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A Computational Study To Detect The Potential Of Phytoconstituents For Drug Development Against Urinary Tract Infection

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Urinary tract infection are global health problem. Antibiotic resistance is a major concern in the treatment of UTI. So, there is necessity for prevention and cure of UTI by alternative therapy. Medicinal plants extracts are used for many ailments. In our study we selected some phytoconstituents from plants which has shown anti uropathogenic activity invitro to detect their potentiality for drug development with computational tools SwissADME and DruMAP along with some existing drugs. We also included potential compound named sunitinib that shows antiviral and anticancer property as drug repurposing query. These methods calculates the many parameters to find out the capability for drug discovery. Out of ten phytoconstituent nine shows potentiality for drug development study in SwissADME prediction. DruMAP prediction also confirms the stability of these phytoconstituents indicating their potential for drug development. Our study will help the researchers in the drug discovery for UTI management.

Keywords: Antibiotics, Physiochemical, Pharmacokinetics, Natural Therapeutics, Uropathogen, Urinary Tract Infection.

Urinary tract infection is defined as when a uropathogen is successful to overcome the host immune response and able to colonize the urinary tract. UTI most common bacterial infection affecting huge population worldwide.[1] Good hygiene, probiotics, antibiotic, probiotics and vaccines are the potential remedies to treat the chronic and recurrent UTIs. Antibiotics are most common treatment for UTI . With alarming rates of multi drug resistance pattern in uropathogen that hinders the treatment of UTI demands an alternative option with no side effects, cost effective treatment. Many studies reported that for the acute UTI, natural therapeutics like cranberry, berberine, estriol cream, uva ursi, supplements of vitamin A, C and potassium salt are prescribed.[2] There are many studies which reported cranberry efficacy in clinical trial to treat the urinary tract infection.[3] Antibiotics are the major therapy for the prevention and treatment of the uncomplicated and complicated UTI. Uropathogens evade the immune responses to survive via different mechanism

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involving morphological variation, biofilm formation and able to invade the uroepithelial cells in bladder. Adhesive fibres , pili, flagella, extracellular DNA helps the uropathogen to form a niche that is protected from immune responses and antimicrobial compounds.[4] Due to these reasons alternative therapeutic approaches for the treatment of UTI are being explored for their ability to be potential drugs. Ethnobotanicals like Natural isothiocyanates (ITC), lemon grass (*Cymbopogon citratus* (DC), *Arctostaphylos uva-ursi*, Cranberry, *Cinnamom verum* J. Presl. (cinnamon), *Ocimum gratissimum, L*, and *Mangifera indica, Zingiber officinale* and *Punica granatum, Ibicella lutea* (Martyniaceae), *Camellia sinensis, Ocimum suave, Cymbopogon citratus* and *Syzygium aromaticum, Coleus aromaticus* and *Ocimum sanctum*, D-Mannose, *Coccinia grandis*, sage (*Salvia officinalis L.*), are found with antiuropathogenic activity against respective uropathogen causing urinary tract infection by the different researchers (Table 1).

One such plant-based medication may be natural isothiocyanates (ITC). [5] The ITC originated from the plant horseradish (*Armoraciae rusticanae radix*) and nasturtium (T*ropaeoli majoris herba)*. ITC antimicrobial activity against the selected isolates of uropathogenic *E. coli* is found very strong.[5] ITC reduces UPEC internalization in human uroepithelial cell. But this effect is varied between the strains. This variation actually comes due to presence of virulence factor that are genetically determined but these genetic differences were not studied.[5] Bioactive substances such as anthocyanins, flavonoids, terpenoids, catechins, and organic acids are abundant in cranberries.[6] Hippuric acid quantity is found very high in urine on consumption of cranberry due to presence of quinic acid that make the urine acidic.[7] Juice of cranberry is found vigorous barrier to the bacterial adherence.[8] The anti-adhesive nature of cranberry is used as therapeutic agent against urinary tract infection. Additionally, it has been discovered that cranberries prevent type I and P-fimbriated uropathogens, mostly E. coli, from adhering to the uroepithelium.[9]

For the bladder infection one of potent herb named *Arctostaphylos uva-ursi*. Antibacterial activity is found against the UPEC due to presence of arbutin in the leaves of *bearberry leaves.*[10] To test the antimicrobial activity against the uropathogen *Proteus mirabilis, Klebsiella pneumonia, E. coli,* and *Pseudomonas aeruginosa, Enterobacteria,* essential oils were isolated from three medicinal herbs: *Salvia officinalis L., O. gratissimum L., and C. citratus* (DC) Stapf. [11] *M.indica* has many medicinal uses and its seed kernel ethanolic extract was found having antioxidant, antibacterial and antiviral property against the clinical isolates causing the urinary tract infection.[12] A potent antibacterial activity of *Punica granatum and Zingiber officinale* against *E. coli* is found in many research studies.[13] In their study they tested acetone, ethanol and aqueous extract of these plants against the major clinical isolate of complicated urinary tract infection.

