docking study. Their 3D molecular structures, along with Compound IDs (CIDs), were obtained from the NCBI PubChem database in SDF format.

For compounds not listed in PubChem or ChemSpider, chemical structures were manually constructed using ChemDraw Ultra 12.0 (CambridgeSoft). To prepare these molecules for docking studies, all ligands were converted from 2D to 3D SDF format using VConf software (VeraChem LLC). Finally, all ligand structures were compiled into a single SDF file using Open Babel (http://openbabel.org) to enable seamless integration into the PyRx virtual screening platform.

Protein Preparation

The crystal structure of the NF-κB protein (specifically the p50 subunit) was obtained from the RCSB Protein Data Bank (https://www.rcsb.org/) in .pdb format, using the PDB ID: 1SVC at a resolution of 2.6 Å. Protein preparation was carried out using BIOVIA Discovery Studio Visualizer 2021 (v21.1.0.20298; Dassault Systèmes: https://www.3ds.com), following the protocol described by Qasayme *et al*. (2019). During this process, all water molecules and heteroatoms were removed, while polar hydrogens were added to optimize the protein structure for docking. The co-crystallized ligands within the protein were used to identify and model the active site. This modeled binding site was further validated by comparing it with experimental references and binding data.

Active Site Prediction

Active site prediction was conducted using a combination of structural data and bioinformatic tools. The active binding residues of NF-κB were predicted using a blend of scholarly references, the PDB database, BIOVIA Discovery Studio, and PrankWeb (P2Rank)—an advanced machine learning-based web server designed for ligand binding site prediction (https://prankweb.cz/). PrankWeb provided both visual prediction and center coordinates for potential binding pockets. Predictions from all sources were cross-compared, and consensus residues were selected for defining the active binding site. These predicted residues were used to configure the grid box for docking in PyRx, ensuring comprehensive coverage of the target binding site.

Molecular Docking Studies

Molecular docking simulations were performed using PyRx version 0.8 (https://pyrx.sourceforge.io), in accordance with the protocol described by Dallakyan and Olson (2015). PyRx is an integrated virtual screening tool that facilitates molecular docking of large compound libraries against target proteins. Ligands in 3D SDF format were loaded into the platform using its built-in Open Babel graphical interface. Energy minimization of ligands was executed using the Universal Force Field (UFF) and the conjugate gradient algorithm, with 200 total steps. The step size was initially set to 1, and subsequently refined to 0.1 for greater precision.

Following minimization, all ligands were converted to AutoDock-compatible pdbqt format to prepare for docking. The docking protocol was executed with an exhaustiveness level of 8, allowing for thorough exploration of potential binding conformations. Ligands were ranked based on binding affinity, with the most negative binding energy values indicating the strongest interaction. The ligand with the highest affinity was identified as the best potential inhibitor of NF-κB, based on its binding energy (Prasanth *et al*., 2020).

Visualization and analysis of ligand–protein interactions at the optimal docking poses were carried out using BIOVIA Discovery Studio Visualizer 2021. Validation of the docking procedure was also undertaken to ensure the accuracy and reliability of the results.

Results

The molecular docking analysis of selected bioactive compounds against NF-κB identified several promising inhibitors (Figure 1 &Table 1), highlighting the therapeutic potential of phytochemicals in modulating NF-κB-mediated pathways associated with inflammation and oncogenesis. Among the screened compounds, hypericin and withanolide exhibited the most potent binding affinities, both scoring −8.4 kcal/mol. These values surpassed those of known NF-κB inhibitors such as olmesartan (−6.3 kcal/mol) and disulfiram (−3.5 kcal/mol), suggesting strong inhibitory potential.

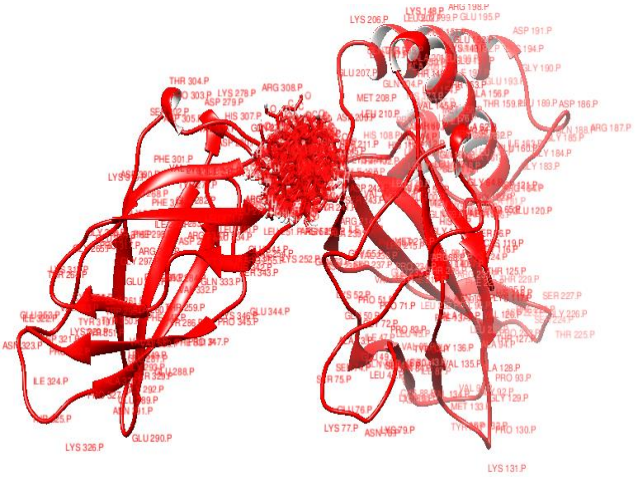

Figure 1: Protein-ligand complex of NF-κB and hypericin.

