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STUDY OF PHARMACOKINETIC PROPERTIES OF SOME SELECTED PHYTOCHEMICALS

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ABSTRACT: Pharmacokinetic properties of selected phytochemicals studied in this article. The phytochemicals for present study were obtained from online databases IMPPAT. The Absorption, Distribution, Metabolism, Excretion and toxicity prediction (ADMET) properties of selected phytochemicals were studied from the online available tools. The seven medicinally important plants were selected for study including Malabar nut, Ashwagandha, Nilgiris, Indian gooseberry (Amla), Aloe vera, sweet flag, Mint. The seven phytochemicals one from each selected plants Kaempferol, Tropine,5,7-Dihydroxy-6-methyl-8-prenylflavanone, Anthraquinone, Lucenin-2, Eucalyptol, Azulene evaluated for pharmacokinetic study. Compound were selected in this study according to their biological activities which was already available in the literature. Online freely available standard databases and some software design by SWISS institute of bioinformatics was used to calculate the pharmacokinetic properties of selected phytochemicals. The seven phytochemicals were coded by S-1, S-2, S-3, S-4, S-5, S-6 and S-7 respectively. Each phytochemical was evaluated for its bioavailability and shown by bioavailability radar maps. They also evaluated for its blood brain barrier (BBB) by boiled egg structure.

KEYWORDS: Pharmacokinetic properties, Organic compounds, Phytochemicals, Toxicity, Online databases, Bioavailability.

INTRODUCTION:

[1]The Pharmacokinetic properties ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) of compound is very important because it explains the role of drug in the body metabolism and hence it plays a vital role in the development of new drug. [2]Pharmacokinetic studies help to determine the concentration of phytochemicals that reach target tissues and organ of body. which is essential for understanding their biological activity. [3]These studies can create roadmap for the development of strategies to improve the bioavailability of phytochemicals. Pharmacokinetic properties evaluate the drug efficiency, helps in minimizing adverse effects, risk of toxicity of drug, guiding drug development and formulations, safe and effective dosing regimens, helps in understanding the variations of drug response with body, therefore here we studied the pharmacokinetic properties of some selected compounds. [4]Literature of review shows that a large number of drug molecules was studied by researchers for their pharmacokinetic properties. These properties are very complex in nature for study but it is very essential to avoid and minimize the side effect and to know health benefits of phytochemicals.

[5]Phytochemicals is the naturally occurring organic compounds exhibiting medicinal properties. The phytochemicals are used directly or indirectly from ancient time to treat, cure and relief of some human diseases continuously. Recently as per the increasing demand of drug Its synthetic homologue is used as indispensable part of medicinal drugs therefore it is necessary to study their various effect on body of living organism including plants, animals and human. A large number of bioactive organic compounds synthesized by the researchers, scientist and pharmaceutical industry globally. [6]Millions of organic compounds occur naturally in the plants and animals having many medicinal properties. [7]Literature review shows that a large number of medicinally important compounds are present in plants like, Neem, Adulsa, Tulsi, Nilgiris, lemongrass, ashwagandha, sweet flag, Indian babel, amla elachi, shatavari, Aloe vera Mint etc. Many plants are mentioned in the Indian medicinal remedies from ancient period known as Indian Ayurveda but at that time actual structure of the chemical compound and their reactivity was not known. It is important to know the structure and reactivity of medicinally important compound because it plays an important role in biochemical reactions and regulates metabolism of human body. Recently many advanced spectroscopic tools and technique is available to determine the structure of chemical compounds like NMR, IR, UV, Mass Spectrometry, XRD, SEM, TEM etc.

Generally, for this kind of study researchers can select the biologically active compounds from literature review, newly synthesized organic compounds, [8]Compound extracted from plants by GC-MS, LC-MS, HPLC, Google Scholar, Online databases etc.

