***In Silico* Pharmacophore Profiling of *Embelia ribes* and *Gloriosa superba* for Potential Therapeutic Applications**

**ABSTRACT**

Traditional Plants of Medicinal Importance (TPMI) are essential components of healthcare systems in developing countries. It is estimated that, out of 300,000 plant species present in the world, only 15% have been assessed for their pharmacological potential. The complexity and high costs associated with lab-based pharmacological assessment have significantly limited the evaluation of many TPMI, restricting research primarily to a small number of plant species, further it has hindered the exploration of numerous potentially bioactive compounds present in medicinal plants. However, *in silico* tools emerged as a powerful alternative that enabling the large-scale screening of plant constituents in a cost-effective and time-efficient manner. Researchers can identify promising bioactive compounds and prioritize them for further *in vitro* and *in vivo* validation by leveraging computational methods like molecular docking, virtual screening, and bioinformatics-based target prediction. Bioinformatics tools like SwissADME, PubChem, and ChemSpider provide effective solutions for large-scale screening of plant bioactive compounds. *Embelia ribes* and *Gloriosa superba*, two rare indigenous plants, have been selected for *in silico* pharmacophore evaluation during the present course of investigation. The researchers have reported that *E. ribes* and *G. superba*, are rich repertoire of bioactive compounds, including caffeic acid, chlorogenic acid, cinnamic acid, o-cumaric acid, embelin, vanillic acid, colchicine, and colchicoside. The identification of key biological targets including MMP-9, HCAR2, SLC22A3, and ALOX5 for these bioactive compounds emphasizes their relevance in treating conditions such as papillary thyroid cancer and inflammatory diseases. Additionally, the favorable physicochemical properties, such as low tPSA values, suggest promising bioavailability and absorption, further supporting their potential as viable drug candidates.

***Keywords:*** *Bioactive compounds, Embelia ribes, Gloriosa superba, SwissADME, in silico pharmacophore, MMP-9, HCAR2, SLC22A3, ALOX5*

**INTRODUCTION**

Populations of Developing countries depend on Traditional Plants of Medicinal Importance (TPMI) for their day-to-day health care needs. According to the WHO report around 65% to 80% of the populations of developing countries use medicinal plants for treating various ailments. The continuous growth in new herbal products is also seen as it is estimated that out of 300,000 plant species reported, only 15% have been assessed for pharmacological potential (Palhares *et al*, 2015). This aforesaid statement justifies the requirement of mass-level *in silico* evaluation of medical plants for their pharmacological potential. The identification and prediction of the pharmacological potential of TPMI is a sophisticated process due to a bunch of experimental setups and high-end modern analysis expenses. The traditional approach for medicinal plant research was done under the following phases; (a) the extraction of a bioactive compound of interest in pure form, (b) qualitative and quantitative identification of extracted bioactive compound (c) screening for *in vitro* pharmacological efficacy (d) validation of *in vivo* pharmacological efficacy in an animal models (e) data collection and significant interpretation (Zhang *et al*., 2017; Yi *et al*., 2016). As seen above, the traditional research approaches are prolonged and expensive. The TPMI comprises numerous bioactive compounds but due to the expensiveness of traditional tactics screening and development of pharmaceutical drugs from medicinal plants demands higher cost and time consumption. Thus, the most of literature has limited their research to *in vitro* pharmaceutical potential rather than *in vivo* pharmaceutical draggability screening. To overcome such limitations, bioinformatics tools are promising due to the availability of a vast and comprehensive biological database of plant-derived bioactive compounds. A variety of bioinformatics tools are accessible for the *in-silico* study of phytochemicals and their application e.g., zinc docking tool, SwissADME, ChEMBL, PubChem, ChemSpider, UniChem and so forth. These tools are significantly used for the large-scale screening of plant-derived bioactive compounds for systematic evaluation of their pharmaceutical potential and target cells or biological components. The advancement of computer and information technology pushes the use of an *in-silico* method for the search for novel plant-derived bioactive compounds for screening draggability and development of drugs using Computer-Aided Drug (CAD) design. The *in-silico* approaches help to predict the possible interaction between simulated compounds and biological targets accurately.