Table 1: Molecular docking scores of NF-kβ protein inhibitors

S/No	Compound	PubChem ID	Binding Energy (kcal/mol)	Sources
1.	Hypericin	3663	-8.4	Genera *Hypericum* (Saint John's wort)
2.	Withanolide	53477765	-8.4	Nightshade plant family e.g. *Datura, Solanum, Withania, Jaborosa*
3.	Diosmin	5281613	-8.3	Citrus fruits (oranges and lemons) and peel extracts, hyssop, figwort
4.	Tomatidine	65576	-8.0	Stems and leaves of tomato plants, and in the fruits at low concentrations
5.	Tubeimoside-I	51346132	-8.0	*Bolbostemma paniculatum*
6.	Solanine	262500	-8.0	Nightshade family e.g. genus Solanum e.g. potato, tomato, eggplants
7.	Mezerein	24832075	-7.8	*Daphne mezereum* (Thymelaeaceae) and related plants
8.	Vicenin-2	442664	-7.8	Sweet oranges, *Ocimum sanctum*, buckwheats, fenugreeks
9.	Neohesperidin	442439	-7.8	Citrus fruits (e.g. oranges and lemons), peel extracts & inedible ones
10.	Polyphyllin	72960700	-7.7	*Paris polyphylla*
11.	Cycloartocarpesin	15224382	-7.6	Genera *Artocarpus e.g. Artocarpus heterophyllus* (Jackfruit)
12.	Platycodin	162859	-7.6	*Platycodon grandiflorus*
13.	Hypoxoside	13785311	-7.5	*Hypoxis obtuse*, star-grass
14.	Glycyrrhizic acid	14982	-7.5	Licorice (Root extract), *Glycyrrhiza glabra* (Fabaceae)
15.	Isovitexin	162350	-7.5	Pigeon pea, Passion flower, bamboo, mimosa (champagne + citrus juice), wheat leaves, rice hull of *Oryza sativa*
16.	Baicalin	64982	-7.4	Plants in Genus *Scutellaria* and in *Oroxylum indicum*
17.	α-Carotene	6419725	-7.4	Carrots, sweet potatoes, pumpkin, avocado, green beans, spinach
18.	Cleistanthin	4485134	-7.4	*Cleistanthus collinus*
19.	Silymarin	5213	-7.4	Seeds of milk thistle *Silybum marianum* (L.)
20.	Verbascoside	5281800	-7.4	Plants of Verbenaceae, Olive, Lamiaceae family
21.	Vitexin	5280441	-7.4	Leaves of *Phyllostachys nigra* (Bamboo), passion flower, Pearl millet
Standard NF-kβ drug				
1.	Olmesartan	158781	-6.8	NF-kβ inhibitor
2.	Disulfiram	3117	-3.5	NF-kβ inhibitor
Other top performing anticancer drugs				
3.	Venetoclax	49846579	-9.1	Bcl-2 inhibitor
4.	Daunorubicin	30323	-8.0	DNA intercalation and inhibits macromolecular biosynthesis
5.	Guadecitabine	135564655	-7.8	DNA (cytosine-5)-methyltransferase 1 (DMNT1) inhibitor
6.	Sonidegib	24775005	-7.6	SMO inhibitor

Hypericin, a polycyclic aromatic compound with well-documented antiviral and anticancer properties, demonstrated strong binding within the DNA-binding cleft of NF-κB. It engaged key residues including VAL254, LEU272, CYS273, ASP274, HIS307, ARG308, PHE310, and ALA311. The interaction profile includes hydrophobic stacking via its extended aromatic system and hydrogen bonding/electrostatic interactions through its hydroxyl groups—particularly with ASP274 and ARG308. These interactions may disrupt NF-κB's ability to bind DNA, thereby inhibiting the transcription of genes involved in inflammation and cell proliferation, aligning with hypericin's reported biological activity. Hypericin, a naturally occurring compound derived from *Hypericum* species (e.g., St. John's Wort), has been shown to suppress NF-κB activity by inhibiting IκBα phosphorylation, which leads to reduced expression of proinflammatory cytokines (Novelli *et al*., 2020). Similarly, withanolide, a bioactive steroidal lactone from *Withania somnifera*, has demonstrated anti-inflammatory and anticancer properties by inhibiting NF-κB signaling through modulation of upstream kinases such as IKK and Akt (White *et al*., 2016).

Following these were diosmin (-8.3 kcal/mol), tomatidine (-8.0 kcal/mol), tubeimoside-I (-8.0 kcal/mol), and solanine (-8.0 kcal/mol). Diosmin, a citrus flavonoid, is known to downregulate inflammatory mediators and suppress NF-κB in models of oxidative liver damage (Hassanein *et al*., 2025). Tomatidine and solanine, both glycoalkaloids from *Solanum* species (e.g., tomatoes and potatoes), have demonstrated NF-κB modulation through the suppression of p65 nuclear translocation and decreased expression of COX-2 and iNOS (Chiu and Lin, 2008). Tubeimoside-I from *Bolbostemma paniculatum* has been reported to downregulate NF-κB and PI3K/Akt pathways in cancer models (Wang *et al*., 2022).

Mezerine (-7.8 kcal/mol) and vicenin (-7.4 kcal/mol) also showed favorable binding affinities. Mezerine, found in *Daphne mezereum* and related *Thymelaeaceae* plants, is associated with apoptotic and cytotoxic activity, although its effects on NF-κB need further experimental validation. Vicenin, a flavonoid present in sweet oranges and herbs like *Ocimum sanctum*, is known for its antioxidant and anti-inflammatory roles, which may relate to its NF-κB inhibitory activity (Marrassini *et al*., 2011).

Other compounds such as neoHesperidin (-7.3 kcal/mol), polyphyllin (-7.2 kcal/mol), cycloartocarpesin (-7.2 kcal/mol), and platycodin (-7.1 kcal/mol) further reinforce the therapeutic diversity of plant metabolites. NeoHesperidin, common in citrus peels, and polyphyllin, a steroidal saponin from *Paris polyphylla*, have shown promising anti-inflammatory effects through inhibition of NF-κB signaling (He *et al*., 2020). Cycloartocarpesin, isolated from *Artocarpus* species (e.g., jackfruit), and platycodin, from *Platycodon grandiflorus*, possess pharmacological traits consistent with NF-κB pathway modulation (Liu *et al*., 2022).

Also noteworthy are hypoxoside (-7.1 kcal/mol), glycyrrhizic acid (-7.0 kcal/mol), and isovitexin (-7.0 kcal/mol). Hypoxoside, from *Hypoxis obtusa*, is a known anti-inflammatory agent. Glycyrrhizic acid from *Glycyrrhiza glabra* (licorice) has been extensively documented to inhibit NF-κB and MAPK signaling cascades, reducing pro-inflammatory cytokines such as IL-6 and TNF-α (Zhao *et al*., 2016). Isovitexin, found in pigeon pea and passion flower, has also demonstrated anti-inflammatory potential, including inhibition of LPS-induced NF-κB activity in macrophages (Lv *et al*., 2016).

Collectively, the superior binding affinities of these phytochemicals, relative to standard drugs, support the hypothesis that they can effectively interact with the NF-κB binding site and potentially block its activation or transcriptional activity. The predicted interactions likely involve a combination of hydrogen bonding, hydrophobic interactions, and van der Waals forces, which stabilize the ligand-receptor complex.

