STM JOURNALS

International Journal of
Cheminformatics

Volume 1, Issue 2, 2023
July- December
DOI (Journal): 10.37591/IJCI

*https://journals.stmjournals.com/ijci/*

Research IJCI

# Unlocking The Bioactivity Potential: Molecular Insights and Predictions of Salen, Salophen, Allicin, Curcumin, and Piperine

Anamika Pandey[1], Udita Singh[2], Mandakini Gupta[3], Sumit Kumar Chaudhary[4], Ranjeet Kumar[5], Piyush Kumar Sonkar[6,*]

***Abstract***

*In this work, the prediction of the biological activity of several significant molecules, including salen, salophen, allicin, curcumin, and piperine, is discussed. Using Molinspiration software, the molecular properties of these compounds were calculated. These molecules arehighly significant due to their extensive potential in medical applications. Salen and salophen, for instance, play crucial roles in cancer chemotherapy and act as inhibitors of angiogenesis. Curcumin is renowned for its antioxidant properties, piperine is recognized as an alkaloid and anti-arthritic agent, and allicin is a phytochemical known for its anti-cancer effects. Biological pharmacological activity refers to the beneficial impacts a drug or molecule has on living organisms. The bioactivity of these molecules was predicted using Mo inspiration, which provides cheminformatics tools for molecular interpretation and processing. This software facilitates the conversion of SMILES and SD files, normalization of molecules, and the calculation of various molecular properties. Consequently, it significantly aids in predicting the bioactivity of these crucial molecules, which can lead to advancements in their medical applications. By understanding their molecular properties and potential biological activities, researchers can better harness these molecules for therapeutic uses, ultimately contributing to improved health outcomes.*

**Keywords:** Salen, salophen, allicin, curcumin, piperine, molinspiration

***Author for Correspondence**
Piyush Kumar Sonkar
E-mail: piyushchem.mmv@bhu.ac.in

[1]Research Scholar, Department of Zoology, Institute of Science, Banaras Hindu University (BHU), Varanasi, India
[2]M. Sc Student, Department of Chemistry, Institute of Science, Banaras Hindu University (BHU), Varanasi, India
[3]Assistant Professor, Department of Chemistry, Sunbeam Women's College Varuna, Varanasi, India
[4]Research Associate, Department of Chemistry, MMV, BHU, India
[5]Assistant Professor, Department of Chemistry, Vikramajit Singh Sanatan Dharma College, Kanpur, India
[6]Assistant Professor Department of Chemistry, MMV, BHU, India

Received Date: June 14, 2023
Accepted Date: June 15, 2023
Published Date: June 28, 2023

**Citation:** Anamika Pandey, Udita Singh, Mandakini Gupta, Sumit Kumar Chaudhary, Ranjeet Kumar, Piyush Kumar Sonkar. Unlocking the Bioactivity Potential: Molecular Insights and Predictions of Salen, Salophen, Allicin, Curcumin, and Piperine. International Journal of Cheminformatics. 2023; 1(2): 14–21p.

## INTRODUCTION

### Salen

Salen is prepared from the salicylaldehyde and ethylenediamine. It is one of the most significant ligands in coordination chemistry used in catalysis [1]. It is also known as N, N bis(salicylidene) ethylenediamine. Salen is a bright yellow compound soluble in polar solvents [1, 2]. It has a significant role in electrocatalysis, material science, pharmaceuticals, and catalysis [2, 3]. Due to its significant properties, salen has been selected for testing molecular parameters in this work (Figure. 1).

