**International Journal of Botany Studies**
**www.botanyjournals.com**
**ISSN: 2455-541X**
**Received: 24-12-2021, Accepted: 08-01-2022, Published: 25-01-2022**
**Volume 7, Issue 1, 2022, Page No. 498-501**

# *In-silico* pharmacokinetic and toxicological prediction of bioactive compounds from *Gymnema sylvestre*

**Kiran Gaikwad[*], Parixit Bhandurge, Shailendra S Suryawanshi**
Department of Pharmaceutical Chemistry, KLE Academy of Higher Education and Research, KLE College of Pharmacy Belagavi, Belagavi, Karnataka, India

**Abstract**
*Gymnema sylvestre* is important medicinal plant distributed throughout the world and it has documented to possess many beneficial effects. It has been reported for the presence of wide variety of simple and complex primary and secondary phytoconstituents. In the present investigation an attempt has been made to carry out *in-silico* prediction of pharmacokinetic and toxicological properties of bioactive compounds from *Gymnema sylvestre*. We have selected "Gymnemic acids (Gymnemic acid I, II, III, IV, V, VI, and VII) Gymnemoside A to F, Quercitol and Stigmasterol" from the plant. PubChem database was used to find out the canonical smiles. Molsoft server was used for the drug likeness and molecular property prediction. The admetSAR, SwissADME servers were used for the determination of pharmacokinetic and toxicity properties prediction. The results of investigation yield the drug likeness score of selected phytoconstituents along with its pharmacokinetic and toxicity properties. The present investigation concludes that computer and server based screening play important role for identification of drug like candidates and to predict pharmacokinetic and toxicological properties of selected bioactive compounds from plant *Gymnema sylvestre.*

**Keywords:** admet SAR, molsoft, *Gymnema sylvestre,* gymnemic acid, pharmacokinetics, swiss ADME, toxicity

## Introduction
*Gymnema sylvestre* is a important herb comes under family Asclepiadaceae, and widely distributed in Malaysia, Japan, Indonesia, Australia, India, tropical Africa, Vietnam, Srilanka, and the Southwestern region of the People's Republic of China. The word "Gymnema" is obtained from "Gurmar" a Hindi word meaning "destroyer of sugar" and it found to neutralize the excess of glucose present in person with "Diabetes Mellitus".

**Therapeutics Uses:** *Gymnema sylvestre* is used therapeutically in the management of various diseases and disorders. It is used as a "destroyer of madhumeha", anti-inflammatory agents, liver tonic, diuretic agent, stomachic, astringent, anthelmenthics, stimulant, cardioprotective agent, anti-pyretic agent, and expectorant. It is widely used to treat dyspepsia, renal calculi, vesicle calculi, asthma and jaundice [1].

**Phytoconstituents:** The chemicals present in the leaves include carbohydrates, inositole alkaloids, albumin, tartaric acid, formic acid, butyric acid, chlorophyll, resins, anthraquinone derivatives, parabin, organic acid, lignin, calcium oxalate, and cellulose derivatives. The leaves part of plant also found to possess the triterpene saponins (Oleanane and dammarene type). The saponins under Oleanane class are mainly Gymnemic acids and Gymnema saponins. The Saponins under dammarene class are gymnemasides [1]. It also contains "Gymnemic acid I, II, III, IV, V, VI, and VII along with Gymnemosides A to F [2].
Lipinskie's rule of five (Ro5) is mainly used to evaluate the physicochemical properties of molecules to identify the likely orally active drug in humans. It evaluates the poor absorption or permeation of the molecule when in the chemical structure of compound we have more than five Hydrogen Bond Donors (HBD), ten Hydrogen Bond Acceptor (HBA), molecular weight (MW) is more than 500, and calculated logP value is more than five.
Literature search revealed that lack of computational studies have been reported on computer based screening on *Gymnema sylvestre* to investigate its drug likeness properties and profile of ADME along with some toxicity investigations. Hence in the present investigation an attempt has been made to study drug likeness properties and ADME profile of selected phytoconstituents from *Gymnema sylvestre* using computer applications and servers.

## Material and Methods
**Servers used:** PubChem database, Molsoft, admetSAR, SwissADME.

**Phytoconstituents used: "**Gymnemic acid I, II, III, IV, V, VI, and VII, Gymnemoside A to F, Quercitol and Stigmasterol" were used in the study.