These findings align with a growing body of evidence advocating the potential of natural compounds as safer and effective alternatives or adjuncts to synthetic NF-κB inhibitors. However, further validation through molecular dynamics simulations, in vitro NF-κB reporter assays, cytokine profiling, and in vivo models is essential to confirm their biological efficacy and pharmacokinetic behavior.

The docking results indicate that most of these phytochemicals exhibit stronger binding affinities than synthetic controls, highlighting their potential as lead molecules for NF-κB-targeted drug development. The diversity in their plant sources—ranging from tropical fruits and herbs to traditional medicinal plants—emphasizes the rich bioactive potential of natural products in modulating transcription factor-mediated inflammation.

As mentioned earlier, natural products have long served as a valuable source of therapeutic agents (Ekesiobi *et al*., 2017; Anameze *et al*., 2023; Abiodun *et al*., 2024a; 2024b; 2024c; Ekesiobi *et al*., 2024; Ekesiobi & Onebunne, 2025; Ekesiobi, 2025; Ekesiobi *et al*., 2025a; 2025b; 2025c; Iheukwumere *et al*., 2025a; 2025b; Ilechukwu *et al* 2025a; 2025b). Their structural diversity and bioactivity offer promising avenues for drug development. As shown in this study, phytochemicals has the potential to target NF-κB, underscoring the role of natural compounds in advancing safe and effective discovery of new drugs for the treatment of inflammation-related diseases.

Conclusion

This study demonstrates the high binding affinity of several phytochemicals to the NF-κB protein, particularly hypericin, withanolide, and diosmin, which showed superior docking scores compared to conventional inhibitors. These results, supported by existing literature, provide a scientific basis for further in vitro and in vivo evaluations of these compounds as natural NF-κB inhibitors. Their application could be pivotal in managing inflammation-driven diseases such as cancer, arthritis, and autoimmune disorders. It is also recommended that the natural sources of these compounds be explored further for therapeutic purposes while edible sources should be consumed regularly as a preventive mechanism against diseases.

Acknowledgements

Authors are thankful to World Bank, University of Port Harcourt, National Universities Commission, and the Association of African Universities for their support.

Conflict of interests: The authors declare that they have no conflict of interests.

Authors Contributions: All authors contributed towards the study design, docking study, interpretation and manuscript drafting.

References

Abiodun, M. O., Ekesiobi, A. O., & Onyenweife, L. C. (2024a). *Anti-trypanosoma activities, histological and kidney function effect of Garcinia kola seed extract and standard drug (Diaminizene aceturate) in trypanosomiasis disease induced rats*. Adeleke University Journal of Science, *3*(1), 238–259.

Abiodun, M. O., Ekesiobi, A. O., Onyenweife, L. C., & Bankole, O. T. (2024b). *Hepatotoxicity effect of Gongronemal latifollium aqueous leaf extract on some biomarker liver enzyme of albino Wister rats*. Dutse Journal of Pure and Applied Sciences, *10*(4a), 343–348. Retrieved from https://www.ajol.info

Abiodun, M. O., Onyenweife, L. C., & Ekesiobi, A. O. (2024c). *Exploring the in-vitro and in-vivo trypanosomal activities of Garcinia kola (bitter kola) seed aqueous extract using animal models: Trypanosomal*. ABUAD International Journal of Natural and Applied Sciences, *4*(2), 113–120. Retrieved from https://www.abuad.edu.ng

Adetuyi, B. O., Adebisi, O. A., Adetuyi, O. A., Ogunlana, O. O., Toloyai, P. E., Egbuna, C., Uche, C. Z., Khan, J., Adumanya, O., & Patrick-Iwuanyanwu, K. C. (2022). *Ficus exasperata* Attenuates Acetaminophen-Induced Hepatic Damage via NF-*κ*B Signaling Mechanism in Experimental Rat Model. *BioMed research international*, *2022*, 6032511. https://doi.org/10.1155/2022/6032511

Adetuyi, B. O., Adebisi, O. A., Adetuyi, O. A., Ogunlana, O. O., Toloyai, P.-E., Egbuna, C., Uche, C. Z., Khan, J., Adumanya, O. C. U., & Patrick-Iwuanyanwu, K. C. (2022). *Ficus exasperata* attenuates acetaminophen-induced hepatic damage via NF-κB signaling mechanism in experimental rat model. *BioMed Research International*, *2022*(1), 6032511. https://doi.org/10.1155/2022/6032511.

Aldosari, S., Egbuna, C., Albadrani, H., Alshareeda, A., Patrick-Iwuanyanwu, K. C., Kamoru, A. A., Imodoye, S. O., Onyeike, E. N., Jahan, S., & Khan, J. (2023). Multi-fold computational analysis to explore JAK2 and STAT5 potential inhibitors for modulation of cancer. BioMed Research International, 2023, Article ID 5513320. https://doi.org/10.1155/2023/5513320.

Anameze, C. I., Emmy-Egbe, I. O., Anyaegbunam, L. C., Ogomaka, I. J., Uba, B. O., Odumodu, O. A., Ezeigwe, C., Kamalu, N. L., Chukwubude, C. B., Akaogu, O., Ezekwueme, E., Emmy-Egbe, C.C., Obiefoka, O. S., Ezenwata, S. I. and Ilechukwu, C. C. (2023). Qualitative and quantitative Phytochemical Analysis of *Gongronema latifolium* Leaf Extract. *IPS journal of Applied Microbiology and Biotechnology*, 2 (1), 16-19.

Chiu FL, Lin JK. (2008). Tomatidine inhibits iNOS and COX-2 through suppression of NF-kappaB and JNK pathways in LPS-stimulated mouse macrophages. FEBS Lett. 9;582(16):2407-12. doi: 10.1016/j.febslet.2008.05.049. Epub 2008 Jun 9. PMID: 18544347.

