



BIOAVAILABILITY AND PHARMACOKINETICS, DRUG LIKELINESS PREDICTIONS OF BIOACTIVE COMPOUNDS OF ALOE VERA USING SWISS ADME AND PHYRE 2.0 SOFTWARE

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ABSTRACT

Medicinal plants gained a lot of importance in health improvement and curing many ailments. The natural flora has become a very useful source in India and has variety of species which is still use in various parts of our world. Though the WHO reported that 60% of population in world represented the use of traditional medicines .A Decade ago, synthetic drugs got much importance in market for its effectiveness and unanticipated side effects whereas herbal drugs has no such side effects and it is safe and efficient has made benefit over synthetic one.In modern pharmacopoeia 25% drugs and great number of synthetic analogues are present derived from plant compounds.Beginning from the morphine which was isolated from opium early 19th century , now active compounds are also isolated from medicinal plants.Several epidemiological studies shows that usage of natural foods and plant derived compounds in diet has less chances of cancer in future.Many studies showed that bioactive compounds are especially had lot of effectiveness towards parasites and infectious diseases. A great number of natural products derived from medicinal products can be prepared as lead compounds to synthesize novel drug compounds. These are known as semi synthetic drugs.For

example modification of salicylic acid that was produced from many plants used regarding pain relieving effects. So, that active constituent acts as synthetic derivative to prepare aspirin.

Aloevera, which is also known as *Aloe barbadensis* mill is presently included in Asphodelaceae family or Liliaceae. It is in triangular leaves with sharp edges, yellow tubular flowers and fruits. It is widely available in arid regions of Africa, Asia, America and Europe. In India, Aloe is mostly cultivated in Maharashtra, Andhra Pradesh, Rajasthan, Gujarat, Tamilnadu. Aloevera leaves comprised of three layers: inside layer, center layer and outer layer. Inside layer consists of 99% of water, amino acids, vitamins, lipids, sterols and glucomannans. Center layer has latex, glycosides and anthraquinones. Synthesis of carbohydrates and proteins occurs in outer layer of leaves.

Aloe vera has 75 potentially active compounds i.e., Vitamins, enzymes, minerals, lignins, saponins and various amino acids. Vitamins like Vitamin A, vitamin C, vitamin E and antioxidants which protect body from free radicals generated by food. Water soluble vitamins like B1, B2, B6 and B12 are the mostly present in leaves of aloevera. Enzymes are present in the gel part of the leaf i.e., amylase, alkaline phosphatase, oxidase, catalase, lipase, bradykinase which helps in breakdown of fats and reduces the inflammation of skin. There are dense package of minerals available, those are calcium, magnesium, manganese, copper, sodium, selenium, and zinc. Some of the sugars are glucomannans, alprogen, which is a glycoprotein has anti allergic activity and C-glucosyl chromone has anti inflammatory activity. Extraction of phenolic compounds shows the presence of Aloisin, aloinoside, aloin, hydroxy aloin, aloedial, aloeveroside, oleoresin, isoaloesin D, Isoaloesin E, Aloe-emodin, emodin, and Physcione. Commonly present amino acids are Phenylalanine, arginine, serine, histidine. High concentration of tannins, saponins, flavonoids, alkaloids and anthraquinones. These potent phytochemical constituents have many health benefits and across the world it acts as traditional medicine for various ailments. Some of them are

BENEFITS OF ALOE VERA:

Moisturising and antiaging effect:

Cohesive action of epidermal cells and amino acids helps to soften skin. Aloevera produces collagen and elastin fibres making skin more elastic and less wrinkles. It improves ability of skin to hydrate and help in removal of dead skins from skin barrier.

Immune system restoration:

Aloe vera helps in generation of metallothionein, which acts as scavenger for hydroxy radicals and hence protecting skin from oxidative damage.

Anti inflammatory action:

The bioactive compounds in aloe vera inhibit cyclooxygenase activity and reduces the production of prostaglandins thereby decreasing inflammation. The extract of aloevera shows the healing properties and mainly involved in treating the *H. pylori* infection.