Ibicella lutea is America's native plant and quasi carnivorous and its aerial parts extract is found to have capacity to interfere the *P. mirabilis* growth, to check on biofilm formation capacity.[14]

Uropathogenic *Escherichia coli* (UPEC) that produce Extended Spectrum of Beta Lactamase (ESBL) and biofilm are both susceptible to the antibacterial activity of *Coccinia grandis*.[15] Many infectious diseases are cured by traditional use of C. grandis, a medicinal plant existing in India. *Coleus aromaticus* and *Ocimum sanctum* essential oils also found with antibacterial activity against uropathogens causing urinary tract infection (UTI).[16] Essential oils of *Coleus aromaticus* containing carvacrol as phytoconstituents found having more efficacy against the uropathogen in comparison with *Ocimum sanctum* containing eugenol and eugenol methyl ether as phytoconstituents. *Syzygium aromaticum* and *Cymbopogon citratus* oils are commonly employed in impoverished nations, especially India, to treat fungal infections of the mouth, skin, and vaginal tract because of their anti-biofilm properties against powerful strains of *Candida albicans* that form biofilms.[17] Green tea made from the *Camellia sinensis leaves have* polyphenolic catechins with strong beneficial component against UTI caused by *E. coli*. [18] Additionally, the essential oils isolated from *Ocimum suave* have antibacterial action against Citrobacter species, *S. aureus, M. morganii, E. coli, P. aeruginosa, Enterobacter species, K. pneumoniae,* and *E. feacalis*.[19] In children receiving prophylactic treatment, the effectiveness and safety of cranberry products, such as cranberry capsules,

are evaluated.[20] Urobactericidal potential in the P.granatum seed extract and Hemidesmus indicus root extract against *Klebsiella pneumonia, E. coli, Staphylococcus aureus* and *Enterococcus faecalis* strains isolated from UTI patient is also reported.[21, 22, 23] Natural glycosides are found in the extract of herbal plants that help in prevention of UTI pathogenesis by hindering the adhesion of bacteria to host cell.

So, in our research we took isothiocyanate, Cyanidin, Quercetin, Limonene, Catechin, Carvacrol, Eugenol, oils, Polyphenolic Catechin and monoterpenes phytoconstituents of herbs which showed an uropathogenic activity in vitro to predict the druglikliness property. Then we also selected some random existing drug named Sulfamethoxazole, Nitrofurantoin, Fosfomycin, Fluroquinolones, and one potential chemical existing under review as antiviral, anticancer and also showing antibacterial property named Sunitinib as drug repurposing candidate to compare the pharmacokinetics and druglikliness parameters against our phytoconstituents in order to find out the potentiality of our selected molecules to be drug molecules.

A significant role in the quick, low-cost approach, evaluation, and discovery of therapeutics is being achieved by computational methods. The application of a reliable and predictive data complement to experimental subjection can be explored by computational method named SwissADME in which ADME stands for (Absorption, Distribution, Metabolism, and Excretion) that predict the pharmacokinetic, physicochemical, and pharmacological characteristics of small molecule in pharmaceuticals. This work sought to predict the biological activity of many phytochemical constituents of herbal medicines and then to compare them with existing drugs to find out their capacity to be potential therapeutics by computational analysis.

MATERIALS AND METHODS

SwissADME

A free online program called SwissADME uses algorithms to determine a small molecule's physicochemical characteristics, pharmacokinetics, and druglikeness. by BOILED-Egg (model to calculate the likelihood of a molecule to be absorbed by the gastrointestinal tract or permeate the blood-brain barrier ,five integrated models named iLOGP , XLOGP3, WLOGP, MLOGP, SILICOS-IT to calculate molecule's lipophilicity and