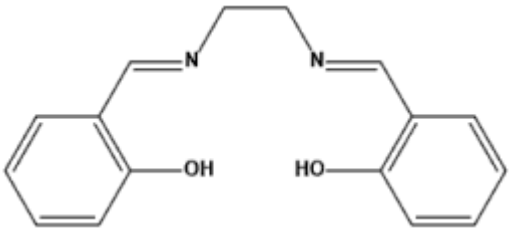


**Figure 1.** Structure of Salen ligand.

 

***Salophen***

Salophen is an organic compound having the chemical formula $C_5H_{13}NO_4$ (Figure. 2). It is an esterification product of salicylic acid and paracetamol [3, 4]. It has biological importance as it is decomposed in the intestine, even when given as an injection. Salophen was also used as a substitute for salicylic acid in acute rheumatism and as an intestinal antiseptic. It is similarly effective and much safer than salol (another antiseptic used earlier). Similar to salen, salophen is also used as a ligand in coordination chemistry and the metal complexes of the salophen have a variety of applications in catalysis, sensing, pharmaceuticals, etc. [3, 4].

**Allicin**

Allicin is obtained from Allium sativum, having the chemical formula $C_6H_{10}OS_2$ (Figure. 3). It is an organic compound obtained from garlic [5]. It is a colourless liquid with a specific pungent smell. It has significant antibacterial and antifungal activities [5, 6] and has various applications such as a free radical scavenger, anti-oxidants, hypoglycemic agents, anti-infective agents, and hypolipidemic agents [5]. Due to the presence of sulfoxide, it also acts as an antifungal agent. It has also significant properties of the anti-bacterial agent [6, 7]. Hence, the allicin molecule has been selected for molecular properties calculation due to its significant biological applications.

***Curcumin***

Curcumin is also known as diferuloylmethane. It is the main natural polyphenol present in the rhizome of Curcuma longa (turmeric), and other Curcuma species [8]. Due to its antioxidant properties, it can also be used as a medicinal herb. It also possesses anti-inflammatory, antimicrobial, and anticancer properties [8]. Curcumin has significant applications in inflammation, metabolic malfunctioning, and pain. It also helps in inflammatory and degenerative eye problems [9–12]. So, it has been selected as a target molecule in this work (Figure. 4).

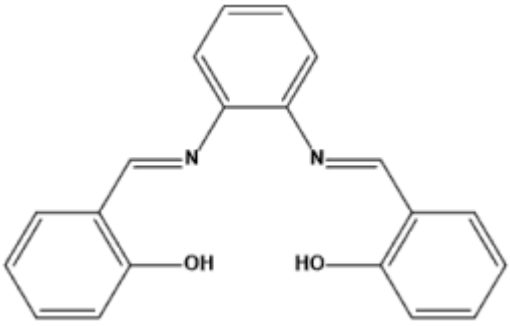


**Figure 2.** Structure of salophen.

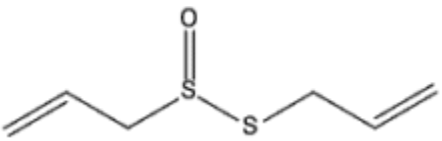


**Figure 3.** Structure of allicin.

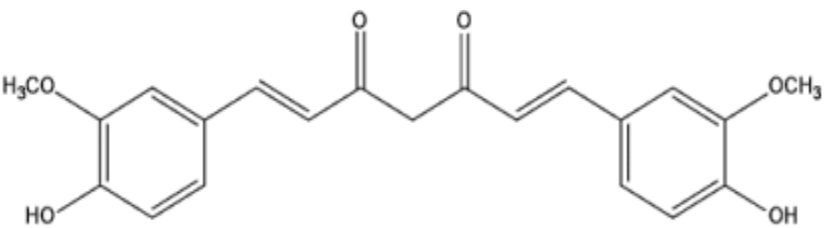


**Figure 4.** Structure of curcumin molecule.

 

**Piperine**

Piperine is obtained from Piper nigrum having molecular formula is $C_{17}H_{19}NO_3$ (Figure. 5). It is an alkaloid and can be derived from piperic acid [13]. It is present in pepper (Piper nigrum) which is responsible for the hot taste of pepper. Piperine is useful in pharmaceuticals [14–17]. Hence, it has been selected for the analysis of molecular properties in this work.

