iJRASET
International Journal For Research in Applied Science and Engineering Technology

# INTERNATIONAL JOURNAL FOR RESEARCH

IN APPLIED SCIENCE & ENGINEERING TECHNOLOGY

**Volume:** 14 **Issue:** III **Month of publication:** March 2026

**DOI:** https://doi.org/10.22214/ijraset.2026.78579

www.ijraset.com

Call: 08813907089 | E-mail ID: ijraset@gmail.com

International Journal for Research in Applied Science & Engineering Technology (IJRASET)
*ISSN: 2321-9653; IC Value: 45.98; SJ Impact Factor: 7.538*
*Volume 14 Issue III Mar 2026- Available at www.ijraset.com*

# Drug-Likeness and ADMET Evaluation of Garlic Non-Sulfur Compounds: A Virtual Screening Approach

Manisha[1], Khushboo[2], Neera Raghav[3], Nitika Mor[4]
[1, 2, 4]*Department of Chemistry, Baba Mastnath University, Asthal Bohar, Rohtak (India) –124021*
[3]*Department of Chemistry, Kurukshetra University, Kurukshetra (India) –136119*

***Abstract:*** ***In modern drug discovery, where some of the most important aspects remain lead compound identification and screening; computational approaches therefore stand out. Here, we systematically compiled and evaluated a library of 18 phytoconstituents from non-sulfur compounds of garlic. The compounds were first screened for their drug-likeness according to Lipinski's Rule of Five and ADMET predictions of the parameters that greatly affect the pharmacological activity of a drug candidate were investigated. All the compounds were meticulously studied for their pharmacokinetic and pharmacodynamic profiles which were compared with standard anticancer drug paclitaxel. These findings suggest that among 18 investigated compounds, gamma-octalactone showed optimal characteristics and was identified as the best candidate for future drug development.***

***Keywords: ADMET predictions, garlic, phytoconstituents, drug development.***

## I. INTRODUCTION

Garlic (Allium sativum) is a beneficial bulbile plant having multifarious biological actions not only limited to its well explored sulfuraceous compounds but also augmented by the non-sulfide bioactive substances present in it. Among these, phenolic acids, flavonoids, polysaccharides, saponins, fructans, steroidal glycosides and organo- nitrogenous components may all play a role adding to the overall pharmacological profile of garlic. Increasing evidence suggests that these non-sulfur components are essential mediators of multiple biological pathways related to human health [1-3].

Two non-sulfur compounds of garlic exhibit significant antioxidant activity, largely through free-radical scavenging and chelation of metal ions, as well as through regulation of endogenous anti-oxidative defense systems. Among them, phenolic acids and flavonoids have special ability to reduce oxidative stress level through preventing lipid peroxidation process as well as protecting macromolecules in the cells against oxidation. Furthermore, polysaccharides and saponins derived from garlic possess potent anti-inflammatory and immunomodulatory activities which are mediated by inhibition of pro-inflammatory cytokines and modulation of inflammatory signalling pathways [4-6].In addition to their antioxidant and anti-inflammatory properties, bioactive non-sulfur component of garlic has more recently been linked with anticancer potential [7]. These sulfur-independent molecular mechanisms have been verified in preclinical studies and shown to modulate critical oncogenic pathways by suppressing the growth of cancer cells, promoting apoptosis and inducing cell-cycle arrest. Additionally, indirect antitumor activities have been documented including immune system activation and inhibition of angiogenesis and processes associated with metastasis [8-9].

Non-sulfur components of garlic exhibit antimicrobial effects against a wide range of disease-causing microorganisms, mainly by compromising the structural integrity of the microbes and affecting critical metabolic processes. In addition, fructans and other polysaccharide derivatives produce prebiotic effects that maintain the balance of gut microbiota and modulating metabolism and immune function indirectly [10-11].

Despite the anticancer potential shown by garlic non-sulfur compounds, their applicability for clinical use as stand-alone therapeutic agents remains low due to its low bioavailability [12-15]. As such, these bioactive components are best referred to as chemo-preventive agents or adjunctive therapeutic candidates in formulations-based strategies focused on improved bioavailability and reduced toxicity along with synergistic actions with established therapies for cancer. Their translational and therapeutic potential shall be substantiated by further careful clinical investigations[16-18].

In this study, 18 non-sulfur phytoconstituents of Allium sativum (garlic) library was generated and thoroughly screened for in silico ADMET studies.

Identification of the most promising non-sulfur bioactive compound was based on extensive filtering of pharmacokinetic properties, drug-likeness criteria and molecular interaction parameters. The central aim of this study is to identify lead molecule which can be a drug-like candidate.

## II. METHODS

### A. *Designing of garlic non sulfur compounds library*

Allium sativum (garlic) a rich source of diverse bioactive phytochemicals including phenolic acids, flavonoids, saponins, fructans and other non-sulfur constituents that fill garlic out its pharmacological activity. The structural diversity of these compounds, especially at the level of functional group substitutions and molecular conformations, is a key determining factor in their biosignificant activities (e.g., anticancer, anti-inflammatory, antioxidant and neuroprotective effects). In this study, we developed a curated library of 18 garlic non sulfur bioactive compounds and performed systematic in silico screening to filter anticancer lead molecules from the compound library. This joint screening strategy combined drug-likeness evaluation, ADME profiling and toxicity prediction in order to select compounds with good behavior concerning pharmacokinetics and safety. Paclitaxel is a clinically proven anticancer medicine, and was used as a reference standard for the computation results. This integrative computational framework fosters a comprehensive comparison of structure-activity relationships and offers a rationale to optimize the anticancer potential of garlic-derived MOXs as safe, natural-product-based therapeutic candidates [19-20].

### B. *Probable drug properties*

The Molinspiration online web server, a java-based prediction tool that assess the molecular properties was used to check drug-likeness nature of compounds included in the designed garlic phytochemical library. Molecular weight, miLogP (octanol/water partition coefficient), hydrogen bond acceptors (HBA), hydrogen bond donors (HBD), topological polar surface area (TPSA), number of rotables bonds (nRotB) and molecular volume were the key physicochemical parameters evaluated. Each of the 18 non sulfur compounds (derived from garlic) wasanalyzed one by one with individual submission of their SMILES representations or manually constructed and modeled using ChemDraw software coupled to Chem3D (version 18 for Windows, PerkinElmer Informatics). The authorized PerkinElmer Download provided access to the software suite. This systematic analysis gave important information on the pharmacokinetic potentiality, drug-likeness properties and medicinal importance of selected garlic derived non sulfur bioactive compounds [21-22].

### C. *Bioactivity score*

The bioactivity potential of garlic-derived non-sulfur compounds was assessed using in silico bioactivity scoring to predict their likelihood of interacting with key biological target classes. The evaluated parameters included G-protein-coupled receptor (GPCR) ligand activity, ion channel modulation, kinase inhibition, nuclear receptor binding affinity, protease inhibition, and general enzyme inhibitory activity. Several non-sulfur constituents demonstrated favorable bioactivity scores, indicating moderate to high biological relevance. In particular, compounds exhibiting enhanced enzyme and protease inhibitory potential are of significant interest due to their established roles in cancer progression, inflammatory processes, and aberrant cellular signaling. Compounds with bioactivity scores greater than -0.5 were classified as biologically active, while those with values between -0.5 and 0.0 were considered moderately active. Collectively, these findings highlight the multitarget pharmacological potential of garlic non-sulfur phytochemicals and support their further exploration as prospective anticancer agents [23].

### D. *ADME Properties*

The in silico ADME analysis was performed related to the ADME properties of the respective compounds through SwissADME, vNN-ADMET and ADMET SAR platforms. All compounds showed favorable physicochemical properties with respect to drug-likeness parameters based on Lipinski's rule of five, which highlights aqueous solubility and permeability as fundamental measures for predicting oral bioavailability, such as appropriate molecular weight (g/mol), lipophilicity (LogP) and hydrogen bond donor and acceptor counts as well as polar surface area. The other non-sulfur constituents were predicted to possess adequate gastrointestinal absorption and bioavailability with minimal orthogonal deviations from parameters of drug-likeness [24] according to Swiss ADME predictions. In addition, the analysis data based on VNN-ADMET and ADMET SAR also indicated that P450 metabolic clearance was moderate to low and they do not present any toxicity risks.