Table 1. List of plants with anti-uropathogenic activity

Plant	Part used	Reference
1. Natural isothiocyanates (ITC)	Nasturtium (*Tropaeoli majoris herba*) and horseradish (*Armoraciae rusticanae radix*) plant extract	Mutters et. al (2018)
2 .*Vaccinium macrocarpon*(cranberry)	Fruit	Bodel et al. (1959), Borukh et al. (1972), Kahn et al. (1967), Sobota, A. E. (1984), Schmidt et al. (1988), Zafriri et al. (1989)
3. Cinnamom verum J. Presl. (cinnamon)	Plant extract	Amalaradjou et al. (2011)
4. Arctostaphylos uva-ursi (L.)Spreng(Bearberry)	Leaves and extract	Ofek et al. (1991), Schindler et al. (2002)
5. *Ocimum gratissimum* L., *Salvia officinalis* L. (Lamiaceae); *Cymbopogon citratus* (DC.) Stapf (Poaceae)	Essential oil	Pereira et al. (2004)
6. *Mangifera indica* L. (Anacardiaceae)	Water and ethanol extract of seed kernel	Sowmiya et al. (2009)
7. *Zinziber officinale* Roscoe (Zinziberaceae); *Punica granatum* L. (Lythraceae)	Ethanol extract of rhizome and seed, respectively	Sharma et al. (2009), Avcioglu et al. (2016)
8. *Ibicella lutea* (Lindl.) Van Eselt. (Martyniaceae)	Plant extract	Sosa, V., & Zunino, P. (2009)
9. D-Mannose	Monosaccharide in fruits and berries	Ala-Jaakkola et al., (2022)
10 *Coccinia grandis* (L.) Voigt (Cucurbitaceae)	Water, acetone, ethanol extract of leaves	Poovendran et al., (2011)
11. *Coleus aromaticus* Lour.; *Ocimum sanctum* L. (Lamiaceae)	Essential oil	Khare et al., (2011)
12. *Cymbopogon citrates* (DC.) Stapf (Poaceae); *Syzygium aromaticum* (L.) Merr. & L.M. Perry (Myrtaceae)	Essential oil	Khan, M. S. A., & Ahmad, I. (2012)
13. *Camellia sinensis* (L.) Kuntze (Theaceae)	Leaf extract	Reygaert, W., & Jusufi, I. (2013)
14.*Ocimum suave* Willd. (Lamiaceae)	Essential oil	Tibyangye et al., (2015)

Support vector machine (SVM) an algorithm to calculate if compound is likely to be a substrate or inhibitor. SwissADME require canonical SMILE information as input, so the first step is to visit the drug bank database (https://go.drugbank.com/) to retrieve chemical formula, structure and smile. The second step is to use SwissADME (http://www.swissadme.ch/). It provide output in ADMET (absorption, distribution, metabolism, and excretion) properties.[24]

DruMAP

DruMAP is a web-based method that help in accessing the early drug discovery development.[25] It needs compounds smile in

Table 2. Phytoconstituents of herbal medicine and existing Drugs

Molecule	Canonical SMILES	Formula
Allyl isothiocyanate	C=CCN=C=S	C4H5NS
Cyanidin	Oc1cc(O)c2c(c1)[o+]c(c(c2)O)c1ccc(c(c1)O)O	C15H11O6+
Quercetin	Oc1cc(O)c2c(c1)oc(c(c2=O)O)c1ccc(c(c1)O)O	C15H10O7
Limonene	CC1=CCC(CC1)C(=C)C	C10H16
Catechin	Oc1cc2OC(c3ccc(c(c3)O)O)C(Cc2c(c1)O)O	C15H14O6
Carvacrol	CC(c1ccc(c(c1)O)C)C	C10H14O
Eugenol	C=CCc1ccc(c(c1)OC)O	C10H12O2
Oils	OC1C[C@H]2C([C@]1(C)CC2)(C)C.C=CC(CCC=C(C)C)C.C=CCc1ccc(c(c1)OC)OC.OC/C=C(\CCC=C(C)C)/C.O=C/C=C(\CCC=C(C)C)/C	C51H84O5
Polyphenolic Catechin	Oc1cc2O[C@H](c3ccc(c(c3)O)O)[C@H](Cc2c(c1)O)O	C15H14O6
Monoterpenes	CC([C@@H]1CC[C@H]([C@]23[C@H]1[C@H]2C(=CC3)C)C)C	C15H24
Sulfamethoxazole	Nc1ccc(cc1)S(=O)(=O)Nc1noc(c1)C	C10H11N3O3S
Nitrofurantoin	O=C1NC(=O)N(C1)/N=C/c1ccc(o1)[N+](=O)[O-]	C8H6N4O5
Fosfomycin	C[C@@H]1O[C@@H]1P(=O)(O)O	C3H7O4P
Fluroquinolones	CN1CCN(CC1)c1cc2c(cc1F)c(=O)c(cn2c1ccc(cc1)F)C(=O)O	C21H19F2N3O3
Sunitinib	CN1CCN(CC1)c1cc2c(cc1F)c(=O)c(cn2c1ccc(cc1)F)C(=O)O	C21H19F2N3O3