## CHEMDRAW SOFTWARE

Chemdraw software is one of the useful chemistry molecules drawing software. It is easy to use and one of the best software used for drawing structures and finding the stereochemistry of the molecules [18]. It has a variety of features such as easy-to-use, stereochemistry, spectra prediction, templates, mass fragmentation, color, rotation, etc. It is helpful in drawing molecular structure, parameter prediction, and research article preparation [19, 20].

**Molinspiration Software**

Molinspiration is one of the useful cheminformatics software for the prediction of molecular properties [21]. It has a range of cheminformatics software tools which is useful in the prediction, and description of different structures, substructure, and molecular properties. It is useful in drug design, molecular parameter prediction, and bioactivity [22]. Molinspiration is an independent platform and also assists in bioactivity prediction, virtual screening, and data visualization. It is compatible with PC, Mac, UNIX, or LINUX machines [21].

## EXPERIMENTAL

**Software Details**

A Chemdraw 12.0 was used for the preparation of the structure of molecules. Molinspiration cheminformatics software (online) was used for the prediction of molecular and biological activity.

***Operating procedure***

The structure of salen, salophen, curcumin, allicin, and piperine was prepared using chemdraw software. The structure of the particular molecule was inserted/drawn in the molinspiration software. A smile notation of the molecules can also be used instead of the structure of the molecule. The molecular properties, and biological parameters were calculated from molinspiration software tool, and the similar procedure was followed for all the molecules (Figure. 6).

## RESULTS AND DISCUSSIONS

The parameters are showing the bioactivity score or biological activity of the molecules which describes the beneficial or adverse effects of a drug on living matter. Its activity depends on the self-fulfilment of the ADME criteria or drug-likeness property. This parameter helps us in concluding the range in which a particular molecule is active or inactive.

**Calculation of Molecular Properties**

The molecular properties such as lipophilicities (LogP) and polar surface areas (PSA) offer eminence roles in determining biological responses and are commonly used in predicting the structural activity relationships of bioactive molecules [22]. Therefore, LogP and PSA are considered a significant parameter in structure-activity relationships study and are the most informative and successful physiochemical properties and is used as a major experimental and theoretical tool in drug design [21–25]. Apart from these two properties, nrotb, molecular volume, etc. are also essential for getting various useful information related to molecules in detail. The parameter value of one molecule differs significantly because of their different molecular formula and their structure in three-dimensional space i.e., participation of different atoms and number of atoms that make each molecule specific and provide it unique identity.

The parameters such as LogP, PSA, n atom, molecular weight, Non, n violations, nrotb, and volume for the different molecules; salen, salophen, allicin, curcumin, and piperine are summarized in Table 1.

 