The combined ADME profiling highlights the beneficial pharmacokinetic properties of non-sulfur compounds of garlic that can reinforce their possible use as promising lead candidates in anticancer drug discovery and development.

*E. Toxicity profile*

In order to determine safety and pharmacological suitability, the ADMET SAR in silico prediction platform was used to systematically investigate the toxicity profiles of non-sulfur compounds derived from garlic. Some toxicological endpoints evaluated included ames mutagenicity, carcinogenicity, acute oral toxicity, hepatotoxicity and human ether-à-go-go-related gene (hERG) inhibition. The analyzed compounds were mostly predicted to be non-mutagenic, non-carcinogenic and low in acute toxicity with very little potential for hepatotoxic effects [25]. Moreover, most constituents exhibited a low probability of HERG channel inhibition translated to a lower risk of cardiotoxicity. Taken together, these results suggest that garlic non-sulfur phytochemicals have a benign toxicity profile, supporting their potential as viable lead candidates in the development of anticancer drugs.

Table 1: Molinspiration (Physiochemical parameters and druglikeness attributes of garlic derived nonsulfur compounds)

| S.N. | Compound | miLogP | TPSA(A) | Atoms | MW (kDa) | nOH | nOHNH | Nrotb | Volume(g/mol) | Violation |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Paclitaxel | 5.19 | 221.31 | 63 | 867.95 | 15 | 4 | 14 | 772.84 | 3 |
| 2 | 2,5-dimethyl pyridine | 1.20 | 12.89 | 8 | 107.16 | 1 | 0 | 0 | 113.01 | 0 |
| 3 | 2,6-dimethyl pyrazine | 0.67 | 25.78 | 8 | 108.14 | 2 | 0 | 0 | 108.85 | 0 |
| 4 | 2-methyl benzaldehyde | 2.13 | 17.07 | 9 | 120.15 | 1 | 0 | 1 | 119.59 | 0 |
| 5 | 5-ethyl2-methyl pyridine | 1.67 | 12.89 | 9 | 121.18 | 1 | 0 | 1 | 129.81 | 0 |
| 6 | 2-acetylfuran | 1.09 | 30.21 | 8 | 110.11 | 2 | 0 | 1 | 101.16 | 0 |
| 7 | Cyclopentanone | 0.89 | 17.07 | 6 | 84.12 | 1 | 0 | 0 | 87.98 | 0 |
| 8 | Heptadecene | 8.53 | 0.00 | 17 | 238.46 | 0 | 0 | 14 | 292.15 | 1 |
| 9 | 3-penten-2-one | 0.75 | 17.07 | 6 | 84.12 | 1 | 0 | 1 | 92.16 | 0 |
| 10 | 5-hexen-2-one | 1.28 | 17.07 | 7 | 98.14 | 1 | 0 | 3 | 109.51 | 0 |
| 11 | 4-pentenal | 1.56 | 17.07 | 6 | 84.12 | 1 | 0 | 3 | 92.95 | 0 |
| 12 | 1-pentadecene | 7.68 | 0.00 | 15 | 210.41 | 0 | 0 | 12 | 258.55 | 1 |
| 13 | Ethylbut-2- enoate | 1.45 | 26.30 | 8 | 114.14 | 2 | 0 | 3 | 117.94 | 0 |
| 14 | Gamma octalactone | 1.11 | 26.30 | 10 | 142.20 | 2 | 0 | 3 | 147.16 | 0 |
| 15 | 2,4-Hexadienaldehyde | 1.55 | 17.07 | 7 | 96.13 | 1 | 0 | 2 | 103.01 | 0 |
| 16 | 2,3-dimethyl pyrazine | 0.67 | 25.78 | 8 | 108.85 | 2 | 0 | 0 | 108.85 | 0 |
| 17 | 2,3,5-trimethyl pyrazine | 0.90 | 25.78 | 9 | 122.17 | 2 | 0 | 0 | 125.41 | 0 |
| 18 | Cholesterol | 7.62 | 20.23 | 28 | 386.86 | 1 | 1 | 5 | 423.13 | 1 |
| 19 | Ethylbutyrate | 1.68 | 26.30 | 8 | 116.16 | 2 | 0 | 5 | 124.13 | 0 |

## III. RESULT AND DISCUSSION

The recurring theme of computational approaches is now becoming a necessity in contemporary drug discovery and development, successfully accelerating the process of identifying novel therapeutic candidates from extensive chemically diverse libraries while substantially reducing experimental time, labor, and cost. Having access to structures of target biomolecules will set stage for the large-scale structure-based virtual screening and molecular docking of lead compounds corresponding to early exclusion of non-viable candidates that enhance the precision as well as performance of drug selection process.

*ISSN: 2321-9653; IC Value: 45.98; SJ Impact Factor: 7.538*
*Volume 14 Issue III Mar 2026- Available at www.ijraset.com*

Herein, 18 Non sulfonate bioactive agents of garlic (Allium sativum) molecule were computationally investigated using in silico tools; the molecule's drug-likeness properties Molinspiration, SwissADME, vNN-ADMET and ADMET-SAR,iGEMDOCK and discovery studio visualiser to assess; pharmacokinetic characteristics and safety profiles.

### *A. Physiochemical screening of garlic derived non sulfur compounds*

Physicochemical features of non-sulfur garlic-related bioactive compounds were thoroughly scrutinized to assess their drug-likeness characteristics. Classical computational tools were applied to learn crucial molecular descriptors (pharmacophore features), namely: molecular weight, lipophilicity, hydrogen bond donors and acceptors, topological polar surface area (TPSA) and conformational flexibility. This analysis was important, as it yielded crucial information regarding parameters influencing molecular stability in the gastrointestinal environment, membrane permeability and oral bioavailability of a given compound, thus enabling rational prioritization for subsequent pharmacokinetic and biological studies [26]. For these purposes, a virtual library of eighteen garlic-originated non-sulfur compounds was constructed, and their physicochemical properties (miLogP; molecular weight; number of rotatable bonds; hydrogen bond) were calculated through the online Molinspiration platform (Table 1). The drug-likeness was determined using Lipinski's Rule of Five (RO5) and paclitaxel was used as a reference standard for comparative pharmacokinetic and pharmacodynamic profiling [27]. According to RO5, four compounds showing one or more rules violations were discarded and the other fourteen satisfying criteria of oral drug-likeness were carried forward for further in silico & experimental studies.

#### *1) miLogP*

A predicted lipophilicity descriptor computing using Molinspiration server and determining octanol-water partition coefficient of compound. This parameter is used in drug discovery for evaluating drug-likeness, membrane permeability, oral bioavailability and ADME characteristics representing one of the key parameters of Lipinski's Rule of Five [28]. Three compounds were removed based on the logP value (if it exceeds from 5), remaining fifteen compounds follows this rule according to RO5 and these compounds have been taken up for further study.

#### *2) Molecular weight*

Molecular weight (computed using Molinspiration server) is an important physicochemical property for drug discovery to check the drug-likeness and pharmacokinetic property in these compounds [29]. Lipinski's Rule of Five states that M.W. of the compounds should be less than 500. As the molecules have not more than 500 Da molecular weight none of the compound will be excluded from this property.

#### *3) Rotational bonds*

Bond rotors, defined as single non-ring bonds between heavy atoms are key determinants of molecular flexibility, and thereby exert strong influence on ligand-target interactions [30]. Lipinski's Rule of Five states that the ideal molecular configuration for increased oral bioavailability is less than 10 rotatable bonds. All garlic-derived non-sulfur compounds from the current library except two (8,12) conform to this parameter; suggesting privileged structural features decisive for bioavailability and biological activity and inviting their evaluations for oral drug development.

#### *4) Number of hydrogen bond donor and acceptors*

Hydrogen bond donors (HBDs) and acceptors (HBAs) play a pivotal role in drug discovery in relation to a compound's solubility, permeability and target interaction.[1] The ideal structure that has >1040 MW for oral bioavailability according to Lipinski's Rule of Five indicates ≤5 HBDs, and ≤10 HBAs, as ↑donors or acceptors ↓membrane permeability and would eventually lower absorption [31]. HBDs and HBAs are well balanced to improve drug-likeness and/or early-stage development optimization. All of compounds except (18) fit the criteria of hydrogen bonds. Of the 18 tested compounds, 14 compounds obeyed both Lipinski's Rule of Three and Five indicating drug-likeness. The fourteen compounds selected were further assessed in terms of their ADME properties and safety profile.