**Role of Servers Used in Study:** PubChem database is used to find out the canonical smiles. PubChem gives freely the molecular data like molecular formula, biological actions, structure, properties, safety and toxicity information. Molsoft server is used for the drug likeness and molecular property prediction. The molecular properties like MW, HBA, HBD, and logP value and Drug Likeness Score (DLS) can be identified by using Molsoft. AdmetSAR and SwissADME servers are used for the determination of ADME and toxicological prediction.

**Determination of Physicochemical Properties and Drug Likeness Score:** In this present study we have identified and taken some 19 phytoconstituents from *Gymnema sylvestre* for determining drug likeness score according to Lipinski's Ro5. Lipinski's rule of five was followed so as to find out drug likeness score of each phytoconstituents. The data about drug likeness was complied with adherence of Lipinski's rule. The canonical SMILES (Simplified Molecular Line Entry System) were obtained from PubChem in order to apply them in Molsoft software to collect the data [3-6].

**Prediction of Pharmacokinetic and Toxicological Profile:** The pharmacokinetic (PK) parameters such as distribution, absorption, metabolism and excretion of phytoconstituents play important role in drug development process. Therefore, we used the online server admetSAR and SwissADME to predict several pharmacokinetic aspects. AdmetSAR and SwissADME evaluate the pharmacokinetic properties such as Blood Brain Barrier (BBB), protein binding, skin permeability, P-glycoprotein, Human intestinal absorption and buffer solubility along with other important aspects of ADME [7-14].

**Results and Discussion**

*Gymnema sylvestre* consists of various phytoconstituents and is found to exert many pharmacological and biological actions. In the present computational screening study, we have selected **"**Gymnemic acid I, II, III, IV, V, VI, and VII, Gymnemoside A to F, Quercitol and Stigmasterol" as important constituents based on Lipinskies Ro5. The molecular weight, hydrogen bond acceptor, hydrogen bond donor, log P value and DLS of selected phytoconstituents were presented in Table 1.

The admetSAR and SwissADME servers are used for describing the properties of molecules which are important for a pharmacokinetics of molecule in body. The admetSAR and SwissADME used to evaluate the pharmacokinetic properties such as plasma protein binding, P-glycoprotein, skin permeability, Human intestinal absorption BBB, and buffer solubility along with some toxicity prediction. The admetSAR and SwissADME profile of selected chemicals were presented in Table 2a and 2b.

**Table 1:** Molecular Properties of Selected Phytoconstituents by Molsoft Analysis

| Sl. No | Phytoconstituents | Mol. Weight | HBA (>10) | HBD (>5) | Log P (>5) | Drug Likeness Score |
|---|---|---|---|---|---|---|
| 1 | Gymnemic acid I | 806.45 | 14 | 7 | 3.23 | 0.91 |
| 2 | Gymnemic acid IV | 764.43 | 13 | 8 | 2.65 | 0.85 |
| 3 | Gymnemic acid V | 846.48 | 14 | 7 | 4.08 | 0.85 |
| 4 | Gymnemic acid VI | 926.49 | 18 | 11 | 0.8 | 0.76 |
| 5 | Gymnemic acid VII | 666.4 | 11 | 8 | 2.06 | 0.69 |
| 6 | Gymnemic acid VIII | 926.49 | 18 | 10 | 0.55 | 0.94 |
| 7 | Gymnemic acid IX | 924.47 | 18 | 10 | 0.21 | 0.76 |
| 8 | Gymnemic acid X | 724.4 | 13 | 8 | 1.79 | 0.78 |
| 9 | Gymnemic acid XI | 846.48 | 14 | 7 | 4.13 | 0.96 |
| 10 | Gymnemic acid XII | 968.5 | 19 | 10 | 1.39 | 0.82 |
| 11 | Gymnemic acid XIV | 764.43 | 13 | 8 | 2.69 | 0.81 |
| 12 | Gymnemoside A | 806.45 | 14 | 7 | 3.1 | 0.9 |
| 13 | Gymnemoside B | 806.45 | 14 | 7 | 3.14 | 0.88 |
| 14 | Gymnemoside C | 828.43 | 14 | 7 | 3.89 | 0.75 |
| 15 | Gymnemoside D | 946.51 | 19 | 13 | -1.7 | 0.17 |
| 16 | Gymnemoside E | 1254.62 | 28 | 18 | -4.48 | 0.08 |
| 17 | Gymnemoside F | 1254.62 | 28 | 18 | -4.22 | 0.14 |
| 18 | Stigmasterol | 412.37 | 1 | 1 | 7.74 | 0.62 |
| 19 | Quercitol | 270.05 | 5 | 3 | 3.22 | 0.39 |