Darwish, N., Sudha, T., Godugu, K., Bharali, D. J., Elbaz, O., El-Ghaffar, H., Azmy, E., Anber, N., & Mousa, S. A. (2019). Novel Targeted Nano-Parthenolide Molecule against NF-kB in Acute Myeloid Leukemia. *Molecules* (Basel, Switzerland), *24*(11), 2103. https://doi.org/10.3390/molecules24112103.

de Gregorio, E., Colell, A., Morales, A., & Marí, M. (2020). Relevance of SIRT1-NF-κB Axis as Therapeutic Target to Ameliorate Inflammation in Liver Disease. *International Journal of Molecular Sciences*. *21*(11), 3858. doi:10.3390/ijms21113858.

Egbuna C, Patrick-Iwuanyanwu KC, Onyeike EN, Khan J, Alshehri B. (2022). FMS-like tyrosine kinase-3 (FLT3) inhibitors with better binding affinity and ADMET properties than sorafenib and gilteritinib against acute myeloid leukemia: in silico studies. J Biomol Struct Dyn. 40(22):12248-12259. doi: 10.1080/07391102.2021.1969286.

Egbuna, C., Awuchi, C. G., Kushwaha, G., Rudrapal, M., Patrick-Iwuanyanwu, K. C., Singh, O., Odoh, U. E., Khan, J., Jeevanandam, J., Kumarasamy, S., Chukwube, V. O., Narayanan, M., Palai, S., Găman, M.-A., Uche, C. Z., Ogaji, D. S., Ezeofor, N. J., Mtewa, A. G., Patrick-Iwuanyanwu, C. C., Kesh, S. S., Shivamallu, C., Saravanan, K., Tijjani, H., Akram, M., Ifemeje, J. C., Olisah, M. C., & Chikwendu, C. J. (2021). Bioactive compounds effective against type 2 diabetes mellitus: A systematic review. *Current Topics in Medicinal Chemistry*, *21*(12), 1067–1095. https://doi.org/10.2174/1568026621666210325141205

Egbuna, C., Kumar, S., Ezzat, S.M., Ifemeje, J.C., & Saravanan, K. (Eds.) (2019). *Phytochemicals as Lead Compounds for New Drug Discovery*. 1st edn. Elsevier, Cambridge, USA, 378 pages, ISBN: 9780128178911.

Egbuna, C., Mishra, A. & Goyal, M.R. (Eds.) (2020). Preparation of Phytopharmaceuticals for the Management of Disorders. 1st edn. Academic Press (Elsevier), ISBN: 9780128202845.

Egbuna, C., Patrick-Iwuanyanwu, K. C., Onyeike, E. N., Khan, J., & Alshehri, B. (2022). FMS-like tyrosine kinase-3 (FLT3) inhibitors with better binding affinity and ADMET properties than sorafenib and gilteritinib against acute myeloid leukemia: In silico studies. *Journal of Biomolecular Structure and Dynamics*, *40*(22), 12248–12259. https://doi.org/10.1080/07391102.2022.2154564

Egbuna, C., Patrick-Iwuanyanwu, K. C., Onyeike, E. N., Khan, J., Aldosari, S., Jahan, S., Adedokun, K. A., Imodoye, S. O., Bello, I. O., Uche, C. Z., Noreen, S., & Ifemeje, J. C. (2025). Anti-proliferative effects of a polyherbal formulation on HL-60, HCT-116, and HeLa cell lines: A docking simulation and response surface design-aided study. *Frontiers in Chemistry*, *13*, 1487887. https://doi.org/10.3389/fchem.2025.1487887

Egbuna, C., Patrick-Iwuanyanwu, K. C., Onyeike, E. N., Uche, C. Z., Ogoke, U. P., Riaz, M., Ibezim, E. N., Khan, J., Adedokun, K. A., Imodoye, S. O., Bello, I. O., & Awuchi, C. G. (2023). Wnt/β-catenin signaling pathway inhibitors, glycyrrhizic acid, solanine, polyphyllin I, crocin, hypericin, tubeimoside-1, diosmin, and rutin in medicinal plants have better binding affinity and ADMET properties than standard anticancer drugs: In silico evidence for cancer therapeutics. *Food Science & Nutrition*, *11*(7), 4155–4169. https://doi.org/10.1002/fsn3.3347

Ekesiobi, A. O. (2025). Evaluation of the Aqueous Leaf Extract of Ocimum gratissimum (Scent Leaf) against Larvae of Musca domestica. *IPS Journal of Drug Discovery Research and Reviews*, *3*(1), 15–22. https://doi.org/10.54117/ijddrr.v3i1.26

Ekesiobi, A. O. ., Iheukwumere, C. M., Iheukwumere, I. H., Ejike, C. E., Ilechukwu, C. C., Dim, C. N., Ike, V. E., Okereke, F. O., & Ochibulu, S. C. (2025c). Natural Product-Based Therapies: Exploring the Potential of Ocimum gratissimum and Vitamin C Combination against Vibrio cholerae Infections. *IPS Interdisciplinary Journal of Biological Sciences*, *4*(3), 119–124. https://doi.org/10.54117/iijbs.v4i3.64

Ekesiobi, A. O., & Onebunne, C. C. (2025). Larvicidal Activity of Ethanolic Leaf Extract of Ocimum gratissimum (Scent Leaf) on Larvae of Musca domestica. *IPS Journal of Applied Microbiology and Biotechnology*, *4*(1), 106–114. https://doi.org/10.54117/ijamb.v4i1.46

Ekesiobi, A. O., Abiodun, M. O., & Onyenweife, C. L. (2024). *Pharmacological potential and effect of bitter kola aqueous seed extract compared with the standard drug in trypanosomiasis disease induced animal*. Funksec Here, *6*(2), 34–49.