Table 3. Physicochemical properties

Molecule	MW	HA	AHA	Fraction Csp3	RB	HBA	HBD	MR	TPSA
Allyl isothiocyanate	99.15	6	0	0.25	2	1	0	30.03	44.45
Cyanidin	287.24	21	16	0	1	6	5	76.17	114.29
Quercetin	302.24	22	16	0	1	7	5	78.03	131.36
Limonene	136.23	10	0	0.6	1	0	0	47.12	0
Catechin	290.27	21	12	0.2	1	6	5	74.33	110.38
Carvacrol	150.22	11	6	0.4	1	1	1	48.01	20.23
Eugenol	164.2	12	6	0.2	3	2	1	49.06	29.46
oils	777.21	56	6	0.59	16	5	2	249.2	75.99
Polyphenolic Catechin	290.27	21	12	0.2	1	6	5	74.33	110.38
monoterpenes	204.35	15	0	0.87	1	0	0	67.14	0
Sulfamethoxazole	253.28	17	11	0.1	3	4	2	62.99	106.6
Nitrofurantoin	238.16	17	5	0.12	3	6	1	62.8	120.73
Fosfomycin	138.06	8	0	1	1	4	2	26.49	79.87
Fluroquinolones	399.39	29	16	0.24	3	6	1	112.68	65.78
Sunitinib	399.39	29	16	0.24	3	6	1	112.68	65.78

a file as an input for new prediction. In vitro parameters (metabolic stability, protein binding in plasma, protein binding in brain homogenate, and blood-to-plasma concentration ratio), in vivo parameters (drug amount in plasma and toxicity data), and numerous physiochemical parameters (solubility and distribution coefficient) are all accessible.[26, 27] DruMAP obtain the pharmacokinetic and physicochemical parameters from ChEMBL database that compiles information from experiments and reformat calculation in it.

RESULTS

The physicochemical characteristics were then examined.

MW stands for molecular weight (g/mol); rotatable bonds (RB); hydrogen bond acceptor and

Table 4. Lipophilicity characteristics

Molecule	iLOGP	XLOGP3	WLOGP	MLOGP	Silicos-IT Log P	Consensus Log P
Allyl isothiocyanate	1.93	2.41	1.28	1.98	2.37	1.99
Cyanidin	-2.62	0.77	2.91	0.32	0.24	0.32
Quercetin	1.63	1.54	1.99	-0.56	1.54	1.23
Limonene	2.72	4.57	3.31	3.27	2.97	3.37
Catechin	1.47	0.36	1.22	0.24	0.98	0.85
Carvacrol	2.24	3.49	2.82	2.76	2.79	2.82
Eugenol	2.37	2.27	2.13	2.01	2.48	2.25
oils	2.37	2.27	13.73	2.01	2.48	2.25
Polyphenolic Catechin	1.33	0.36	1.22	0.24	0.98	0.83
monoterpenes	3.4	4.47	4.27	5.65	3.73	4.3
Sulfamethoxazole	1.03	0.89	2.26	-0.15	0.16	0.84
Nitrofurantoin	0.14	-0.47	-0.69	0.13	-1.6	-0.5
Fosfomycin	0.08	-1.38	-0.09	-1.68	-0.75	-0.76
Fluroquinolones	2.66	0.89	2.8	2.61	2.85	2.36
Sunitinib	2.66	0.89	2.8	2.61	2.85	2.36

Table 5. Water solubility characteristics

Molecule	ESOL Log S	ESOL Solubility (mg/ml)	ESOL Solubility (mol/l)	ESOL Class
Allyl isothiocyanate	-1.84	1.43	0.01	Very soluble
Cyanidin	-2.6	0.715	0.00	Soluble
Quercetin	-3.16	0.211	0.00	Soluble
Limonene	-3.5	0.0433	0.00	Soluble
Catechin	-2.22	1.74	0.01	Soluble
Carvacrol	-3.31	0.074	0.00	Soluble
Eugenol	-2.46	0.569	0.00	Soluble
oils	-2.46	0.569	0.00	Soluble
Polyphenolic Catechin	-2.22	1.74	0.01	Soluble
monoterpenes	-3.86	0.0284	0.00	Soluble
Sulfamethoxazole	-2.25	1.42	0.01	Soluble
Nitrofurantoin	-1.04	21.7	0.09	Very soluble
Fosfomycin	0.24	240	1.74	Highly soluble
Fluroquinolones	-3.09	0.327	0.00	Soluble
Sunitinib	-3.09	0.327	0.00	Soluble

donor (HBA and HBD); heavy and aromatic heavy atoms (HA and AHA, respectively); respectively; molar refractivity, or MR (m3/mol); Topology polar surface area (TPSA) (Å²) (Table 4 and 5): The phytoconstituents were then shown to have lipophilicity and water solubility properties.