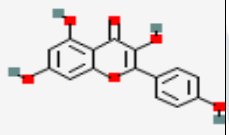
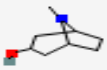
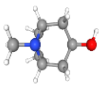
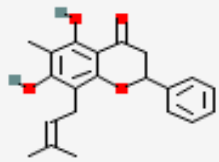
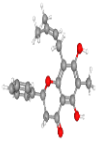
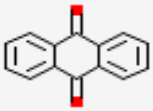
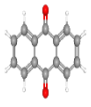
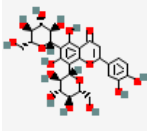
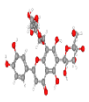
MATERIALS AND METHODS:

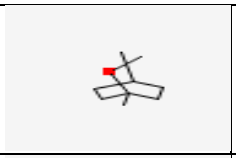
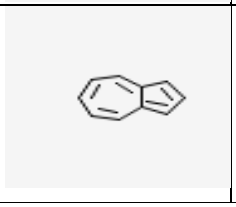
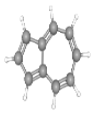
[9]The phytochemicals used for present study was retrieved from online databases IMPPAT, TCMSP, NPASS, TCM-Mesh, CHEMBI these contains a lot of phytochemical libraries in which phytochemicals extracted from different parts of plants and available free to access. [10]The pharmacokinetic properties of compound were studied from the online software's of SWISSADMET websites design by SWISS institute of bioinformatics. Bioactivity prediction and biological score was done calculated from pass online and molinspiration respectively.

RESULT AND DISCUSSION:

The observations and result of present study is given below in tabulated form. Figure 1 shows bioavailability radar map of each compound which visualized the drug likeliness or oral bioavailability, each plot has six axes showing six different parameter LIPO (Lipophilicity), SIZE (Molecular Size), POLAR (Polarity), INSOLU (Insolubility), INSATU (Instauration) FLEX (Flexibility). The red polygon connects the data point of each six parameters and hence represent overall drug likeness profile of a molecules. Pink shaded area shows optimal range of each six parameters indicates better likeness of drug molecule which fall in this area. Figure 2 shows the boiled egg structure main which dark yellow oval part shows the blood Brain barrier (BBB) and human intestinal absorption (HIA)which shows absorption of drug molecule. The molecule S-3, S-4, S-5 and S-6 presents in the yellow blood vein barrier and absorb readily. Molecule S-1 and S-2 are present in white part outside the blood brain barrier which shows high HIA but low BBB they absorb by intestine but not reach at brain.

Table 1: Code of Phytochemicals, List of plants, Name of Phytochemical, Medicinal uses,2D and 3D, Structure of Phytochemicals.

Code of Compound	Name of plant	Name of Phytochemicals	Medicinal use	2-D Structure	3-D Structure
S-1	Malabar nut	Kaempferol	Anti-inflammatory, Antioxidant Antitumor		
S-2	Ashwagandha	Tropine	To treat bradycardia (slow heart rate).		
S-3	Indian gooseberry (Amla)	5,7-Dihydroxy-6-methyl-8-prenylflavanone	antioxidant and anti-inflammatory		
S-4	Aloe vera	Anthraquinone	Laxatives, anti-inflammatories, and anti-cancer agents		
S-5	Sweet flag	Lucenin-2	anti-inflammatory, antibacterial, and antioxidant		

S-6	Nilgiri	Eucalyptol	cough suppressants.		
S-7	Mint	Azulene	antiallergic, antibacterial, and anti-inflammatory		