The expansion of the pharmacology database helps toward the rapid and wide-ranging elucidation of the relationships between plant-derived bioactive compound and their targets& overall regulatory mechanism (i.e., Protein-Ligand interaction) (Rubio-Perez *et al*., 2015; Zhang *et al*., 2016). The network analysis under systems biology is used to predict the numerous characteristics of signal nodes (i.e., plant-derived bioactive compounds) for multiple targets with special reference to draggability. Hence, with such a bioinformatics facility, researchers can explore the chemical composition and pharmacological potential of traditional medicine. The present work was focused on the study of traditional plants of medicinal importance to human health practices. A total of 11538.64 ha is occupied by medicinal & aromatic plant cultivation in Chhattisgarh state as per the Agri-portal database reflected on Horticulture Department, Government of Chhattisgarh. Thereby, the Chhattisgarh state offers tremendous opportunities to screen *in-silico* pharmacophore assessment of indigenous medicinal flora. In-line, two medicinal plants viz., *Embelia ribes* and *Gloriosa superba* have been selected as rare indigenous medicinal flora of Chhattisgarh and processed for the preliminary *in-silico* pharmacophore evaluation.

*Embelia ribes* is traditionally used as anticancer, antioxidant, analgesic, anthelmintic, antibacterial, antidiabetic, antihyperlipidemic, wound healing, and anti-spermatogenic activity. And the tuber of *Gloriosa superba* is also used traditionally for the treatment of cancer, chronic ulcers, haemorrhoids, impotency and other related diseases etc. Choudhary *et al*. (2021) reviewed the pharmacology importance of the phenolic content of *Embelia ribes* for pharmaceutical importance. Haq *et al*., (2005) evaluated fresh berries of *E. ribes* and claimed that they consisted of caffeic acid, chlorogenic acid, cinnamic acid, o-cumaric acid, and vanillic acid. Novel bioactive agents embelin (ver., embelinol, and embeliol) have also been reported in fresh berries of *E. ribes* (Indrayan *et al*., 2005). Jasmine *et al.* (2020) reported that the Colchicine and Colchicoside found in *Gloriosa superba* L as secondary metabolites. Chopra *et al*. (1956) and Sarin *et al*. (1977) revealed that the *Colchicum luteum* and *Gloriosa superba* consisted of colchicines at a range of 0.62 to 0.9%. Later, Srivastava *et al*. (1977) and Bellet and Gaignault (1985) claimed that the *G. superb* has been observed to have more colchicine than *Colchicum luteum*. Hence, the TPMI viz., *E. ribes* and *G. superba* were evaluated for their *in-silico* Pharmacophore efficacy. The aforementioned pieces of literature revealed that caffeic acid, chlorogenic acid, cinnamic acid, o-cumaric acid, colchicine, embelin, and vanillic acid have significantly contributed to the medicinal potency of *E. ribes* and *G. superba*. The present study also highlights the significance of *in silico* tools for the primary screening of *E. ribes* and *G. superba-derived* bioactive agents for their pharmacological potential and possible target assessment. Hence, we documented the *in-silico* pharmacophore profile of caffeic acid, chlorogenic acid, cinnamic acid, o-cumaric acid, colchicine, embelin, and vanillic acid and their target biological moieties.

**MATERIALS AND METHODS**

The present research work was based on the gathering and analysis of the biological database of selected bioactive compounds that belong to *E. ribes* and *G. superba* using bioinformatics tools.

**Selection of Bioactive Compounds**

The bioactive compounds from medicinal plants (namely *E. ribes* and *G. superb*) viz., caffeic acid, chlorogenic acid, cinnamic acid, o-cumaric acid, colchicine, embelin, and vanillic acid have been selected for their pharmacophore analysis based on the literature survey namely Chopra *et al*., 1956; Sarin *et al*., 1977; Srivastava *et al*., 1977; Bellet and Gaignault, 1985; Haq *et al*., 2005; Indrayan *et al*., 2005; Jasmine *et al.,* 2020; Choudhary *et al*., 2021).

**Evaluation of pharmacological potential of TPMI**

To meet the objective of the study the following approach was used to divulge the pharmacological potential of TPMI (viz., *E. ribes* and *G. superba*); (a) exploring the research significance of the TPMI, (b) searching, collection, and organization of biological database available online selected bioactive compounds, (c) prediction of pharmacophore efficacy of selected bioactive compounds and (d) ADME (absorption, distribution, metabolism, and excretion) analysis.