### *B. Bioactivity score*

Further evaluation was performed on the fourteen compounds following Lipinski's rule. Bioactivity scores from the molinspiration server give a quantitative prediction of a compounds ability to interact with important biological targets (GPCRs, ion channels, kinases, nuclear receptors, protease and enzymes) represented in table2 [32].

The results showed that most of compounds have been adopted as negative value (< -0.50) was due to their predicted bioactivity except selected compounds of garlic non-sulfur compounds. Of them Gamma-octalactone has the highest score indicating moderate interaction potential and had physiological effects through its interaction with GPCR, nuclear receptors and inhibition of protease and other enzymes. Individual compound bioactivities for the analytes were as follows:

*1) GPCR ligands*

Across the membrane, GPCRs form a large and diverse family of proteins that modulate physiogically important pathways such as neurotransmission, hormonal signaling and immune responses. GPCR ligands may be either endogenous in the form of hormones or neurotransmitters or synthetic, e.g. drugs aiming to modulate receptor activity. Determining compounds that preferentially bind to certain GPCRs with high specificity and affinity is crucial in drug discovery to modulate disease-associated signaling pathways. Due to their key roles in many diseases and main focus on the pharmacologic aspects, GPCRs are important targets in drug discovery [33]. Based on molinspiration server GPCR ligand bioactivity scores all selected compounds showed value less than -0.50 denoting lack of predicted GPCR activity. Gamma-octalactone possessed a relatively higher score for GPCR ligands but still remained in the inactive range, indicating that these compounds are not suitable for use as GPCR-mediated pharmacological agents.

*2) Ion channel modulator*

Ion channel modulators are a class of compounds that modulate the function of ion channels, which are membrane-bound proteins that control the flow of ions across membranes—including sodium, potassium, calcium and chloride. These channels are critical for fundamental physiological processes, most notably electrical signaling in neurons and muscle contraction, as well as cellular homeostasis. Depending on their function, they can be agonists that increase channel activity or antagonists that block ion conductance and alter the flow of ions in and out of cells. Changes in ion transport can have a profound effect on cellular function, underscoring the therapeutic potential of ion channel modulators in the therapy of neurological disorders, cardiac arrhythmias or chronic pain [34]. All the selected compounds exhibited significant results as ion channel modulator except standard drug Paclitaxel. The ion channel modulator (table 2) has the highest gamma-octalactone.

Table 2: Molinspiration (Bioactivity score of garlic derived non sulfur compounds)

| S.N. | Compounds | GPCR ligand | Ion channel modulator | Kinase inhibitor | Nuclear receptor ligand | Protease inhibitor | Enzyme inhibitor |
|---|---|---|---|---|---|---|---|
| 1 | Paclitaxel | -2.87 | -3.53 | -3.56 | -3.25 | -2.23 | -3.00 |
| 2 | 2,5-dimethyl pyridine | -3.01 | -2.63 | --3.07 | -3.74 | -3.33 | -2.81 |
| 3 | 2,6-dimethyl pyrazine | -2.90 | -2.48 | -2.90 | -3.57 | -3.22 | -2.65 |
| 4 | 2-methyl benzaldehyde | -2.33 | -1.80 | -2.40 | -2.20 | -2.91 | -1.91 |
| 5 | 5-ethyl-2-methyl pyridine | -1.97 | -1.28 | -2.21 | -2.34 | -2.30 | -1.53 |
| 6 | 2-acetyl furan | -3.63 | -3.42 | -3.69 | -3.73 | -3.70 | -3.22 |
| 7 | Cyclopentanone | -3.58 | -3.58 | -3.42 | -3.79 | -3.47 | -3.29 |
| 8 | 3-penten-2-one | -3.78 | -3.66 | -3.96 | -3.57 | -3.65 | -3.48 |
| 9 | 5-hexen-2-one | -3.66 | -3.51 | -3.91 | -3.31 | -3.59 | -3.19 |
| 10 | 4-pentenal | -3.53 | -2.90 | -3.77 | -3.41 | -3.04 | -3.02 |
| 11 | Ethyl but-2-enoate | -3.51 | -2.89 | -3.74 | -3.01 | -3.20 | -2.89 |
| 12 | Gamma-octalactone | -0.80 | -0.55 | -1.28 | -0.75 | -0.94 | -0.23 |
| 13 | 2,4-hexadienaldehyde | -3.55 | -3.07 | -3.70 | -3.06 | -2.92 | -3.03 |
| 14 | 2,3-dimethyl pyrazine | -2.99 | -2.61 | -3.21 | -3.55 | -3.25 | -2.84 |
| 15 | 2,3,5-trimethyl pyrazine | -1.96 | -1.43 | -2.29 | -2.97 | -2.40 | -1.65 |

*3) Kinase inhibitor*

Kinase inhibitorA kinase inhibitor is defined as a compound that inhibits the activity of kinases, which are enzymes that catalyzef the transfer of phosphate groups (usually from ATP) to target proteins in a process called phosphorylation. Phosphorylation is a key step in the control of many cellular processes such as cell growth, proliferation, differentiation and survival. Aberrant overexpression or hyperactivation of kinases leading to uncontrolled cellular proliferation and tumor progression is observed in a number of malignancies. Through the selective inhibition of these enzymes, kinase inhibitors target dysregulated signaling pathways to slow disease progression [35]. As a result, kinase inhibitors have emerged as a critical class of targeted agents for cancer therapy. Data shows that out of 14 selected compounds, gamma-octalactone demonstrates the least negative value of kinase inhibition.
This suggests that gamma-octalactone possesses higher potential of kinase inhibition as compared to paclitaxel and few other selected compounds.

*4) Nuclear receptor ligands*

It is a class of intracellular proteins without which nuclear receptors bind to their target genes, in response to hormonal and environmental signals. These ligands can be from natural sources, such as thyroid hormones, retinoids and steroid hormones including estrogen and testosterone, or they can be organic compounds that have been deliberately designed to selectively bind nuclear receptors. Following ligand binding, the receptor-ligand complex translocates into the nucleus and interacts with specific DNA response element(s) to modulate transcription. This is a fundamental regulatory mechanism that underpins many biological functions, including metabolism, the reproductive systems, and cellular development/differentiation [36]. Because of their significant involvement in pathological conditions such as cancer, metabolic disorders, and inflammatory diseases, nuclear receptors have emerged as crucial components in the drug discovery process. According to the table provided on molinspiration server, glyphioning and non-sulfur compounds of garlic are not highly active towards nuclear receptors. Beta-hydroxy-octanoic acid shows the maximum value among all the selected compounds comparative to standard drug paclitaxel and rest of compounds.

*5) Protease inhibitors*

Protease inhibitors inhibit proteases that hydrolyze peptide bonds and are responsible for protein degradation. ` These enzymes partake in several physiological processes like digestion, immune modulation, and cellular regulation. However, dysregulated activity has been linked to other disease states such as viral infections, neoplasia and inflammatory disorders [37]. Protease inhibitors are also innovated in treatment of hypertension and cancer. Protease inhibition: Table 3 showed that the majority of garlic-derived sulfur compounds demonstrate weaker protease inhibition than paclitaxel, the standard drug. Gamma-octalactone have more protease inhibitory activity comparative to all of them.

*6) Enzyme inhibitors*

The enzyme inhibitors are the kind of molecules that reduce or inhibit enzyme activity. Based on mode of interaction, they are classified into competitive, non-competitive, uncompetitive or irreversible. They also play very essential roles in metabolic pathways, as well as help regulate diverse biological processes [38]. Such inhibitors play a significant role in elucidating the mechanistic pathways of these enzymes. Except for compounds extracted from garlic that contain sulfur, all other non-sulfur garlic compounds demonstrate similar or lower enzyme inhibitor activity to the standard drug paclitaxel. Gamma-Octalactone and 2-methyl benzaldehyde have a comparatively higher enzyme inhibitory action than the paclitaxel shown in table 2.