Ekesiobi, A. O., Anene, C. C., Igbodika, M. C., Nwigwe, H. C., Emmy-Egbe, I. O., & Orji, N. M. (2017). *Evaluation of repellent and larvicidal activity of Cymbopogon citratus (lemon grass) against filarial vector, Culex quinquefasciatus*. African Journal of Education, Science and Technology (AJEST), *3*(4), 25–32. Retrieved from https://ajest.org

Ekesiobi, A. O., Iheukwumere, C. M., Iheukwumere, I. H., Ejike, C. E., Ilechukwu, C. C., Ike, V. E., Dim, C. N., Okereke, F. O., & Ochibulu, S. C. (2025a). Hyping the Inhibitory Activity of Xylopia aethiopica against Vibrio cholerae using Azithromycin. *IPS Journal of Basic and Clinical Medicine*, *2*(3), 93–98. https://doi.org/10.54117/ijbcm.v2i3.16

Ekesiobi, A. O., Iheukwumere, C., Iheukwumere, I. H., Ejike, C. E., Ilechukwu, C. C., Dim, C. N., Ike, V. E., Okereke, F. O., & Ochibulu, S. C. (2025b). Combination Therapy: Investigating the Combined Effects of Zingiber officinale and Azithromycin against Vibrio cholerae. *IPS Journal of Drug Discovery Research and Reviews*, *3*(2), 44–50. https://doi.org/10.54117/ijddrr.v3i2.34

Godwin, P., Baird, A. M., Heavey, S., Barr, M. P., O'Byrne, K. J., & Gately, K. (2013). Targeting nuclear factor-kappa B to overcome resistance to chemotherapy. *Frontiers in oncology*, *3*, 120. https://doi.org/10.3389/fonc.2013.00120.

Hassanein EHM, Althagafy HS, Baraka MA, Amin H. (2025). Hepatoprotective effects of diosmin: a narrative review. Naunyn Schmiedebergs Arch Pharmacol. 398(1):279-295. doi: 10.1007/s00210-024-03297-z. Epub 2024 Aug 21. PMID: 39167171; PMCID: PMC11787178.

He H, Xu C, Zheng L, Wang K, Jin M, Sun Y, Yue Z. (2020). Polyphyllin VII induces apoptotic cell death via inhibition of the PI3K/Akt and NF-κB pathways in A549 human lung cancer cells. Mol Med Rep. 21(2):597-606. doi: 10.3892/mmr.2019.10879. Epub 2019 Dec 12. PMID: 31974591; PMCID: PMC6947863.

Ifemeje, J. C., Egbuna, C., Uche, C. Z., Olisah, M. C., Ezeofor, N. J., Chikwendu, C. J., Orukwowu, U., Patrick-Iwuanyanwu, K. C., Nwaka, A. C., Tijjani, H., Banboye, L. C., Nnagbogu, C., Akram, M., Khan, J., & Saravanan, K. (2021). Effects of four local species of beans consumed in South-eastern Nigeria on selected biochemical indices of Wistar albino rats. *IPS Interdisciplinary Journal of Biological Sciences*, *1*(1), 1–7.

Iheukwumere, C. M., Ekesiobi, A. O., Iheukwumere, I. H., Okoli, U. O., Dim, C. N., Ejike, C. E., Ilechukwu, C. C., Ike, V. E., Okereke, F. O., Nwankwo, A. K., & Ochibulu, S. C. (2025a). Bacteriological Study of Urine Samples from Obstetric Patients in Onitsha Metropolis: Public Health Implications. *IPS Journal of Basic and Clinical Medicine*, *2*(3), 99–107. https://doi.org/10.54117/ijbcm.v2i3.17

Iheukwumere, I. H., Mmaduagha, C. P., Nwike, M. I., Iheukwumere, C. M., Ike, V. E., Obianom, A. O., Ihenatuoha, U. A., Igboanugo, E. U., Ekesiobi, A. O., Okereke, F. O., Obiefuna, O. H., Nnadozie, C. H., Oduoye, O. T., Nwakoby, N. E., Ilechukwu, C. C., Ochibulu, S. C., & Ejike, C. E. (2025b). Mitigating Newcastle Disease Virus Pathogenesis with Allicumin: A Potenting Approach. *IPS Journal of Advanced and Applied Biochemistry*, *1*(1), 11–18. https://doi.org/10.54117/ijaab.v1i1.59.

Jayab NA, Abed A, Talaat IM, Hamoudi R. (2024). The molecular mechanism of NF-κB dysregulation across different subtypes of renal cell carcinoma. J Adv Res. S2090-1232(24)00314-X. doi: 10.1016/j.jare.2024.07.030. Epub ahead of print. PMID: 39094893.

Kumar, S. & Egbuna, C. (Eds.) (2019). *Phytochemistry: In vitro and in silico updates*. 1st edn. *Springer Nature*, Singapore, 589 pages, ISBN: 978-981-13-6919-3. Link: https://link.springer.com/book/10.1007/978-981-13-6920-9.

Lin, Z., Wu, D., Huang, L., Jiang, C., Pan, T., Kang, X., & Pan, J. (2019). Nobiletin Inhibits IL-1β-Induced Inflammation in Chondrocytes *via* Suppression of NF-κB Signaling and Attenuates Osteoarthritis in Mice. *Frontiers in Pharmacology*. *10*, 570. doi:10.3389/fphar.2019.00570.

Liu YM, Cong S, Cheng Z, Hu YX, Lei Y, Zhu LL, Zhao XK, Mu M, Zhang BF, Fan LD, Yu L, Cheng ML. (2020). Platycodin D alleviates liver fibrosis and activation of hepatic stellate cells by regulating JNK/c-JUN signal pathway. Eur J Pharmacol. 5;876:172946. doi: 10.1016/j.ejphar.2020.172946. Epub 2020 Jan 26. PMID: 31996320.

Liu, T., Zhang, L., Joo, D., & Sun, S. C. (2017). NF-κB signaling in inflammation. *Signal transduction and targeted therapy*, *2*, 17023–. https://doi.org/10.1038/sigtrans.2017.23.

Lv H, Yu Z, Zheng Y, Wang L, Qin X, Cheng G, Ci X. (2016). Isovitexin Exerts Anti-Inflammatory and Anti-Oxidant Activities on Lipopolysaccharide-Induced Acute Lung Injury by Inhibiting MAPK and NF-κB and Activating HO-1/Nrf2 Pathways. Int J Biol Sci. 1;12(1):72-86. doi: 10.7150/ijbs.13188. PMID: 26722219; PMCID: PMC4679400.