**Zinc docking and SwissADME**

The online zinc docking tool (<https://zinc.docking.org/substances/>), ChemSpider (<http://www.chemspider.com/>) and SwissADME (<http://www.swissadme.ch/>) were used to predict the pharmacophore properties of selected bioactive compounds. The zinc docking tool was selected because it offers interoperability with the most reliable chemoinformatics tools i.e., ChEMBL (Bento *et al*., 2014), PubChem (Li *et al*., 2010), ChemSpider (RSC ChemSpider), and UniChem (Chambers *et al*., 2014; Chambers *et al*., 2013). The SMILES (Simplified Molecular Input Line Entry System) file of selected bioactive compounds was retrieved from the ZINC database and further, the structure was drawn by ChemDraw.

**Lipinski's rule**

Lipinski's rule of five assists in deciding the drug-likeliness of molecules based on the established rule related to molecular mass, lipophilicity, hydrogen bond donors and acceptor and molar refractivity range for pharmaceutical drug candidates (Lipinski, 2004; Jayaram *et al*., 2012). Lipinski’s rule of five is mentioned in Table 1. The most probable target biological moiety was retrieved from the ChEMBL-20 database. Lipinski's rule of five posits that compounds are more likely to be orally active if they have no more than one violation of the criteria viz., a molecular weight under 500 Daltons, no more than five hydrogen bond donors, no more than ten hydrogen bond acceptors, and a partition coefficient (log P) not exceeding five (Lipinski, 2004).

**Table 1. Lipinski’s rule of five**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Molecular Weight (g/mol)** | **Lipophilicity**  **(MLogP)** | **H-Bond Donors** | **H-bond acceptors** | **Rule Violation/ Molar Refractivity** | **Drug Likeness** |
| <500 | <5 | <5 | <10 | <2 / 40-130 | Yes |

**RESULTS AND DISCUSSION**

The bioactive compounds of medicinal plants *E. ribes* and *G. superb* (viz., caffeic acid, chlorogenic acid, cinnamic acid, o-cumaric acid, colchicine, embelin, and vanillic acid) have been selected for their pharmacophore analysis based on the literature survey. The bioactive compounds viz., Caffeic acid (ID- [ZINC58172](https://zinc.docking.org/substances/ZINC000000058172/)), Chlorogenic acid (ID-[ZINC6482465),](https://zinc.docking.org/substances/ZINC000006482465/) Cinnamic acid (ID- [ZINC16051516](https://zinc.docking.org/substances/ZINC000016051516/)), o-cumaric acid, Colchicine version COLCRYS (ID- [ZINC621853](https://zinc.docking.org/substances/ZINC000000621853/)), Embelin (ID- [ZINC1531764](https://zinc.docking.org/substances/ZINC000001531764/)), Vanillic acid (ID- [ZINC1644138](https://zinc.docking.org/substances/ZINC000001644138/)) were mined using a zinc docking tool for their SMILESand the chemical structures were drew by ChemDrawshown in Table 2.

**Table 2. SMILES of selected bioactive compounds retrieved from the ZINC database and structure drawn by ChemDraw**

|  |  |  |  |
| --- | --- | --- | --- |
| **S.N.** | **Bioactive Compound** | **Structure**  **(drawn by ChemDraw)** | **SMILES** |
|  | **Caffeic acid** [ZINC58172](https://zinc.docking.org/substances/ZINC000000058172/) |  | **O=C(O)/C=C/c1ccc(O)c(O)c1** |
|  | Chlorogenic acid [ZINC6482465](https://zinc.docking.org/substances/ZINC000006482465/) |  | **COC(=O)[C@]1(O)C[C@@H](O)[C@@H](O)[C@H](OC(=O)/C=C/c2ccc(O)c(O)c2)C1** |
|  | **Cinnamic acid** [**ZINC16051516**](https://zinc.docking.org/substances/ZINC000016051516/) |  | **O=C(O)/C=C/c1ccccc1** |
|  | o-cumaric acid (var. 2-Coumarate) |  | **O=C(O)/C=C/c1ccccc1O** |
|  | **Colchicine (COLCRYS)**  [**ZINC621853**](https://zinc.docking.org/substances/ZINC000000621853/) |  | **COc1cc2c(c(OC)c1OC)-c1ccc(OC)c(=O)cc1[C@@H](NC(C)=O)CC2** |
|  | **Embelin**  [**ZINC1531764**](https://zinc.docking.org/substances/ZINC000001531764/) |  | **CCCCCCCCCCCC1=C(O)C(=O)C=C(O)C1=O** |
|  | **Vanillic acid**  [**ZINC1644138**](https://zinc.docking.org/substances/ZINC000001644138/) |  | **COc1cc(C(=O)O)ccc1OS(=O)(=O)O** |

Further, the ZINC database was used to explore molecular weight, molecular formula, tPSA (total Polar Surface Area) and most probable target biological moiety which is tabulated in Table 3.