Anti diabetic Effect:

Aloe vera is the best choice for diabetic conditions. It reduces blood sugar, hepatic transaminase, plasma and tissue cholesterol, free fatty acids and phospholipids. Triglycerides being main key role in many cardiovascular diseases and diabetic conditions, the levels would be drastically reduced by using aloevera juice and shows hypolipidemic effect.

Antibacterial and Antifungal effect:

Aloe vera gel has good skin repairing activity and also prevents the micro organisms mainly *Streptococcus pyogenes* and *Streptococcus faecalis*. Several studies showed that the inhibition of gram positive and gram negative bacteria by the aloevera has fruitful advantage for formulating several dosage forms. Leaf pulp and liquid extract of aloevera acts against plant pathogenic fungi.

Sickle cell Anemia:

The condition of genetic variation and reduced haemoglobin activity in sickle cell anemia has led to many ailments like reduced oxidation state of RBC, inflammation of skin, spleen sequestration, fatigue. Some work at edo state showed that aloe extract on sickle cell anemia attained the positive results on managing the sickle cell disease. Mainly the presence of Alkaloids, Flavanoids and tannins, which are pharmacologically active in treatment. Most of bioactive compounds found in aloe vera like Alkaloids, having the action on ANS, GIT related diseases and respiratory system. Tannins are known for the best Antioxidant and anti-inflammatory action. Flavanoids also perform the antioxidant activity, anticarcinogenic activity and antitumour properties. By isolating these potent bioactive compounds and studying the bioavailability and drug likelihood properties may help us to generate more drugs for treating the sickle cell disease, by improving the oxidation i.e., Fe²⁺/Fe³⁺ ratio and inhibiting the polymerisation of haemoglobin (Hb) in SCA Patients. As per some studies, leaf portion of aloe vera exhibits 78% reduction of polymerisation of Hb and gel exhibits the inhibition about 22.69% in RBC. The extraction of phytochemicals from the leaves and gel of aloe vera and detecting the ADME, bioavailability and toxicity helps further research activities in developing the medicine for sickle anemia.

Drug discovery and development process includes target identification, validation, lead discovery and optimisation methods. With the development of insilico techniques in recent years had emerged numerous new drug entities (NDE), approved by FDA. The major concern was lack of efficiency and safety of using the hit compounds are two serious causes of drug failure and side effects. The concept of drug likelihood introduced by Lipinski and co workers which will be the 'rule of five' in 1997. This speed up the drug development process under emergency and pandemic conditions. Drug likelihood distinguishes the rule of whether bioactive molecule or hit molecule are orally active or not and the conditions were molecular weight should be less than 500, octanol/water partition coefficient (AlogP) ≤ 5 and number of hydrogen bonds donor (HBD) ≤ 5 and ≤ 10 for hydrogen bond acceptor (HBA). Drug would not be active if two or more rules are violated. ADMET SAR helps to predict the toxicity of the bioactive compounds and its derivatives. Data collected from Drugbank, ChEMBL and NCBI, PubChem inputs are given to the insilico techniques. Based on ADMET scoring the molecule would be given preference and used for developing dosage forms.

MATERIALS AND METHODS:

MODELLING PLATFORM:

The SWISS ADME and ADME lab 3.0 were used to perform the computational analysis, which included Absorption, distribution, metabolism and excretion (ADME), toxicity. The operating system was Windows 11 Version 24H2 for x64-based Systems (KB5063878) (26100.4946).

BIOLOGICAL DATA:

PubChem were used to find the bioactive compounds for this investigation (Table 1). Two dimensional (2D) images of the selected compounds and chemical structures are obtained from the ChemBank, PubChem, NCBI and from some literature survey reports.