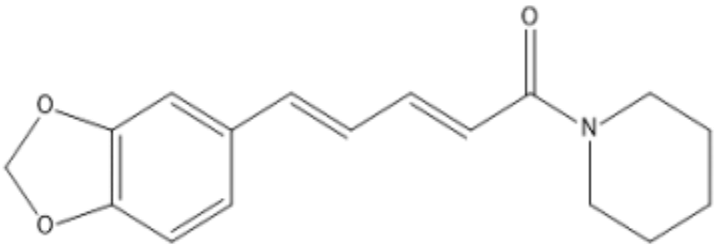


**Figure 5.** Structure of the piperine molecule.

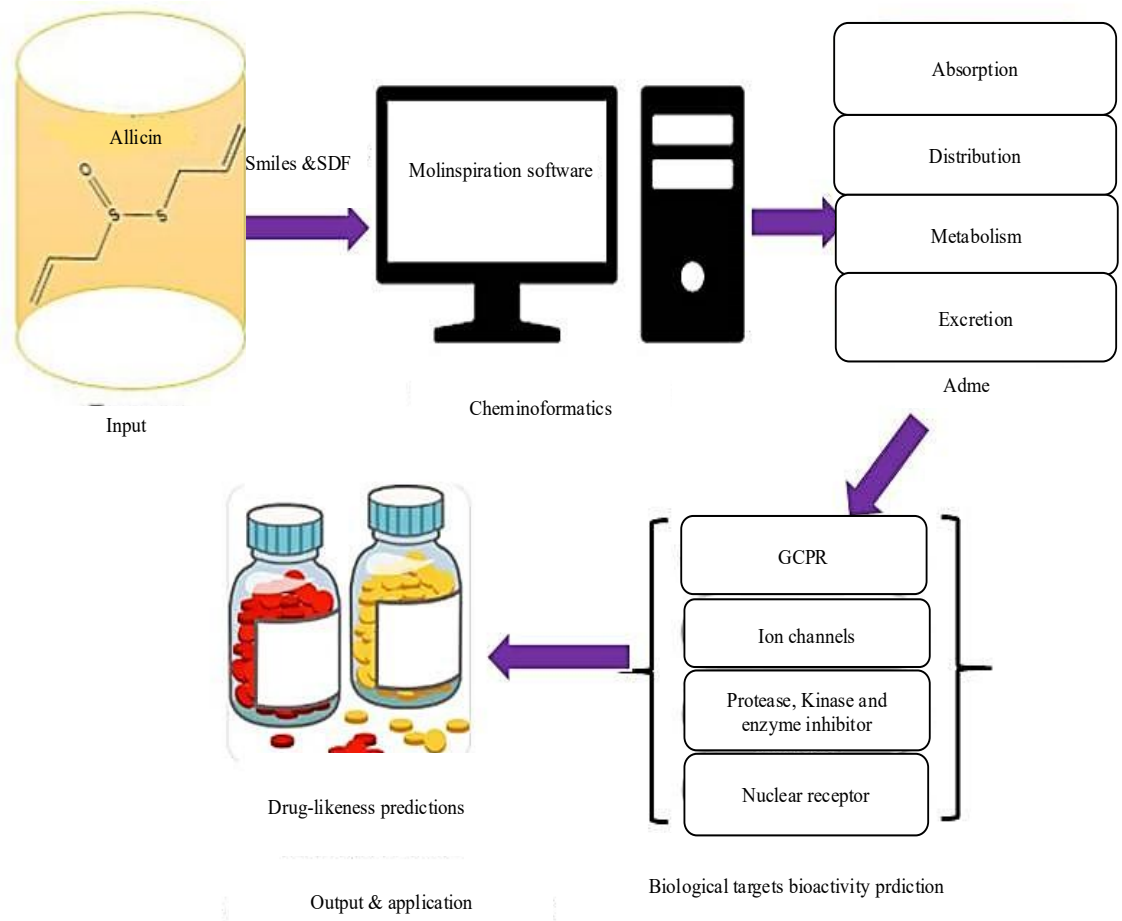


**Figure 6.** Steps for determining biological parameters & applications of molecules.

**Table 1.** shows the molecular properties of the given molecules.

| **Molecule Name** | **Milog P** | **TPSA** | **No. of atoms** | **Molecular Weight** | **nON** | **n OHNH** | **n violations** | **n rotb** | **Volume** |
|---|---|---|---|---|---|---|---|---|---|
| Molecule Name | MilogP | TPSA | $N_{at}$ | Molecular Weight | $N_{ON}$ | $N_{OHNH}$ | NViolations | Nrotb | Volume |
| Salen | 1.66 | 58.20 | 20 | 268.32 | 4 | 2 | 0 | 5 | 251.83 |
| Salophen | 3.05 | 75.63 | 20 | 271.27 | 5 | 2 | 0 | 4 | 239.38 |
| Allicin | 2.06 | 17.07 | 9 | 162.28 | 1 | 0 | 0 | 5 | 145.51 |
| Curcumin | 2.30 | 93.07 | 27 | 368.38 | 6 | 2 | 0 | 8 | 332.18 |
| Piperine | 3.33 | 38.78 | 21 | 285.34 | 4 | 0 | 0 | 3 | 267.74 |

 