*C. Determination of ADME properties*

Using drug-likeness properties and bioavailability score, fourteen compounds that met the primary criteria of beingdrug moleculecandidates were shortlisted. Their ADME (absorption, distribution, metabolism and excretion) profiles were then predicted using SwissADME and admetSAR tools provided in table 3&4. Assessment of ADME properties at an early stage, is crucial before drug development and clinical evaluation to optimize pharmacokinetic behavior. Compounds with favorable ADME profiles should be rapidly absorbed into systemic circulation, reach plasma concentrations at or near optimal levels for therapeutically relevant time frames—and fall to minimal concentrations before being eliminated efficiently from the body. The compounds were then assessed for key pharmacokinetic parameters as solubility, bioavailability, plasma protein binding and blood–brain barrier (BBB) permeability, human intestinal absorption (HIA), maximum recommended therapeutic dose (MRTD, mg/day), Caco-2 cell permeability using the PK PoP Core software [12] and inhibition of P-glycoprotein and CYP enzyme interactions also based on in-house databases.

*1) BBB*

The blood brain barrier (BBB) is a semi-permeable highly selective physiological barrier that separates the circulating blood from the brain and extracellular fluid in the CNS, thus inhibiting or permitting passage of substances across the bloodstream into neural tissue. It protects the brain against toxic agents and pathogen microorganisms while also maintaining physiological homeostasis by allowing entry of essential nutrients like glucose and oxygen and restricting access to harmful substances. But, effective drug delivery is hampered by the fact that a number of therapeutic agents cannot cross the blood-brain barrier (BBB), which imposes great challenge for treating neurological diseases including Alzheimer's disease and brain cancer [39]. All the 14 chosen compounds show positive results whereas paclitaxel cannot cross the barrier having most negative result with respect to these 14 compounds shown in table3.

*2) HIA*

Human Intestinal Absorption (HIA) is an important parameter in the evaluation of ADME properties, specifically within the absorption stage. Bioavailability is a term that refers to the fraction of an administered compound that reaches systemic circulation and thus, the extent to which a compound is absorbed through gastrointestinal tract into the central blood stream. The more a compound is absorbed, the higher its bioavailability and pharmacological effects [40]. That said, the results in general are consistent with garlic-derived non-sulfur compounds having higher predicted human intestinal absorption than paclitaxel, providing support for greater oral bioavailability of these three constituents. These results motivated investigations from ADME parameters to discover a potential pharmacotherapy from natural compounds.

*3) Bioavailability and Solubility*

Solubility is a critical parameter in lead discovery and drug development, as it influences the absorption and bioavailability of a drug candidate. Increasing lipophilicity tends to improve bioavailability; that is, compounds are more readily absorbed into the systemic circulation following oral administration if they have higher aqueous and lipid solubility. This leads to a fast acting response and more effective therapeutic action [41]. Out of all the screened compounds, all selected compounds exhibited positive results except standard drug paclitaxel which showed negative human oral bioavailability. And the garlic-derived non-sulfur selected compounds, which were relatively more soluble as compared to that of paclitaxel and demonstrated high absorption, better pharmacokinetic properties.

*4) % Absorption*

Zhao et al. used the following equation to quantify percent absorption (%Ab):

$\%Ab = 109 - (0.345 \times TPSA)$,

where TPSA is the topological polar surface area, a descriptor that relates to hydrogen bonding capacity and is regarded as an obvious predictor for molecular absorption [42] Absorption higher value (%) of non sulfur compounds of garlic (97.15%- 104.56%) indicates that it has better oral bioavailability as compare to paclitaxel shows lower absorption %35 indicate that it has low intestinal permeability.

*5) Caco-2 permeability*

Merc Haggaz et al. developed a mathematical model using Caco-2 cells, which are human colon epithelial carcinoma derived cancer cells [4]. They express numerous transporter proteins, efflux pumps, and Phase II metabolizing enzymes, thus mimicking several transcellular transport pathways as well as metabolic processes relevant for the absorption and biotransformation of investigated compounds [43]. Paclitaxel has negative (-0.9373) Caco-2 permeability values, which revealed poor intestinal permeability but garlic compounds had positive value (0.5232-0.9738), showing good intestinal transport properties.

*6) P-glycoprotein inhibition*

P-glycoprotein (P-gp) is a transmembrane glycoprotein that mainly serves as an important active efflux transporter in the membranes of cells. It is ubiquitous in the body and can translocate a wide array of substrates. As a result, it can improve the overall ADME profile of therapeutic compounds by using inhibitors to reduce efflux activity and increase drug bioavailability [44]. For most garlic non−sulfur compounds, as they had more negative values than the standard drug paclitaxel of P-glycoprotein (PGP) is positive and are less probable to be in a position to inhibit it.

*7) Subcellular localization*

The results of subcellular localization indicated that paclitaxel mainly localized in mitochondria and non-sulfur compounds from garlic localized at M, L, and PM suggesting heterogeneous intracellular distribution patterns [45].

*8) MRTD*

The Maximum Recommended Therapeutic Dose (MRTD) is an estimation of the highest daily dose that is unlikely to cause adverse toxicity. A high intracellular peak concentration of drug-like compounds generally corresponds to a low MRTD, which is indicative of increased potential therapeutic effect [46]. While all selected compounds except compound 11 showed MRTD value lesser than 100 mg per day illustrated in table3.

*9) Plasma protein binding*

Drugs in the blood can bind to proteins (also called plasma protein binding), and this is important when considering drugs for absorption, distribution, metabolism and excretion. This is an important parameter since it has a profound impact on pharmacokinetic and pharmacodynamic properties. In general, lipophilic compounds tend to have a higher degree of plasma protein binding [47]. Non sulfur garlic compounds have less plasma protein binding than Paclitaxel shown in table4.

| S. No. | Name of ligand | %AB= 109-(0.345* TPSA) | Human intestinal absorption | Blood brain barrier | CaCO2 | Human oral bioavailability | Subcellular localization | P-glycoprotein inhibitor | Solubility (mg/ml) | MRTD (mg/day) |
|---|---|---|---|---|---|---|---|---|---|---|
| 1. | Paclitaxel | 32 | +0.9470 | -1.0000 | -0.9373 | -0.9413 | M 0.6557 | +0.7874 | 0.066 | 283 |
| 2. | 2,5-Dimethyl pyridine | 104.56 | +0.9931 | +0.1000 | +0.7153 | +0.8000 | L 0.4776 | -0.9845 | 2.50 | 66 |
| 3. | 2,6-dimethyl pyrazine | 100.1 | +0.9922 | +0.6250 | +0.6571 | +0.7714 | M 0.6577 | -0.9898 | 4.25 | 69 |
| 4. | 2-methyl benzaldehyde | 103.1 | +0.9970 | +0.9500 | +0.9738 | +0.7714 | M 0.7683 | -0.9890 | 0.44 | 73 |
| 5. | 5-ethyl-2-methyl pyridine | 104.5 | +0.9944 | +01.000 | +0.8960 | +0.8286 | M 0.4728 | -0.9881 | 0.59 | 81 |
| 6. | 2-acetyl furan | 98.58 | +0.9951 | +0.8000 | +0.8552 | +0.6857 | M 0.6252 | -0.9865 | 6.24 | 86 |
| 7. | Cyclopentanone | 97.15 | +0.9939 | +0.8000 | +0.8436 | +0.8857 | M 0.6539 | -0.9874 | 21.1 | 41 |
| 8. | 3-penten-2-one | 103.1 | +0.9946 | +0.9250 | +0.8199 | -0.5000 | M 0.5208 | -0.9868 | 20 | 83 |
| 9. | 5-hexen-2-one | 103.1 | +0.9921 | +1.0000 | +0.7932 | -0.5000 | PM 0.3937 | -0.9878 | 1.28 | 90 |
| 10. | 4-pentenal | 103.1 | +0.9868 | +0.9750 | +0.7665 | +0.6857 | PM 0.4646 | -0.9871 | 1.89 | 53 |
| 11. | Ethyl-but-2-enoate | 99.93 | +1.0000 | +0.9500 | +0.8690 | -0.5571 | M 0.6570 | -0.9914 | 7.63 | 1942 |
| 12. | Gamma octalactone | 99.93 | +1.0000 | +0.8000 | +0.8055 | +0.5857 | PM 0.5012 | -0.9849 | 3.95 | 55 |
| 13. | 2,4-hexadienaldehyde | 97.23 | +0.9910 | +0.9250 | +0.8864 | +0.7000 | M 0.5689 | -0.9857 | 47.1 | 65 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 14. | 2,3-Dimethyl pyrazine | 100.11 | +0.9921 | +0.9500 | +0.5232 | +0.9857 | M 0.7431 | -0.9893 | 4.25 | 76 |
| 15. | 2,3,5-trimethyl pyrazine | 100.11 | +0.9915 | +0.9250 | -0.5204 | +0.7000 | M 0.7274 | -0.9816 | 2.50 | 86 |