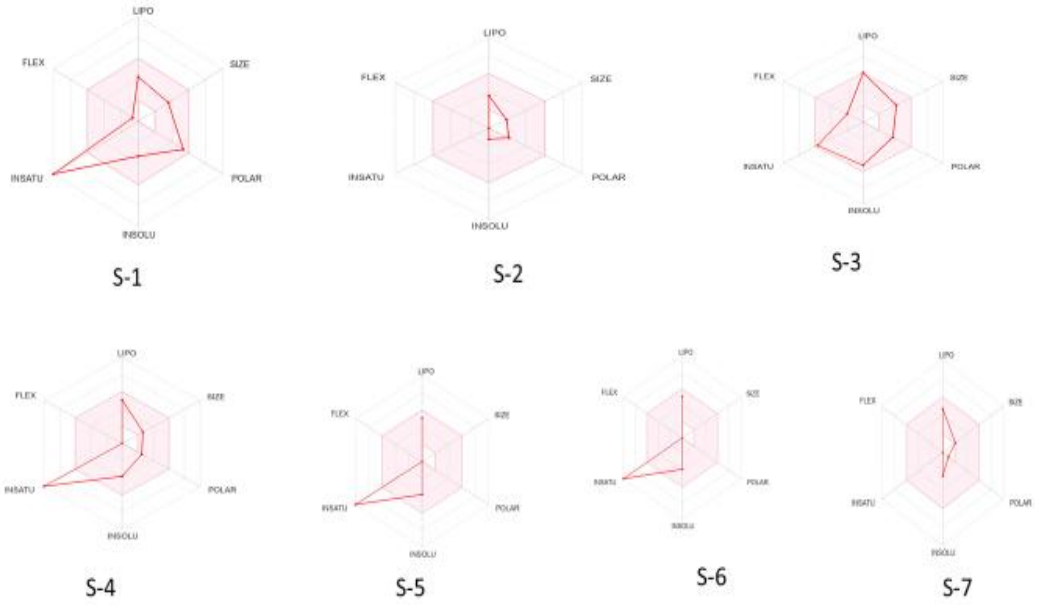


Fig 1: Bioavailability Radar Map of Phytochemicals.

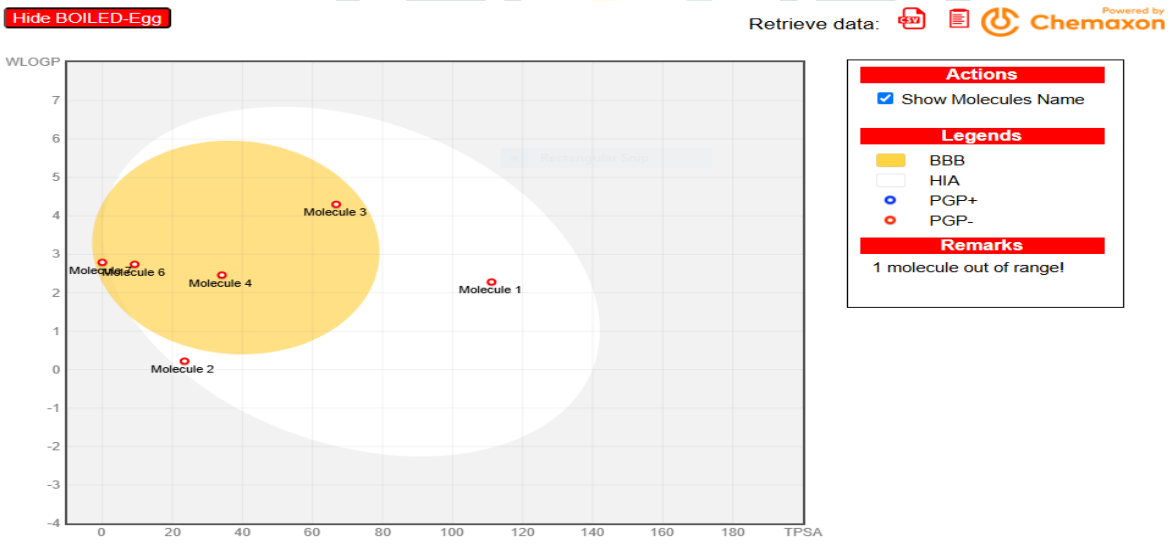


Fig 2: Boiled egg structure of Map of selected Phytochemicals.

Table 2: Pharmacokinetic parameters of the selected phytochemicals of plants.