Marrassini C, Davicino R, Acevedo C, Anesini C, Gorzalczany S, Ferraro G. (2011). Vicenin-2, a potential anti-inflammatory constituent of Urtica circularis. J Nat Prod. 24;74(6):1503-7. doi: 10.1021/np100937e. Epub 2011 May 24. PMID: 21608987.

Mehta, S. V., Shukla, S. N., & Vora, H. H. (2013). Overexpression of Bcl2 protein predicts chemoresistance in acute myeloid leukemia: its correlation with FLT3. *Neoplasma*, *60*(6), 666–675. https://doi.org/10.4149/neo_2013_085

Novelli M, Masiello P, Beffy P, Menegazzi M. (2020). Protective Role of St. John's Wort and Its Components Hyperforin and Hypericin against Diabetes through Inhibition of Inflammatory Signaling: Evidence from In Vitro and In Vivo Studies. Int J Mol Sci. 30;21(21):8108. doi: 10.3390/ijms21218108. PMID: 33143088; PMCID: PMC7662691.

Paur, I., Balstad, T.R., Kolberg, M., Pedersen, M.K., Austenaa, L.M., Jacobs, D.R., & Blomhoff, R. (2010). Extract of oregano, coffee, thyme, clove, and walnuts inhibits NF-kappaB in monocytes and in transgenic reporter mice. *Cancer Prevention Research*. *3*(5), 653–663. doi:10.1158/1940-6207.CAPR-09-0089

Qasaymeh, R. M., Rotondo, D., Oosthuizen, C. B., Lall, N., & Seidel, V. (2019). Predictive Binding Affinity of Plant-Derived Natural Products Towards the Protein Kinase G Enzyme of *Mycobacterium tuberculosis* (*Mt*PknG). *Plants (Basel, Switzerland)*, *8*(11), 477. https://doi.org/10.3390/plants8110477.

Saravanan K., Egbuna, C., Averal, H.I., Soundarapandian, K. Siddhayan, E. and Behadur, B. (Eds.) (2020). *Drug Development for Cancer and Diabetes*. 1st edn. Apple Academic Press/Taylor & Francis, 392 pages, ISBN 9781771888608.

Singla, R. K., Behzad, S., Khan, J., Tsagkaris, C., Gautam, R. K., Goyal, R., Chopra, H., & Shen, B. (2022). Natural kinase inhibitors for the treatment and management of endometrial/uterine cancer: Preclinical to clinical studies. *Frontiers in Pharmacology*, *13*, 801733. https://doi.org/10.3389/fphar.2022.801733.

Vlahopoulos, S.A. (2017). Aberrant control of NF-κB in cancer permits transcriptional and phenotypic plasticity, to curtail dependence on host tissue: molecular mode. *Cancer Biology & Medicine*. *14*(3), 254–270. doi:10.20892/j.issn.2095-3941.2017.0029.

Wang CL, Gao MZ, Gao DM, Guo YH, Gao Z, Gao XJ, Wang JQ, Qiao MQ. (2022). Tubeimoside-1: A review of its antitumor effects, pharmacokinetics, toxicity, and targeting preparations. Front Pharmacol. 15;13:941270. doi: 10.3389/fphar.2022.941270. PMID: 35910383; PMCID: PMC9335946.

White PT, Subramanian C, Motiwala HF, Cohen MS. (2016). Natural Withanolides in the Treatment of Chronic Diseases. Adv Exp Med Biol. 928:329-373. doi: 10.1007/978-3-319-41334-1_14. PMID: 27671823; PMCID: PMC7121644.

Zhao H, Zhao M, Wang Y, Li F, Zhang Z. (2016). Glycyrrhizic Acid Prevents Sepsis-Induced Acute Lung Injury and Mortality in Rats. J Histochem Cytochem. 64(2):125-37. doi: 10.1369/0022155415610168. Epub 2015 Sep 18. PMID: 26385569; PMCID: PMC4812678.

Appendices

Appendix I

List of compounds for molecular docking simulation

S/No	PubChem ID	Bioactive compounds
1.	91535337	5,3'-Dihydroxy-6,7,8,4'-tetramethoxyflavanone
2.	442793	[6]-Gingerol
3.	72512	9-Methoxyellipticine
4.	5280442	Acacetin or Linarigenin
5.	393472	Acetogenins (total annonaceous acetogenins)
6.	5280896	Abscisic acid
7.	72965	Ailanthone
8.	65036	Allicin
9.	5971	Allyl isothiocyanate
10.	11503749	Amooranin
11.	656516	Amygdalin
12.	167551	Anacardic acid
13.	5318517	Andrographolide
14.	No PubChem ID. 000100* Drawn	Annocatacin A
15.	No PubChem ID. 000200* Drawn	Annocatacin B
16.	10054251	Annocatalin
17.	10054746	Annohexocin
18.	157682	Annomurine A
19.	354398	Annonacin
20.	44259709	Annulatin
21.	637563	Anethole
22.	5280443	Apigenin
23.	9812534	Aplidine
24.	10698768	Arianacin
25.	558221	(R)-Ar-Turmerone
26.	5320351	Artemetin
27.	68827	Artemisinin
28.	6917864	Artesunate
29.	399491	Artocarpesin
30.	54670067	Ascorbic acid
31.	44583916	Asterosaponin-1
32.	5282102	Astragalin
33.	6710748	Avocatin B
34.	5280682	Ayanin
35.	5281303	Azadirachtin
36.	5281604	Azaleatin
37.	12308714	Azadiradione
38.	64982	Baicalin
39.	10337211	Bavachinin
40.	6456014	Belotecan
41.	21600402	Benzyl glucosinolate
42.	72326	Betulin
43.	275182	Berbamine
44.	2353	Berberine
45.	2355	Bergapten
46.	64971	Betulinic acid
47.	3080597	Bigelovin
48.	5280373	Biochanin A
49.	3778105	β-Boswellic acid acetate
50.	6473739	Bryostatin-1
51.	5281304	Bruceantin
52.	11124994	Bullatacin
53.	11101102	Burseran
54.	264	Butyric acid
55.	689043	Caffeic acid
56.	5281787	Caffeic acid phenethyl ester
57.	2519	Caffeine
58.	5280453	Calcitriol
59.	5280448	Calycosin
60.	6616	Camphene
61.	2537	Camphor
62.	24360	Camptothecin
63.	5944	Cantharidin
64.	10321	Capillin