Table 3: ADME profile of 14 compounds taken paclitaxel as a standard drug

| S. No. | Compounds | OATP1B1 inhibition | OATP1B3 inhibition | OCT2 inhibition | Plasma protein binding | CYP2C9 inhibition | CYP2C19 inhibition | CYP2D6 inhibition | CYP1A2 inhibition | CYP2C8 inhibition | CYP3A4 substrate |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. | Paclitaxel | -0.7738 | +0.9479 | -0.9500 | +0.919 | -0.9071 | -0.9025 | -0.9231 | -0.9045 | +0.9817 | +0.7980 |
| 2. | 2,5-Dimethyl pyridine | +0.9689 | +0.9662 | -0.9500 | +0.640 | -0.8373 | -0.5728 | -0.6862 | -0.5815 | -0.9292 | -0.7249 |
| 3. | 2,6-dimethyl pyrazine | +0.9582 | +0.9607 | -0.9500 | +0.294 | -0.9835 | -0.9412 | -0.9329 | -0.6575 | -0.9556 | -0.8181 |
| 4. | 2-methyl benzaldehyde | +0.8942 | +0.9753 | -0.9750 | +0.783 | -0.9211 | -0.8783 | -0.9626 | +0.5729 | -0.9608 | -0.7315 |
| 5. | 5-ethyl-2-methyl pyridine | +0.9561 | +0.9581 | -0.9000 | +0.453 | -0.8413 | -0.6358 | -0.6272 | +0.6561 | -0.7460 | -0.6960 |
| 6. | 2-acetyl furan | +0.9597 | +0.9682 | -1.0000 | +0.461 | -0.9079 | -0.7016 | -0.9542 | +0.5718 | -0.9728 | -0.7097 |
| 7. | Cyclopentanone | +0.9842 | +0.9670 | -0.8250 | -0.014 | -0.8830 | -0.9138 | -0.9603 | -0.8011 | -0.9980 | -0.8261 |
| 8. | 3-penten-2-one | +0.9531 | +0.9683 | -1.0000 | +0.128 | -0.9562 | -0.9035 | -0.9607 | -0.7766 | -0.9937 | 0.7436 |
| 9. | 5-hexen-2-one | +0.9410 | +0.9360 | -0.9000 | +0.225 | -0.9489 | -0.8757 | -0.9650 | +0.6345 | -0.9872 | -0.7194 |
| 10. | 4-pentenal | +0.9363 | +0.9456 | -0.9000 | -0.050 | -0.9291 | -0.9027 | -0.9700 | -0.6156 | -0.9872 | -0.7391 |
| 11. | Ethyl-but-2-enoate | +0.9416 | +0.9571 | -0.9750 | +0.264 | -0.9342 | -0.9406 | -0.9547 | -0.6777 | -0.9471 | -0.6396 |
| 12. | Gamma octalactone | +0.9222 | +0.9493 | -0.7500 | +0.351 | -0.8382 | -0.6159 | -0.9434 | -0.6366 | -0.9395 | -0.6309 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 13. | 2,4-hexadienaldehyde | +0.9545 | +0.9619 | -1.0000 | +0.695 | -0.9247 | -0.9381 | -0.9584 | -0.8903 | -0.9947 | -0.7936 |
| 14. | 2,3-Dimethyl pyrazine | +0.9791 | +0.9614 | -0.9500 | +0.147 | -0.9583 | -0.7757 | -0.9216 | +0.5456 | -0.9722 | -0.8184 |
| 15. | 2,3,5-trimethyl pyrazine | +0.9775 | +0.9588 | -0.9500 | +0.457 | -0.9356 | -0.7115 | -0.9017 | +0.6110 | -0.9574 | -0.7319 |

Table 4: (Swiss ADME) ADME profile of 14 selected compounds taken paclitaxel as a standard drug

*10) OATP inhibition*

Organic anion-transporting polypeptides (OATPs) are also membrane-bound proteins that mediate the hepatic uptake of drugs, hormones, and other endogenous and exogenous compounds for subsequent elimination [48]. But inhibition of these transporters markedly impacts hepatic drug uptake and will affect the ADME profile, which may lead to increased systemic exposure. The results show garlic-derived non-sulfur compounds are good inhibitors for OATP1B1/3 transporters, and paclitaxel shows good inhibition too but only against this transporter presented in table4. Thus, the chosen garlic compounds have higher overall OATP inhibitory potential toward OATP1B1 in particular.

*11) CYP inhibition*

Cytochrome P450 (CYP) inhibitors are substances that inhibit hepatic enzymes involved in the metabolism of many drugs and xenobiotics, resulting in decreased clearance from the liver. The selectivity of these inhibitors is significant for minimizing risk of potential drug–drug interactions in patients on multiple concurrent medications [49]. The comparison of results in the table indicates that non-sulfur substances in a garlic structure illustrate patterns of protest known as CYP limitation similar to that of paclitaxel for different isoforms, essentially CYP2C9, CYP2C19, and CYP2D6 (shown in table4). However, unlike CYP1A2, CYP2C8 and CYP3A4 show different interaction patterns suggesting diverse metabolic properties that can affect their pharmacokinetics.

*D. Determination of toxicity profile*

Moreover, a bioactive agent with good pharmacokinetic parameters should also display a strong safety margin for humans or the environment. However, evaluating various compounds typically involves substantial cost and time; as such, computational toxicity prediction models can help ease this burden and represent an important class of early-stage drug development tools. Toxicity screening helps recognize and address potential negative effects of potential drugs. Tables 5and 6 show the predicted outcomes for organ toxicity, genotoxicity, and environmental toxicity of selected compounds in descending order; they are discussed below:

*1) Organ toxicity*

As for paclitaxel, it produced positive prediction(s) towards human Ether-a-go-go Related Gene (hERG), a tetrameric potassium ion channel that plays an important role in the potential for cardiac activity and is suspected to be blocked by drug molecules as one of the major of cardiac arrhythmias .All selected compounds of garlic derived non-sulfur compounds indicated negative prediction presented in table5 & 6. However, all the compounds selected (except compound 11) and paclitaxel show hepatotoxicity, which is a leading cause of acute liver failure. Nephrotoxicity: The occurrence of kidney toxicity; all but three compounds (3, 5, & 14) exhibit nephrotoxic behaviour which can lead to poor functioning of kidneys along with the paclitaxel. While only 2 and 13 represent II class acute oral toxic compounds, all other compounds can be classified for III or III class toxicity [50].

*2) Genomic toxicity*

Genomic toxicity refers to the potential of chemical agents to damage a cell's genetic material, causing mutations that can lead to cancer. A commonly used assay for determining the mutagenicity of chemicals is the Ames test. A test result which is positive in the Ames test indicates that a compound has the potential to cause genomic instability, leading to valuable information for chemical safety assessment and supporting regulatory decision making. Besides, among the 14 selected components of garlic, 11 component shows no or low mutagenic toxicity while 3 showed some mutagenic potential (compounds 3,6 and 13). Selected compounds are harmful to the eyes. Of the 14 chosen compounds, six compounds indicated negative qualities with regards to skin corrosion thus indicating that they are less prone to cause skin corrosion.

Out of the selected 14 compounds, 10 were either negative or had no respiratory toxicity while along with paclitaxel, there are positive results of respiratory toxicity by 4 compounds (2,3,5,15). All 14 compounds toolbar placements were negative for the hormonal receptors like estrogen, androgen, thyroid or gluco-corticoids receptors, suggested garlic derived non-sulfur compounds have not significant interaction with the hormonal receptors. 10 compounds have negative results of carcinogenicity it means these compounds have no carcinogenic potential. Based on the results garlic non-sulfur compounds are better biological compound then standard drug paclitaxel [51].

*3) Eco-toxicity*

Seven out of fourteen compounds show negative crustacean toxicity that means they are not toxic. 9 compounds are showing the negative activity of tetrahymena pyriformis and 5 compounds along with the paclitaxel in positive demonstrated in table6. The fish aquatic toxicity of 14 compounds was performed out of which the 10 were found to be negative so these are not harmful and 4 along with paclitaxel displayed positive results. Most garlic non-sulfur compounds are environmentally-friendly. All the selected compound on honey bee toxicity shows negative results except 1 compound [52].