**Table 3. The probable targets of selected bioactive compounds retrieved ZINC database associated with ChEMBL 20 database**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **S.N.** | **Bioactive Compound** | **Molecular weight** | **Molecular formula** | **tPSA**  **(from ZINC)** | The most probable target as per the ChEMBL 20 database | |
|  |  |  |  | pKi (L.E.) |  |
|  | **Caffeic acid** | 180.159 | C9H8O4 | 80 | 8 | [MMP9\_HUMAN](https://zinc.docking.org/orthologs/MMP9_HUMAN/) |
|  | **Chlorogenic acid** | 368.338 | C17H20O9 | 153 | There is no known activity for this compound. | |
|  | **Cinnamic acid** | 148.161 | C9H8O2 | 40 | 5.31 | [HCAR2](https://zinc.docking.org/genes/HCAR2/) |
|  | **o-cumaric acid** | **No Data Available (NDA)** | | | | |
|  | **Colchicine** | 399.443 | C22H25NO6 | 83 | 6.11 | [TUBB2B](https://zinc.docking.org/genes/TUBB2B/) |
|  | **Embelin** | 294.391 | C17H26O4 | NDA | 7.22 | [ALOX5](https://zinc.docking.org/genes/ALOX5/) |
|  | **Vanillic acid** | 248.212 | C8H8O7S | NDA | There is no known activity for this compound. | |

The analysis of bioactive compounds retrieved from the ZINC database and their probable targets in the ChEMBL 20 database highlights several key findings. Caffeic acid exhibits a high binding affinity (pKi = 8) for MMP-9, suggesting its potential as a matrix metalloproteinase-9 inhibitor, which is significant in cancer metastasis and inflammatory diseases. Similarly, Cinnamic acid targets HCAR2 (pKi = 5.31), a receptor involved in anti-inflammatory and metabolic regulatory pathways. Colchicine, a well-known microtubule inhibitor, demonstrates a notable interaction with TUBB2B (pKi = 6.11), reinforcing its therapeutic relevance in cancer and inflammatory conditions. Additionally, Embelin shows strong binding to ALOX5 (pKi = 7.22), indicating potential anti-inflammatory and anti-cancer properties. However, Chlorogenic acid and Vanillic acid lack known activity in the ChEMBL 20 database, suggesting the need for further experimental validation to confirm their pharmacological potential. The absence of molecular weight and target data for o-Coumaric acid highlights possible gaps in computational screening, warranting additional research. Overall, this study underscores the significance of MMP-9, HCAR2, ALOX5, and TUBB2B as key pharmacological targets for these plant-derived compounds, reinforcing their potential applications in cancer, inflammatory diseases, and metabolic disorders.Prasanna and Doerksen (2009) mentioned that the tPSA (total Polar Surface Area) values below 140 Å indicated that good intestinal absorption is expected for the new drug candidates. However, Chlorogenic acid and Vanillic acid did not show any known activity in the database. Furthermore, o-Coumaric acid and Vanillic acid were marked as NDA (No Data Available) in the Zinc database, indicating a lack of documented interaction with known biological targets. Conclusively, the present research work revealed that Caffeic acid, Cinnamic acid, Colchicine, and Embelin had potential biological activity, whereas Chlorogenic acid and Vanillic acid lacked recorded target interactions. The absence of data for o-Coumaric acid and Vanillic acid highlighted the need for further investigation into their bioactivity.