**Table 2a:** Pharmacokinetic and Toxicity Profile of Bioactive Compounds

| Parameters | | Compounds | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** |
| **ABSORPTION** | HIA | + | + | + | + | + | + | + | + | + | + |
| | Caco-2 | - | - | - | - | - | - | - | - | - | - |
| | HOB | 0.11 | 0.11 | 0.11 | 0.11 | 0.11 | 0.11 | 0.11 | 0.11 | 0.11 | 0.11 |
| **DISTRIBUTION** | BBB | + | + | + | + | + | + | + | + | + | + |
| | P-glycoprotein (i) | + | + | + | - | + | + | - | + | + | - |
| | P-glycoprotein (s) | + | + | + | + | + | + | + | + | + | + |
| | PPB (P-gp substrate) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| **METABOLISM** | CYP3A4 (s) | + | + | + | + | + | + | + | + | + | + |
| | CYP2C9 (s) | - | - | - | - | - | - | - | - | - | - |
| | CYP2D6 (s) | - | - | - | - | - | - | - | - | - | - |
| | CYP3A4 (i) | - | - | - | - | - | - | - | - | - | - |
| | CYP2D6 (i) | - | - | - | - | - | - | - | - | - | - |
| | CYP1A2 (i) | - | - | - | - | - | - | - | - | - | - |
| **EXCREATION** | Plasma t1/2 | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| | Renal clearance | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| **TOXICITY** | HERG | - | - | - | - | - | - | - | - | - | - |
| | Hepatotoxicity | + | + | + | + | + | + | + | + | + | + |
| | AOT | III | III | III | III | III | III | III | III | III | III |
| | Eye corrosion | - | - | - | - | - | - | - | - | - | - |
| | Carcinogenicity | - | - | - | - | - | - | - | - | - | - |
| | Ames mutagenesis | - | - | - | - | - | - | - | - | - | - |

"1-Gymnemic acid I, 2-Gymnemic acid IV, 3-Gymnemic acid V, 4-Gymnemic acid VI, 5-Gymnemic acid VII, 6-Gymnemic acid VIII, 7-Gymnemic acid IX, 8-Gymnemic acid X, 9-Gymnemic acid XI, 10-Gymnemic acid XII. Human either-a-go-go inhibition: HERG, Plasma protein binding: PPB, Blood Brain Barrier: BBB, Human Intestinal Absorption: HIA, Human Oral Bioavailability: HOB, Acute Oral Toxicity: AOT, (i): Inhibitor, (s): Substrate"

**Table 2b:** Pharmacokinetic and Toxicity Profile of Bioactive Compounds

| Parameters | | Compounds | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | **11** | **12** | **13** | **14** | **15** | **16** | **17** | **18** | **19** |
| **ABSORPTION** | HIA | + | + | - | + | + | + | + | + | + |
| | Caco-2 | - | - | - | - | - | - | - | - | - |
| | HOB | 0.11 | 0.11 | 0.11 | 0.11 | 0.17 | 0.17 | 0.17 | 0.55 | 0.55 |
| **DISTRIBUTION** | BBB | + | + | + | - | + | + | - | + | - |
| | P-glycoprotein (i) | + | + | + | + | - | - | - | - | - |
| | P-glycoprotein (s) | + | + | + | + | + | + | + | + | - |
| | PPB (P-gp substrate) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes |
| **METABOLISM** | CYP3A4 (s) | + | + | + | + | + | + | + | + | - |
| | CYP2C9 (s) | - | - | - | - | - | - | - | - | - |
| | CYP2D6 (s) | - | - | - | - | - | - | - | - | - |
| | CYP3A4 (i) | - | - | - | - | - | - | - | - | - |
| | CYP2D6 (i) | - | - | - | - | - | - | - | - | - |
| | CYP1A2 (i) | - | - | - | - | - | - | - | - | - |
| **EXCREATION** | Plasma t1/2 | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| | Renal clearance | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| **TOXICITY** | HERG | - | - | - | - | - | - | - | - | - |
| | Hepatotoxicity | + | + | + | + | + | + | + | + | + |
| | AOT | III | III | III | III | III | III | III | I | III |
| | Eye corrosion | - | - | - | - | - | - | - | - | - |
| | Carcinogenicity | - | - | - | - | - | - | - | - | - |
| | Ames mutagenesis | - | - | - | - | - | - | - | - | - |