From the above findings, Gamma-octalactone was selected as the best compound by comparing ADME properties and toxicity profiles of screened compounds based on Lipinski's rule since it had better kinetics with lower toxicity profile, increased solubility and low MRTD values.

Table 5:Toxicology profile of different compounds (1)

| S.N. | Compounds | Carcinogenicity(binary) | Eyecorrosion | Eyeirritation | Skinirritation | Skincorrosion | Skinsensitisation | Amesmutagenesis | Humanether-a-go-go-relatedGeneinhibition | Micro-nuclear | Hepato-toxicity | Respiratorytoxicity |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Paclitaxel | -0.8800 | -0.9872 | -0.9100 | -0.7657 | -0.9352 | -0.8230 | -0.9500 | +0.7442 | +0.7300 | +0.6749 | +0.9333 |
| 2 | 2,5-dimethylpyridine | -0.6300 | +0.9601 | +0.9968 | +0.9487 | -0.5675 | +0.7833 | -0.7900 | -0.6704 | -0.7000 | +0.8375 | +0.6000 |
| 3 | 2,6-dimethylpyrazine | -0.7900 | +0.8446 | +0.9918 | +0.8923 | +0.6160 | +0.5428 | +0.6800 | -0.6941 | -0.5500 | +0.6750 | +0.5222 |
| 4 | 2-methylbenzaldehyde | -0.5100 | +0.9937 | +1.0000 | +0.9563 | +0.5932 | +0.9799 | -0.8600 | -0.8365 | -0.7341 | +0.7125 | -0.6444 |
| 5 | 5-ethyl-2-methylpyridine | -0.5000 | +0.8045 | +0.9907 | +0.8775 | -0.6320 | +0.8357 | -0.9400 | -0.5252 | -0.6800 | +0.5875 | +0.7333 |
| 6 | 2-acetylfuran | -0.7117 | +0.9742 | +0.9955 | +0.8700 | -0.5881 | +0.7814 | +0.6900 | -0.7826 | +0.8000 | +0.6000 | -0.7222 |
| 7 | Cyclopentanone | -0.8500 | +0.9874 | +0.9951 | +0.7828 | -0.5424 | -0.5818 | -0.9900 | -0.7934 | -0.9000 | +0.8875 | -0.9333 |
| 8 | 3-penten-2-one | +0.6583 | +0.9942 | +0.9921 | +0.9106 | +0.6472 | +0.9130 | -0.6800 | -0.8275 | -0.5300 | +0.6500 | -0.7444 |
| 9 | 5-hexen-2one | -0.5300 | +0.9872 | +0.9914 | +0.8822 | -0.6436 | +0.8596 | -0.8900 | -0.8116 | -0.9700 | +0.6625 | -0.9333 |
| 10 | 4-pentenal | +0.5100 | +1.0000 | +0.9947 | +0.8431 | +0.5693 | +0.8585 | -0.6200 | -0.7708 | -0.9000 | +0.5875 | -0.8111 |
| 11 | Ethyl-but-2enoate | +0.5874 | +0.9743 | +0.9946 | +0.9358 | -0.6906 | +0.8587 | -0.7700 | -0.7806 | -0.9900 | -0.5774 | -0.8444 |
| 12 | Gamma-octalactone | -0.9100 | +0.7454 | +0.9690 | +0.7308 | -0.8572 | -0.5906 | -0.8700 | -0.7002 | -1.0000 | +0.6250 | -0.8333 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 13 | 2,4-hexa-dienaldehyde | +0.7540 | +1.0000 | +1.0000 | +0.9552 | +0.9928 | +0.9636 | +0.8300 | -0.8614 | +0.6300 | +0.8375 | -0.7667 |
| 14 | 2,3dimethyl-pyrazine | -0.8100 | -0.6150 | +0.9879 | +0.8487 | -0.6817 | +0.5431 | -0.9700 | -0.6619 | -0.5300 | +0.8625 | -0.8111 |
| 15 | 2,3,5-trimethylpyrazine | -0.8300 | -0.7666 | +0.9601 | +0.8003 | -0.7114 | +0.6667 | -0.8300 | -0.5910 | -0.5700 | +0.6802 | +0.6667 |

Table 6: Toxicology profile of different compounds (2)

| S.N. | Compounds | Nephro-toxicity | Estrogen receptor binding | Androgen receptor binding | Thyroid receptor binding | Glucocorticoid receptor binding | Tetrahymena pyriformis | Honey bee toxicity | Crustacea Aquatic toxicity | Fish aquatic toxicity |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Paclitaxel | +0.6119 | +0.8148 | +0.8337 | +0.7275 | +0.7632 | +0.803 | -0.6301 | +0.5700 | +2.0102 |
| 2 | 2,5 Dimethyl pyridine | +0.4504 | -0.9568 | -0.9795 | -0.8803 | -0.8806 | -0.041 | -0.9093 | +0.7700 | -0.8541 |
| 3 | 2,6 dimethyl pyrazine | -0.5895 | -0.9604 | -0.9494 | -0.8123 | -0.9109 | -0.846 | -0.9714 | +0.7800 | -0.8906 |
| 4 | 2-methyl benzaldehyde | +0.6127 | -0.9696 | -0.9321 | -0.7969 | -0.9233 | +0.095 | 0.9732 | +0.6900 | +0.9060 |
| 5 | 5-ethyl 2 methyl pyridine | -0.8441 | -0.9507 | -0.9546 | -0.8816 | -0.8410 | +0.528 | -0.9209 | +0.5900 | -0.8018 |
| 6 | 2 acetyl furan | +0.5267 | -0.9676 | -0.9388 | -0.8853 | -0.8953 | -0.745 | -0.9829 | -0.7100 | -0.7964 |
| 7 | Cyclopentanone | +0.5619 | -0.9654 | -0.9576 | -0.9210 | -0.9185 | -1.463 | -0.9165 | -0.5400 | -0.8685 |
| 8 | 3-Penten-2 one | +0.7432 | -0.9695 | -0.9438 | -0.9101 | -0.8965 | +0.423 | -0.9039 | -0.9200 | -0.6311 |
| 9 | 5-hexen-2 one | +0.6579 | -0.9531 | -0.7848 | -0.9079 | -0.8942 | -1.374 | -0.9868 | +0.8600 | +0.8592 |
| 10 | 4-pentenal | +0.4697 | -0.9807 | -0.9645 | -0.9143 | -0.9341 | -0.221 | -0.8838 | -0.7500 | -0.3672 |
| 11 | Ethyl-but 2-enoate | +0.6069 | -0.9406 | -0.9020 | -0.8785 | -0.8596 | -0.774 | -0.9266 | -0.7955 | +0.7920 |
| 12 | Gamma octalactone | +0.5385 | -0.9455 | -0.8742 | -0.8629 | -0.9011 | -0.334 | -0.9897 | +0.5448 | +0.8247 |
| 13 | 2,4 hexadienaldehyde | +0.7218 | -0.9329 | -0.7961 | -0.7859 | -0.7779 | +0.523 | -0.6726 | -0.5700 | -0.4315 |
| 14 | 2,3 Dimethyl pyrazine | -0.5792 | -0.9605 | -0.8840 | -0.7774 | -0.9319 | -0.063 | -0.9741 | +0.7800 | -0.7465 |
| 15 | 2,3,5 trimethyl pyrazine | -0.5728 | -0.9578 | -0.8899 | -0.8020 | -0.9178 | +0.027 | -0.9815 | -0.8000 | -0.7274 |

## IV. CONCLUSION

Computational approaches provide an efficient and precise means of screening organic molecules as potential lead drugs, offering significant advantages over manual methods by reducing labor, cost, and time. In this study, a virtual screening of 18 non-sulfur compounds derived from garlic was conducted.

Garlic is recognized as a rich source of bioactive molecules, including phenolic acids, flavonoids, polysaccharides, saponins, fructans (such as inulin), steroidal glycosides, and organo-nitrogenous compounds, all of which contribute to its diverse pharmacological properties. The selected compounds were evaluated using Lipinski's rule of five and subjected to ADMET predictions, with paclitaxel serving as the reference standard. Among the screened molecules, gamma-octalactone emerged as the most promising candidate, demonstrating compliance with all key drug-likeness parameters. Based on these findings, gamma-octalactone shows potential as an alternative anticancer agent, with prospects of greater effectiveness compared to paclitaxel.