Notably in our study, Cinnamic acid has a most significant tPSA of 40 Å (Table 3). A low tPSA is typically favoured as it signifies a molecule's enhanced capacity to cross cell membranes and access its target site within the organism, whereas a high TPSA implies inadequate membrane permeability and potentially restricted absorption, rendering it less advantageous for drug development. However, the tPSA value of 153 was recorded for Chlorogenic acid which indicates its poor membrane permeability efficacy.Rashid and Bardaweel (2023) stated that the MMPs belong to a family of zinc-dependent proteolytic metalloenzymes. MMP-9, a member of the gelatinase B family, is characterized as one of the most intricate MMPs. They also pointed the crucial involvement of MMP-9 in extracellular matrix (ECM) remodeling underscores its significant correlation with each stage of cancer pathogenesis and progression. Pan *et al*. (2023) documented that the HCAR2 belongs to the family of class A G protein-coupled receptors with key roles in regulating lipolysis and free fatty acid formation in humans. It is deeply involved in many pathophysiological processes and serves as an attractive target for the treatment of cardiovascular, neoplastic, autoimmune, neurodegenerative, inflammatory, and metabolic diseases. Nguyen *et al*. (2023) divulged that the SLC22A3 gene encodes the organic cation transporter (OCT)-3 and is associated with the prognosis of various cancer types. Nonetheless, its function in lung squamous cell carcinoma (LSCC) remains unexplored in other studies. Poirier *et al*. (2020) mentioned that the 5-lipoxygenase (5-LO), encoded by the ALOX5 gene, is expressed in leukocytes and facilitates the synthesis of leukotrienes, which are pro-inflammatory lipid mediators. Leukotrienes play a crucial role in immune responses and are implicated in inflammatory disorders, with 5-LO expression linked to the persistence of leukaemia stem cells. Understanding the biological processes that regulate 5-LO expression is essential. Additionally, they examined the regulation of 5-LO expressing themselves and leukotriene production during the maturation process of human monocytic cells.

**Table 4.** Pharmacokinetics (ADME) prediction of selected bioactive compounds using SWISS ADME

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Bioactive Compound** | **Caffeic acid** | **Chlorogenic acid** | **Cinnamic acid** | **o-cumaric acid**  **(Chemspider databse)** | **Colchicine** | **Embelin** | **Vanillic Acid** |
| **Formula** | **C9H8O4** | **C17H20O9** | **C9H8O2** | **C9H8O3** | **C22H25NO6** | **C17H26O4** | **C8H8O7S** |
| **Molecular Weight (g/mol)** | **180.16** | **368.34** | **148.16** | **164.16** | **399.44** | **294.39** | **248.21** |
| **H-Bond Acceptors** | **4** | **9** | **2** | **3** | **6** | **4** | **7** |
| **H-Bond Donor** | **3** | **5** | **1** | **2** | **1** | **2** | **2** |
| **Molar Refractivity**  **(40-130)** | **47.16** | **87.82** | **43.11** | **45.13** | **109.36** | **84.31** | **52.11** |
| **TPSA**  **(SWISS ADME)** | **77.76** | **153.75** | **37.30** | **57.53** | **83.09** | **74.60** | **118.51** |
| **Average Lipophilicity**  **(LogPo/w)** | **0.93** | **-0.00** | **1.79** | **1.40** | **2.36** | **3.68** | **0.39** |
| **Water Solubility**  **(LogS, ESOL)** | **Soluble**  **(-1.89)** | **Soluble**  **(-1.84)** | **Soluble**  **(-2.37)** | **Soluble**  **(-2.37)** | **Soluble**  **(-2.90)** | **-4.42** | **-1.83** |
| **Pharmacokinetics**  **(GI absorption)** | **High** | **Low** | **High** | **High** | **High** | **Moderately soluble** | **High** |
| **DrugLikeness**  **(Lipinski)** | **Yes,**  **0 violation** | **Yes,**  **0 violation** | **Yes;**  **0 violation** | **Yes;**  **0 violation** | **Yes;**  **0 violation** | **Yes,**  **0 violation** | **Yes;**  **0 violation** |
| **Bioavailability Score** | **0.56** | **0.55** | **0.85** | **0.85** | **0.55** | **0.85** | **0.56** |
| **Synthetic accessibility** | **1.81**  **(Very easy)** | **4.27**  **(Moderate)** | **1.67** | **1.85** | **3.87** | **3.66** | **2.25** |
| **Leadlikeness** | **No;**  **1 violation: MW<250** | **No;**  **1 violation: MW>350** | **No;**  **1 violation: MW<25** | **No;**  **1 violation: MW<250** | **No;**  **1 violation: MW>350** | **No;**  **2 violations** | **No;**  **1 violation** |