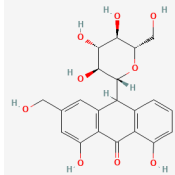
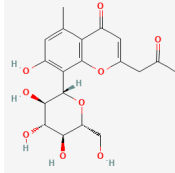
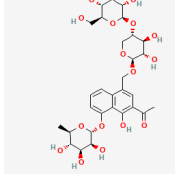
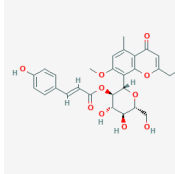
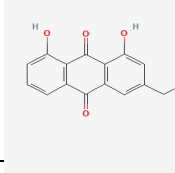
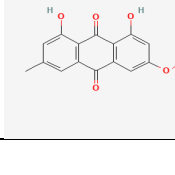
SUBMISSION WEB PAGE:

Accessing the ... web link displays directly the submission page of Swiss adme where molecules are estimated for ADME, Physico chemical properties, Pharmacokinetics, drug likelihood and recommended chemical properties as shown in given table 2

ADME TOXICITY:

ADMET lab 3.0 predicts the toxicity of bioactive compounds either by giving the SMILES or uploading the file format. We need to observe the potentially harmful phytochemicals that were Ames carcinogens, mutagens, and inhibitors of human ether go-go-gene (hERG).

Table1: General characteristics and Pubchem ID of Bioactive compounds of *Aloe barbadensis mill*

S.No	Bioactive compound	Pubchem ID	Part of the plant	Structure
1.	Aloin	CID9866696	Leaves and gel	
2.	aloesin	CID160190	Leaves and gel	
3.	aloeveroside	CID 163064546	Leaves and gel	
4.	Isoaloeresin D	CID 76332505	Leaves and gel	
5.	Aloe emodin	CID 10207	Leaves and gel	
6.	Physcione	CID 10639	Leaves and gel	

RESULTS:

The 2D Structure are retrieved from Pubchem database through Literary work. All are verified and authenticated by CID given in table. The standard range of pharmacokinetics and pharmacodynamics and druglikeness is compared with our results.

Table2: Physico-chemical properties of Bioactive compounds of *aloe barbadensis mill*

S.NO	Bioactive compound	Molecular weight (g/mole)	lipophilicity	Hydrogen bond donor	Hydrogen bond acceptor	TPSA	Number of Lipinski rule violations
1.	Aloin	556.56	1.57	5	11	176.2A ²	2
2.	Aloesin	394.37	-0.57	5	9	157.66 A ²	0
3.	Iso aloeresin	556.56	1.57	5	11	176.2 A ²	2
4.	aloeveroside	672.63	-2.33	10	17	274.75 A ²	3
5.	Aloe emodin	270.24	1.50	3	5	94.83 A ²	0
6.	physcione	284.26	2.27	2	5	83.83 A ²	0

Table3:Pharmacokinetic properties of Bioactive compounds of *aloe barbadensis mill*

S.NO	Bioactive compound	Molecular formula	Water solubility	GIT absorption	BBB penetration	Abbot score
1.	Aloin	C ₂₉ H ₃₂ O ₁₁	Moderately soluble	low	no	0.17
2.	Aloesin	C ₁₉ H ₂₂ O ₉	soluble	Low	no	0.55
3.	Iso aloeresin	C ₂₉ H ₃₂ O ₁₁	Moderately soluble	Low	no	0.17
4.	aloeveroside	C ₃₀ H ₄₀ O ₁₇	Soluble	Low	no	0.17
5.	Aloe emodin	C ₁₅ H ₁₀ O ₅	soluble	high	no	0.55
6.	phycione	C ₁₆ H ₁₂ O ₅	Moderately soluble	high	no	0.55

Table 4: Drug likeness properties of Bioactive compounds of *aloe barbadensis mill*

S.no	Bioactive compound	Pgp substrate	CYP1A2	CYP2C19	CYP2C9	CYP2D6	CYP3A4
1.	Aloin	YES	NO	NO	NO	NO	YES
2.	Aloesin	NO	NO	NO	NO	NO	NO
3.	Iso aloeresin	YES	NO	NO	NO	NO	YES
4.	aloeveroside	NO	NO	NO	NO	NO	NO
5.	Aloe emodin	NO	YES	NO	NO	NO	YES
6.	phycione	NO	YES	NO	YES	NO	YES

The research of our outcome showed