Pharmacokinetic Properties		Selected Phytochemicals						
Properties	**Model Name**	**S-1**	**S-2**	**S-3**	**S-4**	**S-5**	**S-6**	**S-7**
Absorption	**Water solubility**	-3.04	-0.514	- 4.342	-3.435	-2.881	-2.63	-3.654
	Caco2 permeability	0.032	-0.514	1.437	1.31	-2.881	1.485	1.389
	Intestinal absorption (human)	74.29	93.575	88.997	99.057	11.639	96.505	95.451
	Skin Permeability	-2.735	-3.343	-2.786	-2.122	11.639	-2.437	No
	P-glycoprotein substrate	Yes	Yes	Yes	No	Yes	Yes	No
	P-glycoprotein I inhibitor	No	No	Yes	No	No	No	No
	P-glycoprotein II inhibitor	No	No	No	No	No	No	No
Distribution	**VDss (human)**	1.274	0.54	-0.107	0.232	0.733	0.491	0.519
	Fraction unbound (human)	0.178	0.796	0	0.136	0.269	0.553	0.441
	BBB permeability	-0.939	-0.023	-0.285	0.372	-2.114	0.368	0.77
	CNS permeability	-2.228	-3.339	-1.749	-1.421	-4.957	-2.972	-2.064
Metabolism	**CYP2D6 substrate**	No	No	No	No	No	No	No
	CYP3A4 substrate	No	No	Yes	Yes	No	No	No
	CYP1A2 inhibitor	Yes	No	Yes	Yes	No	No	No
	CYP2C19 inhibitor	No	No	Yes	No	No	No	No
	CYP2C9 inhibitor	No	No	Yes	No	No	No	No
	CYP2D6 inhibitor	No	No	No	No	No	No	No
	CYP3A4 inhibitor	No	No	Yes	No	No	No	No
Excretion	**Total Clearance**	0.477	1.063	0.178	0.181	-0.333	1.009	0.208
	Renal OCT2 substrate	No	No	No	No	No	No	No
Toxicity	**AMES toxicity**	No	No	No	Yes	No	No	No
	Max. tolerated dose (human)	0.531	0.896	-0.31	0.291	0.469	0.553	0.507
	hERG I inhibitor	No	No	No	No	No	No	No
	hERG II inhibitor	2.449	No	Yes	No	Yes	No	No
	Oral Rat Acute Toxicity (LD50)	2.505	1.91	2.008	1.979	2.483	2.01	1.66
	Oral Rat Chronic Toxicity (LOAEL)	------	1.152	1.554	2.219	5.574	2.029	2.271
	Hepatotoxicity	No	Yes	No	Yes No	No	No	No
	Skin Sensitization	No	Yes	No		No	Yes	Yes
	T.Pyriformis toxicity	0.312	-0.662	0.563	1.29	0.285	0.171	0.347

	Minnow toxicity	2.885	2.961	0.535	1.032	12.935	1.735	1.425

Table 3: Toxicity parameters of the selected phytochemicals of Selected Plants.

	Acute Inhalation Toxicity						
Code of Phytochemicals	**Toxicity (Conf)**	**Confidence**	**Acute Oral Toxicity**	**Acute Dermal Toxicity**	**Eye Irritation and Corrosion**	**Skin Sensitization**	**Skin Irritation and Corrosion**
S-1	Non-Toxic (-)	68.0%	Non-Toxic (-)	Toxic (+)	Non-Toxic (-)	Sensitizer (+)	Negative (-)
S-2	Toxic (+)	57.0%	Toxic (+)	Non-Toxic (-)	Toxic (+)	Non-Sensitizer (-)	Positive (+)
S-3	Non-Toxic (-)	53.0%	Non-Toxic (-)	Toxic (+)	Non-Toxic (-)	Sensitizer (+)	Negative (-)
S-4	Non-Toxic (-)	56.0%	Toxic (+)	Non-Toxic (-)	Non-Toxic (-)	Sensitizer (+)	Negative (-)
S-5	Non-Toxic (-)	77.0%	Non-Toxic (-)	Toxic (+)	Non-Toxic (-)	Non-Sensitizer (-)	Negative (-)
S-6	Non-Toxic (-)	58.0%	Non-Toxic (-)	Non-Toxic (-)	Non-Toxic (-)	Sensitizer (+)	Positive (+)
S-7	Non-Toxic (-)	69.0%	Non-Toxic (-)	Toxic (+)	Toxic (+)	Sensitizer (+)	Positive (+)

CONCLUSION:

Selected phytochemicals exhibited very important medicinal properties and biological activities including antioxidant, anti-inflammatory, antibacterial, antiallergic, anti-cancer, Laxatives properties and they can inhibit the growth and development of some human disease. The molecule S-2, S-3, S-4, S-5 and S-6 exhibit better bioavailability and hence present in the blood brain barrier and absorb readily and plays vital role in metabolism. Molecule S-1 are present in white part outside the blood brain barrier which shows high HIA but low BBB they absorb by intestine but not reach at brain hence it is medicinally less valuable. Bioavailability radar map S-1, S-3, S-4, and S-7 have the most promising profiles S-2 has a major issue with solubility. S-5 and S-6 have poor profiles overall and are unlikely to have good oral bioavailability. Evaluation of ADMET properties shows that the all seven compound exhibit medicinal properties.

CONFLICT OF INTEREST: The authors have no any conflict of interest.

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