The present study analyzed seven bioactive compounds—Caffeic acid, Chlorogenic acid, Cinnamic acid, o-Coumaric acid, Colchicine, Embelin, and Vanillic acid—based on their molecular characteristics, pharmacokinetics, and drug-likeness. Their molecular weights ranged from 148.16 g/mol for Cinnamic acid to 399.44 g/mol for Colchicine. The hydrogen bond acceptors varied between 2 (Cinnamic acid) and 9 (Chlorogenic acid), while the number of hydrogen bond donors ranged from 1 (Cinnamic acid, Colchicine) to 5 (Chlorogenic acid). Molar refractivity values fell between 43.11 (Cinnamic acid) and 109.36 (Colchicine), indicating differences in molecular size and electronic distribution. The lipophilicity (LogP) values demonstrated a wide range, with Chlorogenic acid having the lowest (-0.00) and Embelin the highest (3.68). Most of the compounds exhibited good water solubility, except for Embelin, which had a LogS value of -4.42, indicating poor solubility. Regarding pharmacokinetics, most compounds showed high gastrointestinal (GI) absorption, except for Chlorogenic acid, which exhibited low absorption, and Embelin, which was moderately absorbed.

In terms of drug-likeness, all compounds complied with Lipinski’s Rule of Five, suggesting their potential as drug candidates. The bioavailability scores varied, with Cinnamic acid, o-Coumaric acid, and Embelin achieving the highest score of 0.85, while the others ranged between 0.55 and 0.56. However, none of the compounds fully met lead-likeness criteria due to molecular weight constraints or other structural limitations. Synthetic accessibility scores indicated that Cinnamic acid (1.67) and Caffeic acid (1.81) were the easiest to synthesize, whereas Chlorogenic acid (4.27), Colchicine (3.87), and Embelin (3.66) presented moderate synthetic difficulty. Overall, these bioactive compounds exhibited diverse pharmacokinetic and physicochemical properties. Most of them were highly soluble, drug-like, and bioavailable, though Chlorogenic acid showed poor GI absorption and Embelin displayed low solubility, which could impact their pharmacological applications. Another crucial point was noted that ZINC and SWISS ADME database has little variation in tPSA value.

Despite its numerous advantages, *in silico* evaluation of plant secondary metabolites for pharmacological applications has several limitations. One major challenge is the accuracy and reliability of computational predictions, as these models rely on existing databases and algorithms that may not fully capture the complexity of biological interactions. The lack of comprehensive datasets on plant metabolites, their bioavailability, and metabolic pathways can lead to misleading results. Additionally, molecular docking and virtual screening approaches often overlook crucial factors such as solubility, pharmacokinetics, and dynamic interactions within biological systems, limiting their predictive power. Furthermore, in silico evaluations cannot replace *in vitro* and *in vivo* experimental studies, making experimental validation essential to confirm predicted bioactivities. The structural diversity and complexity of phytochemicals also pose challenges in standardizing computational models, increasing the risk of errors in binding affinity predictions. Despite these limitations, *in silico* approaches remain valuable for preliminary screening but must be integrated with experimental methodologies for a more comprehensive and reliable assessment of plant-derived compounds in drug discovery.Bottom of Form

**CONCLUSION**

The investigation of TPMI is crucial for identifying novel treatment approaches, particularly in underdeveloped nations where traditional medicine plays a vital role in healthcare. The integration of bioinformatics-driven *in silico* techniques for primary screening and validation of pharmacologically potent bioactive agents, has revolutionized the pharmacological evaluation of TPMI which significantly reducing the time and cost constraints associated with conventional experimental methods. In this study, we emphasize the substantial therapeutic potential of medicinal plants, particularly *E. ribes* and *G. superba*, by highlighting their diverse array of bioactive compounds as key that can target MMP-9, HCAR2, SLC22A3, and ALOX5. These interactions underscore their relevance in treating disorders such as papillary thyroid carcinoma and inflammatory diseases. This integrated approach aligns with ongoing efforts to bridge traditional medicinal knowledge with modern drug discovery, fostering sustainable and innovative healthcare solutions.

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**References**

Bento, A. P., Gaulton, A., Hersey, A., Bellis, L. J., Chambers, J., Davies, M., Kruger, F. A., Light, Y., Mak, L., McGlinchey, S., Nowotka, M., Papadatos, G., Santos, R., Overington, J. P. (2014). The ChEMBL bioactivity database: an update. *Nucleic Acids Res.*, 42 DOI-D1083–109010.1093/nar/gkt1031.