*LogP:* is the octanol-water partition ratio and is the most common way of expressing the lipophilicity of a compound. The lipophilicity character of a molecule is based on two important factors: hydrophobicity and polarity, which help the molecules to cross or irreversible damage the cellular membrane [22–25]. It is also known as octanol/water partition coefficients (clogP). It is defined as the ratio of the concentration of a solute in water-saturated octanolic phase to its concentration in octanol-saturated aqueous phase. It is described by the following expression:

$K_{ow}$ = [solute]octanol/[solute]water Both the polar and the hydrophobic character of a compound are reasonably described by the partition coefficient between octanol and water $K_{OW}$ (or $P_{ow}$). Positive values for log $K_{ow}$ indicate some hydrophobic character and larger values show more hydrophobicity among the above molecule [21–25]. Also, a molecule with low or negative values for Kow is frequently indicated as polar or possessing hydrophilic character.

Among the above discussed compounds, Piperine is most hydrophobic because it shows the highest positive Kow values while salen is least hydrophobic or most hydrophilic because it shows the lowest negative Kow value which indicates its non-polar property.

Molecular polar surface area (PSA) is a useful parameter for the estimation of drug transport properties. PSA belongs to the total surfaces of polar atoms (generally O, N, and attached H atoms), it plays a significant role in determining quantitative structure-activity relationships (QSAR) of a molecule, n atoms represent the number of atoms present in a molecule. It is the cumulative surface belonging to polar atoms. In the above table, curcumin has the highest total polar surface area (TPSA), and allicin has the lowest number of atoms interacting in the molecules. Curcumin possesses the highest number of interacting atoms in its structure while allicin possesses the lowest number of interacting atoms in its structure.

*Molecular weight:* is the weight of each atom present in the chemical structure or molecular formula. The larger the structure i.e. the larger the number of atoms involved in the structure, the larger is the molecular weight of the molecule. Among the above-listed molecules, curcumin has the highest molecular weight while allicin has the lowest.

*nON*: is the number of nitrogen-oxygen bonds present in the molecule. curcumin shows the highest number of O-N bonds and allicin has the lowest number of O-N bonds.

*n Violations- "Rule of 5 properties*", is also known as Lipinski's Rule of 5. n violations signifies the drug-likeness or Lipinski's rule of 5 property of a molecule. The rule is based on drug properties like absorption, distribution, metabolism, and excretion on some specific molecular properties [21–25].

*n rotb (number of rotatable bonds):* is a measure of molecular flexibility representing simple topological parameters and represents no. of rotatable bond present in the molecules. It is a significant parameter of oral bioavailability of drugs [21-25]. From the above-tabulated molecule, Curcumin has a maximum number (8) of rotable bonds while piperine has the lowest (3).

*Volume:* Molecular volume provides information about transport properties of molecules (e.g. blood-brain barrier penetration and intestinal absorption). It is generally used in QSAR studies of molecules and biological activities. Curcumin shows the highest molecular volume, while allicin shows the lowest.

**Prediction of Bioactivity**

Biological parameters or bioactivity deals with the favourable or adverse effects of a drug on living matter. It plays a crucial role since it suggests the use of compounds in medical applications. Bioactivity or biological activity depends critically on self-reliance on the (ADME) absorption, distribution, metabolism, and excretion criteria. To act as an effective compound or drug, a compound not only must

 

be active against a target but also possess the appropriate ADME properties that make it suitable for use as a drug whereas a compound is considered bioactive if it interacts with or effects on any cell tissue in the human body.

Biological activity is usually taken to describe beneficial effects, i.e., the effects of the compound candidate as well as the toxicity of the substance. The parameters for the biological activity of different molecules are summarized in Table 2.

The bioactivity parameters are defined here and discussed for the following molecules.

*GPCR ligand:* GPCR represents G-protein coupled receptors (GPCRs), it is one of the biggest and most significant integral membrane protein families, and it has an essential role in many signalling pathways. Piperine (0.15) compound was found to be highly bioactive towards GPCR ligands (>0) and others were found to be moderately active (< -5 – 0) [21–25].