Acknowledgement:One of the authors Manisha acknowledged Baba Mastnath University, Rohtak, India for providing support and library facilities.

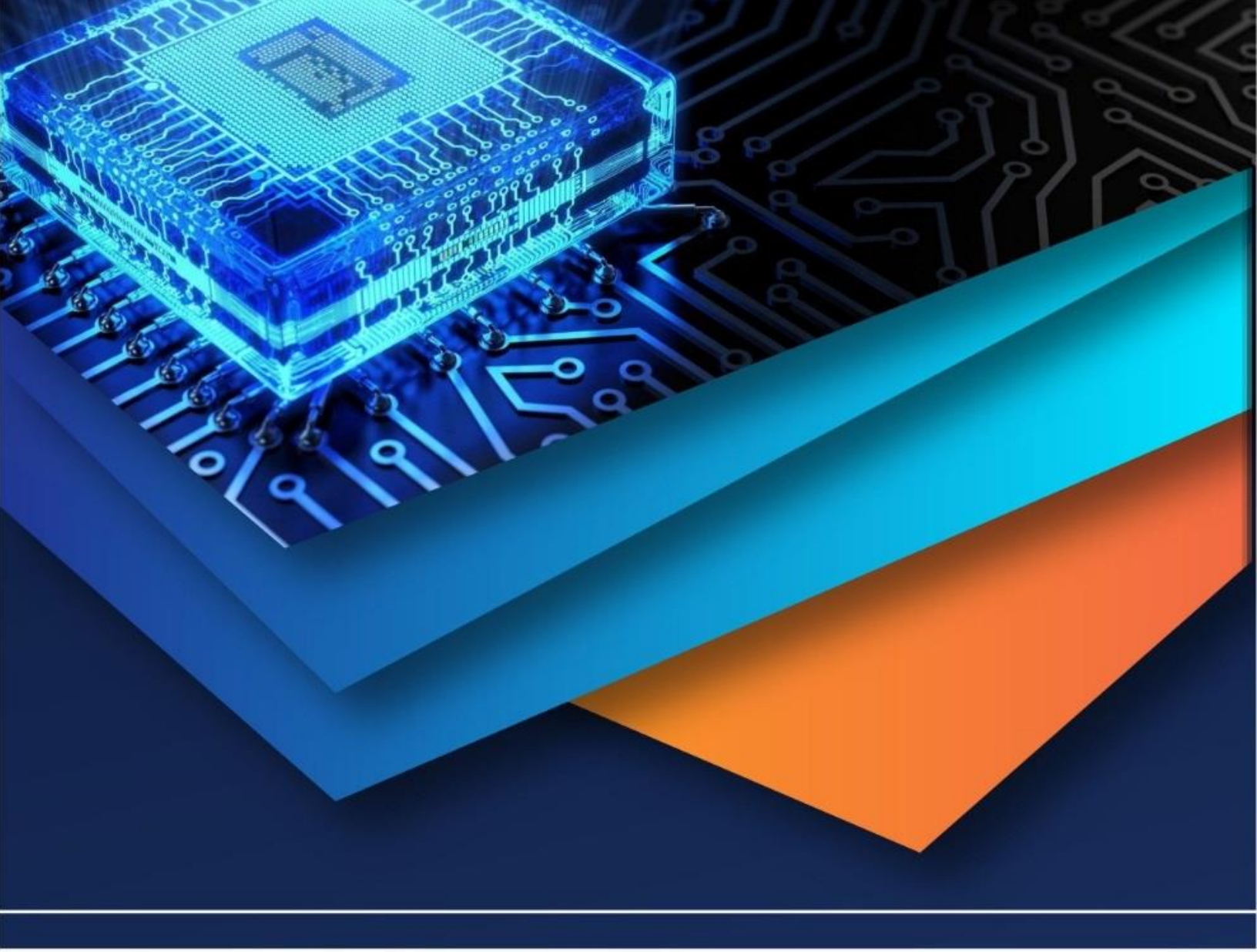
Conflict of Interest:The authors have no conflict of interest.

## REFERENCES

[1] Shang, A., Cao, S. Y., Xu, X. Y., Gan, R. Y., Tang, G. Y., Corke, H., ... & Li, H. B. (2019). Bioactive compounds and biological functions of garlic (Allium sativum L.). Foods, 8(7), 246.
[2] Bayan, L., Koulivand, P. H., & Gorji, A. (2014). Garlic: a review of potential therapeutic effects. Avicenna journal of phytomedicine, 4(1), 1.
[3] Malik, A., Raghav, N., & Mor, N. (2024). Garlic (Allium sativum L.): A mini review on its multiple pharmacological benefits for human health. Chemistry & Biology Interface, 14(3).
[4] Lanzotti, V. (2006). The analysis of onion and garlic. Journal of chromatography A, 1112(1-2), 3-22.
[5] El-Saber Batiha, G., Magdy Beshbishy, A., G. Wasef, L., Elewa, Y. H., A. Al-Sagan, A., Abd El-Hack, M. E., ... & Prasad Devkota, H. (2020). Chemical constituents and pharmacological activities of garlic (Allium sativum L.): A review. Nutrients, 12(3), 872.
[6] Tudu, C. K., Dutta, T., Ghorai, M., Biswas, P., Samanta, D., Oleksak, P., ... & Dey, A. (2022). Traditional uses, phytochemistry, pharmacology and toxicology of garlic (Allium sativum), a storehouse of diverse phytochemicals: A review of research from the last decade focusing on health and nutritional implications. Frontiers in Nutrition, 9, 949554.
[7] El-Saadony, M. T., Saad, A. M., Korma, S. A., Salem, H. M., Abd El-Mageed, T. A., Alkafaas, S. S., ... & Ibrahim, S. A. (2024). Garlic bioactive substances and their therapeutic applications for improving human health: a comprehensive review. Frontiers in immunology, 15, 1277074.
[8] Iciek, M., Kwiecień, I., & Włodek, L. (2009). Biological properties of garlic and garlic-derived organosulfur compounds. Environmental and molecular mutagenesis, 50(3), 247-265.
[9] Talib, W. H., Baban, M. M., Azzam, A. O., Issa, J. J., Ali, A. Y., Alsuwais, A. K., ... & Al Kury, L. T. (2024). Allicin and cancer hallmarks. Molecules, 29(6), 1320.
[10] Ahmed, H. G. M. D., Yang, J., Zhu, T., Iqbal, R., Sheng, Q., Dong, R., Tian, W., Xiao, L., Zeng, Y., & Ding, Y. (2025). Beyond seasoning: Nutrients, bioactive ingredients, and healthcare effects of Allium vegetables. Frontiers in Nutrition, 12, 1597788.
[11] Han, D., Guan, X., Zhu, F., Yang, Q., & Su, D. (2024). Oral aged garlic (Allium sativum) alleviates ulcerative colitis in mice by improving gut homeostasis. Food & Function, 15(17), 8935-8951.
[12] Iwar, K., Ochar, K., Seo, Y. A., Ha, B. K., & Kim, S. H. (2024). Alliums as potential antioxidants and anticancer agents. International Journal of Molecular Sciences, 25(15), 8079.
[13] De Greef, D., Barton, E. M., Sandberg, E. N., Croley, C. R., Pumarol, J., Wong, T. L., ... &Bishayee, A. (2021, August). Anticancer potential of garlic and its bioactive constituents: A systematic and comprehensive review. In Seminars in cancer biology (Vol. 73, pp. 219-264). Academic Press.
[14] Ansary, J., Forbes-Hernández, T. Y., Gil, E., Cianciosi, D., Zhang, J., Elexpuru-Zabaleta, M., ... & Battino, M. (2020). Potential health benefit of garlic based on human intervention studies: A brief overview. Antioxidants, 9(7), 619.
[15] Mondal, A., Banerjee, S., Bose, S., Mazumder, S., Haber, R. A., Farzaei, M. H., &Bishayee, A. (2022). Garlic constituents for cancer prevention and therapy: From phytochemistry to novel formulations. Pharmacological research, 175, 105837.
[16] Lagorce, D., Sperandio, O., Galons, H., Miteva, M. A., &Villoutreix, B. O. (2008). FAF-Drugs2: free ADME/tox filtering tool to assist drug discovery and chemical biology projects. BMC bioinformatics, 9(1), 396.
[17] Das, A. P., & Agarwal, S. M. (2024). Recent advances in the area of plant-based anti-cancer drug discovery using computational approaches. Molecular Diversity, 28(2), 901-925.
[18] Azam, F., Anwar, M. J., Kahfi, J., Almahmoud, S. A., &Emwas, A. H. (2025). Cracking the sulfur code: Garlic bioactive molecules as multi-target blueprints for drug discovery. Pharmaceuticals, 18(11), 1766.
[19] Daina, A., Michielin, O., & Zoete, V. (2017). SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Scientific reports, 7(1), 42717.
[20] Borlinghaus, J., Albrecht, F., Gruhlke, M. C., Nwachukwu, I. D., & Slusarenko, A. J. (2014). Allicin: chemistry and biological properties. Molecules, 19(8), 12591-12618.
[21] Lipinski, C. A. (2000). Drug-like properties and the causes of poor solubility and poor permeability. Journal of pharmacological and toxicological methods, 44(1), 235-249.
[22] Ertl, P., Rohde, B., & Selzer, P. (2000). Fast calculation of molecular polar surface area as a sum of fragment-based contributions and its application to the prediction of drug transport properties. Journal of Medicinal Chemistry, 43(20), 3714-3717.
[23] Li, Y., Zhang, H., & Chen, Q. (2026). In-silico molecular properties and bioactivity prediction of plant-derived compounds for drug discovery. Computational and Structural Biotechnology Journal.
[24] da Silva, R. C. C., Alves, M. C. S., Matos, D. F., & Quaresma, S. A. C. (2024). Bioinformatics approaches to explore the discovery of new plant-derived drugs: a brief review.