Chambers, J., Davies, M., Gaulton, A., Hersey, A., Velankar, S., Petryszak, R., Hastings, J., Bellis, L., McGlinchey, S., Overington, J.P. (2013). UniChem: a unified chemical structure cross-referencing and identifier tracking system, *J. Cheminf*., 5, 3-310. DOI-1186/1758-2946-5-3.

Chambers, J., Davies, M., Gaulton, A., Papadatos, G., Hersey, A., Overington, J. P. (2014). UniChem: extension of InChI-based compound mapping to salt, connectivity and stereochemistry layers, *J. Cheminf*., 6, 43–4310. DOI-1186/s13321-014-0043-5.

Choudhary, S., Kaurav, H., Chaudhary, G. (2021). Vaibidang (Embeliaribes): A Potential Herbal Drug in Ayurveda with Anthelmintic Property, *International Journal for Research in Applied Sciences and Biotechnology*, 8, 237-243. DOI-10.31033/ijrasb.8.2.31.

Haq, K., Ali, M., Siddiqui, A.W. (2005). New compounds from the seeds of *Embeliaribes* Burm. Die Pharmazie, *An International Journal of Pharmaceutical Sciences*, 60(1), 69-71.

Horticulture Department of Chhattisgarh Government, 2012) <http://agriportal.cg.nic.in/horticulture/PDF/Budget/12th%20Five%20Year%20Plan%20Discription.doc>).

Indrayan, A.K., Sharma, S., Durgapal, D., Kumar, N., Kumar, M. (2005). Determination of nutritive value and analysis of mineral elements for some medicinally valued plants from Uttaranchal, *Current Science*, 10, 1252-5.

Jasmine, J.A., Sundari, T., Balakrishan, V. (2020). HPLC analysis of *Gloriosa superba* L., from five different accessions of Tamil Nadu state, India, *J New Biol Rep*, 9(2), 223-227.

Jayaram B., Tanya Singh, Goutam Mukherjee, Abhinav Mathur, Shashank Shekhar, and Vandana Shekhar, "Sanjeevini: a freely accessible web-server for target directed lead molecule discovery", *BMC Bioinformatics*,**2012**, *13*, S7. <http://www.biomedcentral.com/1471-2105/13/S17/S7>.

Li, Q., Cheng, T., Wang. Y., Bryant, S.H. (2010). PubChem is a public resource for drug discovery. Drug Discovery Today, 15, 1052–1057 DOI-10.1016/j.drudis.2010.10.003.

Lipinski, C. A. (2004). Lead- and drug-like compounds: the rule-of-five revolution. *Drug Discovery Today. Technologies*, *1*(4), 337–341. https://doi.org/10.1016/j.ddtec.2004.11.007

Nguyen, T. A., Le, M. K., Nguyen, P. T., Tran, N. Q. V., Kondo, T., & Nakao, A. (2023). SLC22A3 that encodes organic cation transporter-3 is associated with prognosis and immunogenicity of human lung squamous cell carcinoma. Translational lung cancer research, 12(10), 1972–1986. <https://doi.org/10.21037/tlcr-23-334>

Palhares RM, Gonçalves Drummond M, Dos Santos Alves Figueiredo Brasil B, Pereira Cosenza G, das Graças Lins Brandão M, Oliveira G. Medicinal plants recommended by the world health organization: DNA barcode identification associated with chemical analyses guarantees their quality. PLoS One. 2015 May 15;10(5):e0127866. <https://doi.org/10.1371/journal.pone.0127866>

Pan, X., Ye, F., Ning, P., Zhang, Z., Li, X., Zhang, B., Wang, Q., Chen, G., Gao, W., Qiu, C., Wu, Z., Li, J., Zhu, L., Xia, J., Gong, K., & Du, Y. (2023). Structural insights into ligand recognition and selectivity of the human hydroxycarboxylic acid receptor HCAR2. Cell Discovery, 9(1). <https://doi.org/10.1038/s41421-023-00610-7>

Poirier, S. J., Boudreau, L. H., Flamand, N., & Surette, M. E. (2020). LPS induces ALOX5 promoter activation and 5-lipoxygenase expression in human monocytic cells. Prostaglandins, Leukotrienes, and Essential Fatty Acids, 154(102078), 102078. https://doi.org/10.1016/j.plefa.2020.102078

Prasanna, S., & Doerksen, R. (2009). Topological polar surface area: A useful descriptor in 2D-QSAR. Current Medicinal Chemistry, 16(1), 21–41. <https://doi.org/10.2174/092986709787002817>.