65.	1548943	Capsaicin
66.	5315263	Casticin
67.	9064	Catechin (Cianidanol)
68.	65126	Carnosic acid
69.	6419725	α-Carotene
70.	5281515	β-Caryophyllene
71.	7439	Carvone
72.	122724	Celastrol
73.	637760	Chalcone
74.	1794427	Chlorogenic acid
75.	5281607	Chrysin
76.	5280666	Chrysoeriol
77.	637511	Cinnamaldehyde
78.	444539	Cinnamic acid
79.	638011	Citral
80.	311	Citric acid
81.	4485134	Cleistanthin
82.	6167	Colchicine
83.	9895264	Combretastatin
84.	12303802	Combretol
85.	5281233	Crocin
86.	5281235	β-Cryptoxanthin
87.	326	Cuminaldehyde (4-Isopropylbenzaldehyde)
88.	167812	Curcumenol
89.	442360	α -Curcumene
90.	969516	Curcumin
91.	6441391	Curdione (Germacr-1(10)-ene-5,8-dione)
92.	5281232	Crocetin
93.	15224382	Cycloartocarpesin
94.	442972	Cyclopamine
95.	119093	Cynaropicrin
96.	128861	Cyanidin
97.	5281708	Daidzein
98.	68245	Delphinidin
99.	73440	Dehydroleucodin
100.	220401	Demecolcine
101.	16590	Diallyl disulphide
102.	11617	Diallyl sulphide
103.	12232	Dimethyl disulphide
104.	5281612	Diosmetin
105.	5281613	Diosmin
106.	8118	Dipropyl sulphide
107.	5281855	Ellagic acid
108.	3213	Ellipticine
109.	42723	Elliptinium (derivative of the alkaloid ellipticine)
110.	3220	Emodin
111.	65064	Epigallocatechin gallate
112.	105111	Epipodophyllotoxin
113.	6476031	Escin IB
114.	5281417	Esculin
115.	259331	Estramustine
116.	36462	Etoposide
117.	3314	Eugenol
118.	5317291	Eupatolitin
119.	44259636	Europetin
120.	445858	Ferulic acid
121.	5281614	Fisetin
122.	5356121	Flavokawin B
123.	5287969	Flavopiridol (Alvocidib)
124.	92023653	Fucoidan
125.	5281239	Fucoxanthin
126.	400072	Galangal acetate
127.	96539	Gardenin B
128.	370	Gallic acid
129.	12004512	Gedunin
130.	5280961	Genistein
131.	5281617	Genkwanin
132.	637566	Geraniol
133.	101697178	Gigantetrocin
134.	9909368	Ginkgolide-A
135.	65243	Ginkgolide-B

136.	9867869	Ginkgolide-C
137.	24721483	Ginkgolide-J
138.	9918693	Ginsenoside Rg3
139.	124052	Glabridin
140.	5464032	Gluconasturtin
141.	9548634	Glucoraphanin
142.	656498	Glucotropaeolin
143.	5317750	Glycitein
144.	14982	Glycyrrhizic acid
145.	44593503	Goniothalamicin
146.	3503	Gossypol
147.	400772	Halofuginone
148.	276389	Harringtonine,
149.	23205	Helenalin
150.	72281	Hesperetin
151.	10082188	Hispolon
152.	73635	Homoeriodictyol
153.	285033	Homoharringtonine (Omacetaxine mepesuccinate)
154.	72303	Honokiol
155.	5281520	α -Humulene
156.	3663	Hypericin
157.	13785311	Hypoxoside
158.	10614148	Icariside D_2
159.	10212	Imperatorin
160.	6096870	Indicaxanthin
161.	10177	Indirubin
162.	3712	Indole-3-carbinol (I3C)
163.	15560333	Intermedeol
164.	638014	β-Ionone
165.	5464170	Irigenin
166.	5281255	Isobavachalcone
167.	390361	Isochamaejasmin
168.	638278	Isoliquiritigenin
169.	68079	Isopimpinellin
170.	5281654	Isorhamnetin
171.	162350	Isovitexin
172.	5281166	Jasmonic acid
173.	10326193	Javoricin
174.	102316418	Jatrophane IV
175.	442882	Justicidin B
176.	5280863	Kaempferol
177.	100633	Karanjin
178.	20345	Kinetin riboside
179.	3885	β-Lapachone
180.	102401707	Laricitin
181.	5318998	Licochalcone A
182.	5280450	α -Linoleic acid
183.	5280445	Luteolin
184.	446925	Lycopene
185.	72300	Magnolol
186.	159287	Malvidin
187.	5281650	α -Mangostin
188.	25147451	Mannan
189.	160490	Matteucinol
190.	91466	Matrine
191.	5281828	Maytansine
192.	5281929	Methyl Jasmonate
193.	24832075	Mezerein
194.	169581	Miconidine
195.	9415	Monocrotaline
196.	160679561	Montamine
197.	3035657	Muricatacin
198.	44560014	Muricatetrocin
199.	133072	Muricatocin B
200.	11124830	Muricin A
201.	31253	β-Myrcene
202.	5281672	Myricetin
203.	4276	Myristicin
204.	932	Naringenin
205.	442428	Naringin
206.	442439	Neohesperidin