*Ion channel modulator:* are also known as channel modulator. It is a type of drug which controls ion channels. It can work either by blocking or opening the respective ion channels. The Ion channel modulator property of Piperine (-0.18) is higher, as its value is not zero (>0) but its value is greater than other compounds whose value is (< 0).

*Kinase Inhibitor*: Kinase Inhibitor blocks the activity of kinase (a type of enzyme). It blocks its activity by adding phosphate to it. Kinase Inhibitor activities of salen (-0.42), salophen (- 0.29), allicin (-2.95), curcumin (-0.26), piperine (-0.13) were found to be moderate as their score values were found to be less than zero [21–25].

*Nuclear receptor ligand*: These are ligand-regulated transcription factors. Its activities are controlled by a range of lipophilic extracellular signals.

*Protease inhibitor:* are synthetic drugs that restrict the action of protease (cleave protein). It is also involved in inhibiting viral replication by specific binding, cleaving, and preventing the site that leads to viral replication. Piperine was found to be active as a protease inhibitor (- 0.10) as its value is not (>0) but it is quite close to zero as compared to other compounds that were found to be moderately active as their values of more negative or farther from zero [21–25].

*Enzyme inhibitor*: Enzyme inhibitors are the inhibitory molecules that reduce its activity. Curcumin (0.08) and Piperine (0.04) were exhibited the enzyme inhibitor action higher (>0) than other compounds (<0). Among these two compounds, Curcumin (0.08) has a high enzyme inhibitor activity.

In Table 2, different parameters have described the effects as well as the activity level of a particular compound. It also talks about its interaction with other compounds or its absorption (penetration inside the human body). The values of each molecule vary from the other due to its specific molecular formula or structure and the interacting atom that are participating in the structure. The activities of the complex can be determined based on bioactive score (>0 = active, -0.5 to 0.0 = moderately active, < -0.5 = inactive) [26]. Among all 6 molecules, piperine was found to be more bioactive because its bioactivity score is more than zero or close to zero as compared to other molecules.

**Table 2.** Showing the bioactivity of the given molecules.

| Molecule Name | GPCR ligand | Ion channel modulators | Kinase Inhibitor | Nuclear Receptor ligand | Protease Inhibitor | Enzyme Inhibitor |
|---|---|---|---|---|---|---|
| Salen | 1.66 | 58.20 | 20 | 268.32 | 5 | 251.83 |
| Salophen | 3.05 | 75.63 | 20 | 271.27 | 4 | 239.38 |
| Allicin | 2.06 | 17.07 | 9 | 162.28 | 5 | 145.51 |
| Curcumin | 2.30 | 93.07 | 27 | 368.38 | 8 | 332.18 |
| Piperine | 3.33 | 38.78 | 21 | 285.34 | 3 | 267.74 |

 

Curcumin, a phytochemical has antioxidant and anti-inflammatory properties. Due to its unfavourable physicochemical properties such as low aqueous solubility, chemical solubility, and in vivo bioavailability it appears to be a gridlock for successful clinical applications.

## CONCLUSIONS

In the present work, molecules such as salen, salophen, allicin, curcumin, and piperine have been studied. The work mainly emphasizes the study of the structure and molecular properties of these molecules. It also restrains information about various software such as chemdraw which is used to draw the structure of molecules and molinspiration. Molinspiration supports enormous tools and features to study molecular properties, bioactivity, and other data visualization techniques. Also, the information related to the procedure involved in calculating the data using the parameters is gathered. Afterward, the bioactivities of the listed molecules as well as the parameters associated with its prediction are analyzed. These bioactivity or biological activities give information about their interaction with other targets or drugs. The piperine molecule was found the most bioactive compound among all five compounds. The beneficial applications of these molecules may be useful in the treatment of diseases, drug discovery, molecular modeling, etc.

**Acknowledgments**

Piyush Kumar Sonkar acknowledges Institute of Eminence (IoE), Banaras Hindu University, India for Seed Grant and Trans-Disciplinary Research Project for the financial assistance.

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