Rashid ZA, Bardaweel SK. Novel Matrix Metalloproteinase-9 (MMP-9) Inhibitors in Cancer Treatment. Int J Mol Sci. 2023 Jul 28;24(15):12133. doi: 10.3390/ijms241512133. PMID: 37569509; PMCID: PMC10418771.

RSC (2015). ChemSpider. [http://chemspider.com](http://chemspider.com/) (accessed Nov 18, 2021).

Rubio-Perez, C., Tamborero, D., Schroeder, M.P., Antolín, A.A., Deu-Pons, J., Perez-Llamas, C., Mestres, J., Gonzalez-Perez, A., Lopez-Bigas, N. (2015). In silico prescription of anticancer drugs to cohorts of 28 tumor types reveals targeting opportunities, *Cancer Cell*, 27(3), 382-96. DOI-10.1016/j.ccell.2015.02.007. PMID: 25759023.

Yi, F., Li, L., Xu, L., [Meng](https://cmjournal.biomedcentral.com/articles/10.1186/s13020-018-0190-0#auth-Hong-Meng), H.,  [Dong](https://cmjournal.biomedcentral.com/articles/10.1186/s13020-018-0190-0" \l "auth-Yin_mao-Dong), Y., [Liu](https://cmjournal.biomedcentral.com/articles/10.1186/s13020-018-0190-0#auth-Hai_bo-Liu), H., [Xiao](https://cmjournal.biomedcentral.com/articles/10.1186/s13020-018-0190-0" \l "auth-Pei_gen-Xiao), P. (2018). In silico approach reveals traditional medicine plant's pharmacological material basis, *Chin Med*., 13, 33. DOI-https://doi.org/10.1186/s13020-018-0190-0

[Yi](https://www.frontiersin.org/people/u/347115), F., Sun, L., Xu, L., Peng, Y., Liu, H., He, C., Xiao, P. (2016). In silico approach for anti-thrombosis drug discovery: P2Y1R structure-based TCMs screening, *Front. Pharmacol*., DOI-<https://doi.org/10.3389/fphar.2016.00531>

Zhang, [X.](https://www.ncbi.nlm.nih.gov/pubmed/?term=Zhang%20X%5BAuthor%5D&cauthor=true&cauthor_uid=28769792), [Zheng](https://www.ncbi.nlm.nih.gov/pubmed/?term=Zheng%20W%5BAuthor%5D&cauthor=true&cauthor_uid=28769792), W., Wang, [T.](https://www.ncbi.nlm.nih.gov/pubmed/?term=Wang%20T%5BAuthor%5D&cauthor=true&cauthor_uid=28769792), Ren, [P.](https://www.ncbi.nlm.nih.gov/pubmed/?term=Ren%20P%5BAuthor%5D&cauthor=true&cauthor_uid=28769792), Wang, [F.](https://www.ncbi.nlm.nih.gov/pubmed/?term=Wang%20F%5BAuthor%5D&cauthor=true&cauthor_uid=28769792), Ma, [X](https://www.ncbi.nlm.nih.gov/pubmed/?term=Ma%20X%5BAuthor%5D&cauthor=true&cauthor_uid=28769792)., Wang, [J.](https://www.ncbi.nlm.nih.gov/pubmed/?term=Wang%20J%5BAuthor%5D&cauthor=true&cauthor_uid=28769792), Huang, [X.](https://www.ncbi.nlm.nih.gov/pubmed/?term=Huang%20X%5BAuthor%5D&cauthor=true&cauthor_uid=28769792) (2017). Danshen-Chuanxiong-Honghua Ameliorates cerebral impairment and improves spatial cognitive deficits after transient focal ischemia and identification of active compounds, *Front Pharmacol*., 8, 452. DOI-[10.3389/fphar.2017.00452](https://dx.doi.org/10.3389%2Ffphar.2017.00452)

Zhang, Y., Mao, X., Guo, Q., Bai, M., Zhang, B., Liu, C., Sun, Y., Li, S., Lin, N. (2016). Pathway of PPAR-gamma coactivators in thermogenesis: a pivotal traditional Chinese medicine-associated target for individualized treatment of rheumatoid arthritis, *Oncotarget*, 29, 7(13), 15885-900.DOI-10.18632/oncotarget.7419. PMID: 26895106.