"11-Gymnemic acid XIV, 12-Gymnemoside A, 13-Gymnemoside B, 14-Gymnemoside C, 15-Gymnemoside D, 16-Gymnemoside E, 17-Gymnemoside F, 18-Stigmasterol, 19-Quercitol.
Human either-a-go-go inhibition: HERG, Plasma protein binding: PPB, Blood Brain Barrier: BBB, Human Intestinal Absorption: HIA, Human Oral Bioavailability: HOB, Acute Oral Toxicity: AOT, (i): Inhibiter, (s): Substrate"

**Conclusion**

The present investigation concludes that computer and server based screening plays an important role for the identification of drug like candidates from *Gymnema sylvestre* and also data obtained from admetSAR and Swiss ADME is valuable for research on *Gymnema sylvestre.* The selected constituents such as **"**Gymnemic acid I, II, III, IV, V, VI, and VII, Gymnemoside A to F, Quercitol and Stigmasterol" were found to better drug like candidates.

**References**


1. Saneja A, Sharma C, Aneja KR, Pahwa R. *Gymnema sylvestre* (Gurmar): A review. Der Pharmacia Lettre,2010:2(1):275-84.
2. Tiwari P, Ahmad K, Hassan Baig M. *Gymnema sylvestre* for diabetes: From traditional herb to future's therapeutic. Current pharmaceutical design,2017:23(11):1667-76.
3. Patil RS, Khatib NA, Patil VS, Suryawanshi SS. Cholonergic acid may be a potent inhibitor of dimeric SARS-CoV-2 main protease 3CLpro: an in silico study. Traditional Medicinal Research.2020;1-14.
4. Suryawanshi SS, Jayannache PB, Patil RS, Palled MS, SG A. Molecular Docking Studies on Screening and Assessment of Selected Bioflavonoids as Potential Inhibitors of COVID-19 Main Protease. Asian Journal of Pharmaceutical and Clinical Research,2020:31:174-8.
5. Suryawanshi SS, Maruche S, Patil P, Palled MS, Pancham Y. Comparative *in-vitro* antioxidant activity of fruit extracts of *Embelica officinalis* Gaertn and drug likeness profile of selected phytoconstituents. International Journal of Botany Studies,2020:5(6):704-9.
6. Sampat G, Suryawanshi SS, Sawant R, Khanal P, Palled MS, Alegaon SG *et al*. Molecular docking studies and antibacterial activity of leaves of *Tabernamontana divaricate*. Journal of Global Trends in Pharmaceutical Sciences,2020:11(2):7818-24.
7. Suryawanshi SS, Patil RS, Jayanache PB, Palled MS, Alegoan SG, Zaranappa. Screening and assessment of selected alkaloids as potential inhibitors of COVID-19 protease enzyme. Journal of Global Trends in Pharmaceutical Science,2020:11(2):7711-18.
8. Ibrahim ZY, Uzairu A, Shallangwa G, Abechi S. Molecular docking studies, drug likeness and in-silico ADMET prediction of some novel β-amino alcohol grafted 1,4,5-trisubstitued 1,2,3-triazoles derivatives as elevators of p53 protein levels. Scientific African,2020:10:e00570.
9. Suhud F, Tjahjono DH, Yniarta TA. Molecular docking, drug likeness and ADMET study of 1-benzyl-3-benzoylurea and its analogs against VEGFR-2.Natural Resources and life sciences,2019:6:2-10.
10. Chakravarthi KK, Avadhani R. Effect of *Glycyrrhiza glabra* root extract on learning & memory in Wistar albino rats. Drug Invention Today,2012:4:387-90.
11. Yazdi A, Sardari S, Sayyah Md. Evaluation of anticonvulsant activity of leaves of *Glycyrrhiza glabra* grown in Iran as a possible renewable source for anticonvulsant compounds. Iranian journal of Pharmaceutical research,2011:10(1):75-82.
12. Sowmya M, Kumar S. Antistress property of *Glycyrrhiza glabra* on stress induced Drosophila melanogaster. Journal of Stress Physiology & Biochemistry,2010:6:18-27.
13. Rastogi RP, Mehrotra BN. Compendium Indian medicinal plants published by CDRI, Lucknow and National Institute of Science & information resources. ND,1990-94:6:395-98.
14. Subash KR. *In silico* Pharmacokinetic and toxicological properties prediction of bioactive compounds from Andrographis paniculata. National Journal of Physiology, Pharmacy and Pharmacology,2020:10(7):537-542.