[25] Cheng, F., Li, W., Zhou, Y., Shen, J., Wu, Z., Liu, G., ... & Tang, Y. (2012). admetSAR: a comprehensive source and free tool for assessment of chemical ADMET properties.
[26] Veber, D. F., Johnson, S. R., Cheng, H. Y., Smith, B. R., Ward, K. W., & Kopple, K. D. (2002). Molecular properties that influence the oral bioavailability of drug candidates. Journal of medicinal chemistry, 45(12), 2615-2623.
[27] Aggarwal, S., Raghav, N., Dahiya, H., & Mor, N. (2025). A virtual screening of Withaniasomnifera compounds using ADMET predictions, molecular docking, MD simulation and DFT calculations: Withasomniferol C an effective drug and potent inhibitor of anti-inflammatory targets. Computational Biology and Chemistry, 118, 108488.
[28] Leeson, P. D., & Springthorpe, B. (2007). The influence of drug-like concepts on decision-making in medicinal chemistry. Nature Reviews Drug Discovery, 6(11), 881–890.
[29] Ferreira, L. G., Dos Santos, R. N., Oliva, G., &Andricopulo, A. D. (2015). Molecular docking and structure-based drug design strategies. Molecules, 20(7), 13384-13421.
[30] Benet, L. Z., Hosey, C. M., Ursu, O., & Oprea, T. I. (2016). BDDCS, the Rule of 5 and drugability. Advanced drug delivery reviews, 101, 89-98.
[31] Lipinski, C. A., Lombardo, F., Dominy, B. W., & Feeney, P. J. (1997). Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Advanced drug delivery reviews, 23(1-3), 3-25.
[32] Rashid, M., Afzal, O., & Altamimi, A. S. A. (2021). Benzimidazole molecule hybrid with oxadiazole ring as antiproliferative agents: In-silico analysis, synthesis and biological evaluation. Journal of the Chilean Chemical Society, 66(2), 5164-5182.
[33] Rosenbaum, D. M., Rasmussen, S. G., & Kobilka, B. K. (2009). The structure and function of G-protein-coupled receptors. Nature, 459(7245), 356-363.
[34] Alsaloum, M., Dib-Hajj, S. D., Page, D. A., Ruben, P. C., Krainer, A. R., & Waxman, S. G. (2025). Voltage-gated sodium channels in excitable cells as drug targets. Nature Reviews Drug Discovery, 24(5), 358-378.
[35] Hassan, D., Menges, C. W., Testa, J. R., & Bellacosa, A. (2024). AKT kinases as therapeutic targets. Journal of Experimental & Clinical Cancer Research, 43(1), 313.
[36] Evans, R. M., & Mangelsdorf, D. J. (2014). Nuclear receptors, RXR, and the big bang. Cell, 157(1), 255-266.
[37] Dunn, B. M. (2002). Structure and mechanism of the pepsin-like family of aspartic peptidases. Chemical reviews, 102(12), 4431-4458.
[38] Schneider, G. (2018). Automating drug discovery. Nature reviews drug discovery, 17(2), 97-113.
[39] Wu, D., Chen, Q., Chen, X., Han, F., Chen, Z., & Wang, Y. (2023). The blood–brain barrier: Structure, regulation and drug delivery. Signal transduction and targeted therapy, 8(1), 217.
[40] Benet, L. Z., Broccatelli, F., & Oprea, T. I. (2011). BDDCS applied to over 900 drugs. The AAPS journal, 13(4), 519-547.
[41] Huang, L. F., Dong, J., & Karki, S. B. (2018). Formulation strategies and practice used for drug candidates with water-insoluble properties for toxicology, biology, and pharmacology studies in discovery support. In Water-insoluble drug formulation (pp. 125-148). CRC press
[42] Zhao, Y. H., Abraham, M. H., Le, J., Hersey, A., Luscombe, C. N., Beck, G., ... & Cooper, I. (2002). Rate-limited steps of human oral absorption and QSAR studies. Pharmaceutical research, 19(10), 1446-1457.
[43] Fredlund, L., Winiwarter, S., & Hilgendorf, C. (2017). In vitro intrinsic permeability: a transporter-independent measure of Caco-2 cell permeability in drug design and development. Molecular pharmaceutics, 14(5), 1601-1609.
[44] Zhou, S. F. (2008). Structure, function and regulation of P-glycoprotein and its clinical relevance in drug disposition. Xenobiotica, 38(7-8), 802-832.
[45] Mccormick, B., Lowes, D. A., Colvin, L., Torsney, C., & Galley, H. F. (2016). MitoVitE, a mitochondria-targeted antioxidant, limits paclitaxel-induced oxidative stress and mitochondrial damage in vitro, and paclitaxel-induced mechanical hypersensitivity in a rat pain model. BJA: British Journal of Anaesthesia, 117(5), 659-666.
[46] Schyman, P., Liu, R., Desai, V., &Wallqvist, A. (2017). vNN web server for ADMET predictions. Frontiers in pharmacology, 8, 889.
[47] Smith, D. A., Di, L., & Kerns, E. H. (2010). The effect of plasma protein binding on in vivo efficacy: misconceptions in drug discovery. Nature reviews Drug discovery, 9(12), 929-939.
[48] Shitara, Y. (2011). Clinical importance of OATP1B1 and OATP1B3 in drug–drug interactions. Drug metabolism and pharmacokinetics, 26(3), 220-227.
[49] Zanger, U. M., & Schwab, M. (2013). Cytochrome P450 enzymes in drug metabolism: regulation of gene expression, enzyme activities, and impact of genetic variation. Pharmacology & therapeutics, 138(1), 103-141.
[50] Chen, M., Suzuki, A., Borlak, J., Andrade, R. J., & Lucena, M. I. (2015). Drug-induced liver injury: Interactions between drug properties and host factors. Journal of hepatology, 63(2), 503-514.
[51] Bak, S. M., Back, S. M., Kim, D. Y., Jung, S., Jeung, N. Y., Kim, N. Y., ... & Park, S. H. (2024). Differential genotoxicity of PolygoniMultiflori in rat and human: insights from Ames test and S9 metabolic activation system. Scientific Reports, 14(1), 21433.
[52] Raies, A. B., & Bajic, V. B. (2016). In silico toxicology: computational methods for the prediction of chemical toxicity. Wiley Interdisciplinary Reviews: Computational Molecular Science, 6(2), 147-172.



10.22214/IJRASET

45.98

IMPACT FACTOR: 7.129

IMPACT FACTOR: 7.429

# INTERNATIONAL JOURNAL FOR RESEARCH

IN APPLIED SCIENCE & ENGINEERING TECHNOLOGY