207.	5317284	Nepetin
208.	108058	Nimbin
209.	12313376	Nimbolide
210.	72344	Nobiletin
211.		Noscapine
212.	332427	Lariciresinol
213.	5318998	Licochalcone A
214.	73636	Liriodendrin
215.	114829	Liquiritigenin
216.	259846	Lupeol
217.	100771	Obovatol
218.	5320287	Ombuin
219.	5321010	Oridonin
220.	5320315	Oroxylin A
221.	5281677	Pachypodol
222.	7251185	Parthenolide
223.	637542	P-Coumaric acid (4-Hydroxycinnamic acid)
224.	36314	Paclitaxel
225.	6918506	Peloruside A
226.	6440892	Picroside I
227.	638024	Piperine
228.	637858	Piperlongumine
229.	10995620	Pervilleine
230.	101844812	Phanginin D
231.	219100	Phenoxodiol (Idronoxil)
232.	442070	Phorbol
233.	11558520	Phoyunbene B
234.	130796	Picrocrocin
235.	91508	α -Pinene
236.	73399	Pinoresinol
237.	162859	Platycodin
238.	10205	Plumbagin
239.	10607	Podophyllotoxin
240.	72960700	Polyphyllin
241.	4871	Pomiferin
242.	5281803	Pratensein
243.	135455579	Prodigiosin
244.	9920281	Protopanaxadiol
245.	5281804	Prunetin
246.	5353911	Psi-tectorigenin
247.	6199	Psoralen
248.	101324849	Pterokaurane
249.	5281727	Pterostilbene
250.	5280343	Quercetin
251.	445154	Resveratrol
252.	5352005	Retusin
253.	5281691	Rhamnetin
254.	10168	Rhein
255.	13422573	Rohitukine
256.	160355	(R)-Roscovitine (Seliciclib)
257.	5281792	Rosmarinic
258.	5280805	Rutin
259.	61041	Safranal
260.	3085092	Salinomycin
261.	73571	Sakuranetin
262.	5280460	Scopoletin
263.	5281697	Scutellarein
264.	9917980	Secoisolariciresinol diglucoside
265.	442872	Securinine
266.	479503	Shikonin
267.	145659	Sinensetin
268.	23682211	Sinigrin (Allyl glucosinolate)
269.	11787114	Silvesterol
270.	5213	Silymarin
271.	11376469	Solamin
272.	262500	Solanine
273.	509245	Sophoraflavanone B
274.	1268276	Sterubin (7-O-Methyleriodictyol)
275.	5280794	Stigmasterol
276.	222284	β-sitosterol
277.	5350	Sulforaphane

278.	51683	Swainsonine
279.	7172	Synephrine
280.	5281699	Tamarixetin
281.	68077	Tangeretin
282.	875	Tartaric acid
283.	215159	Taspine
284.	9548828	Taxane
285.	452548	Teniposide
286.	476861	Terameprocol
287.	443162	α -Terpineol
288.	73078	Tetrandrine
289.	10281	Thymoquinone
290.	122206355	Tinosporin A
291.	65576	Tomatidine
292.	60700	Topotecan
293.	5281701	Tricetin
294.	5570	Trignolline
295.	51346132	Tubeimoside-1
296.	5281426	Umbelliferone
297.	135515151	Undecylprodigiosin
298.	64945	Ursolic acid
299.	8468	Vanillic acid
300.	5281800	Verbascoside (Acteoside)
301.	442664	Vicenin-2
302.	13342	Vinblastine
303.	5978	Vincristine
304.	40839	Vindesine
305.	6918295	Vinflunine (Javlor)
306.	5311497	Vinorelbine
307.	5280441	Vitexin
308.	74947464	Vitisin B
309.	479756	Wikstromol ((+)-Nortrachelogenin)
310.	53477765	Withanolide
311.	5281703	Wogonin
312.	629965	Zapotin
313.	92776	Zingiberene

Appendix II

List of standard inhibitors for molecular docking study with their respective PubChem IDs

S/No	Name of Inhibitor/drug	PubChem ID	Target
1.	Sorafenib	216239	FLT3
2.	Gilteritinib	49803313	FLT3
1.	Ivosidenib	71657455	IDH1
2.	Enasidenib	89683805	IDH2
3.	Ipatasertib	24788740	AKT1
4.	A-674563	11314340	AKT1
5.	Wortmannin	312145	PI3K
6.	LY294002	3973	PI3K
7.	Rapamycin	5284616	mTOR
8.	Temsirolimus	6918289	mTOR
9.	T4K-733	24963252	MEK1
10.	Selumetinib	10127622	MEK1
11.	Trametinib	11707110	MEK1
12.	Cobimetinib	16222096	MEK1
13.	Fedratinib	16722836	JAK2
14.	Gandotinib	46213929	JAK2
15.	Baricitinib	44205240	JAK2
16.	AC-4-130	154701370	STAT5
17.	BP-1-108	56663448	STAT5
18.	Daurismo (Glasdegib)	25166913	SMO
19.	Sonidegib	24775005	SMO
20.	IWP -4	2155264	β-Catenin
21.	Cardionogen 1	663145	β-Catenin
22.	Dithiocarbamate	3037131	NF-kB
23.	Disulfiram	3117	NF-kB
24.	Olmesartan	158781	NF-kB
25.	Venetoclax (ABT-199)	49846579	Bcl-2
26.	Abt-737 (ABT-737)	11228183	Bcl-2, Bcl-xL and Bcl-w
27.	Navitoclax (ABT-263)	24978538	Bcl-2
28.	Obatoclax	11404337	Inhibitor of the Bcl-2 family of proteins
29.	Guadecitabine	135564655	DMNT1
30.	Azacitidine	9444	DMNT1
31.	Vorinostat	Vorinostat	HDAC
32.	Pracinostat	49855250	HDAC
33.	2,4-pyridinedicarboxylic acid	10365	HDM
34.	Disulfiram	3117	HDM
35.	AS8351	135400486	HDM
36.	LTK-14	25226432	HAT
37.	C646	1285941	HAT
38.	Garcinol	5281560	HAT
39.	Geldanamycin	5288382	Hsp90
40.	Radicicol	6323491	Hsp90
41.	Tanespimycin	6505803	Hsp90
42.	Luminespib	135539077	Hsp90
43.	MKT-077	6912334	Hsp70
44.	VER-155008	25195348	Hsp70
45.	Apoptozole	24894064	Hsp70
46.	Indazole	9221	CYP2E1
47.	4-Methylpyrazole	3406	CYP2E1
48.	Disulfiram	3117	CYP2E1
49.	Idarubicin	42890	Topoisomerase II poison (Prevents DNA unwinding)
50.	Daunorubicin	30323	Interacts with DNA by intercalation and inhibition of macromolecular biosynthesis