Poorly < -6 < Moderately < -4 < Insoluble < -10 < Soluble < -2 Very < 0 < Highly

Then, using Lipinski's principles, pharmacokinetic characteristics, bioavailability, and druglikeness were also assessed (Table 6 and 7).

The terms "GI absorption" and "BBB permeant" refer to intestine and blood-brain barrier permeation, respectively.

MW < 500 Dalton; MR (molar refractivity should be between 40 and 130); H-bond donors - < 5; H-bond acceptors - < 10; Consensus Log P - high lipophilicity (written as LogP < 5); Overall.

Table 6. Bioavailability and pharmacokinetic characteristics

Molecule	GI absorption	BBB permeant	Bioavailability Score
Allyl isothiocyanate	High	Yes	0.55
Cyanidin	High	No	0.55
Quercetin	High	No	0.55
Limonene	Low	Yes	0.55
Catechin	High	No	0.55
Carvacrol	High	Yes	0.55
Eugenol	High	Yes	0.55
oils	High	Yes	0.55
Polyphenolic Catechin	High	No	0.55
monoterpenes	Low	Yes	0.55
Sulfamethoxazole	High	No	0.55
Nitrofurantoin	High	No	0.55
Fosfomycin	High	No	0.56
Fluroquinolones	High	Yes	0.55
Sunitinib	High	Yes	0.55

Table 7. Score for druglikeness rules

Molecule	MW	H-bond acceptors	H-bond donors	MR	Consensus Log P	Overall
Allyl isothiocyanate	YES	YES	YES	NO	YES	YES
Cyanidin	YES	YES	NO	YES	YES	YES
Quercetin	YES	YES	NO	YES	YES	YES
Limonene	YES	YES	YES	YES	YES	YES
Catechin	YES	YES	NO	YES	YES	YES
Carvacrol	YES	YES	YES	YES	YES	YES
Eugenol	YES	YES	YES	YES	YES	YES
oils	No	YES	YES	NO	YES	YES
Polyphenolic Catechin	YES	YES	NO	YES	YES	YES
monoterpenes	YES	YES	YES	YES	YES	YES
Sulfamethoxazole	YES	YES	YES	YES	YES	YES
Nitrofurantoin	YES	YES	YES	YES	YES	YES
Fosfomycin	YES	YES	YES	NO	YES	YES
Fluroquinolones	YES	YES	YES	YES	YES	YES
Sunitinib	YES	YES	YES	YES	YES	YES

DISCUSSION

The physicochemical properties include molar refractivity, TPSA, sum total of heavy atoms, sum total of aromatic heavy atoms, sum total of rotatable bonds, sum total of H-bond acceptors, sum total of H-bond donors, molecular formula, and molecular weight. The PSA is calculated utilizing the polar atoms phosphorus and sulphur as well as a fragmental method called topological polar surface area (TPSA). The molecular weights of all the compounds were less than 500 Da, which is a critical requirement for compounds to be considered drug-like.

We employed the SwissADME models XLOGP3, WLOGP, MLOGP, SILICOS-IT, and iLOGP to evaluate a molecule's lipophilicity. XLOGP3, an atomistic method that incorporates a knowledge-based library and correction elements. MLOGP, the archetype of the topological technique, operates on a linear relation with 13 chemical attributes. SILICOS-IT is a method that employs 27 components and seven topological attributes. The physics-based iLOGP technique uses the generalized-born and solvent accessible surface area (GB/SA) model to calculate the solvation free energies in n-octanol and water. The log P o/w is the mathematical mean of the numbers predicted by the five suggested approaches.

The water solubility properties are displayed in Table 5. The most of compounds were soluble, moderately soluble and two were found highly soluble. The solubility of a substance is greatly influenced by the solvent employed, the ambient temperature, and the pressure. The point at which the solute's concentration in the solution does not rise with the addition of more solute is known as the saturation concentration. The fractional logarithm of the molar solubility in water (log S) is used to calculate all predicted values. SwissADME further offers solubility in mol/l and mg/ml, as well as qualitative solubility classes.

Pharmacokinetic characteristics and bioavailability are displayed in Table 6. A large number of the compounds possess good GI absorption, that has a direct connection with the compound's BBB. The accuracy of the model for GI passive absorption and prediction for brain access by passive diffusion to lay the BOILED-Egg (Brain or Intestinal L Estimate D permeation predictive model) was assessed using the Egan

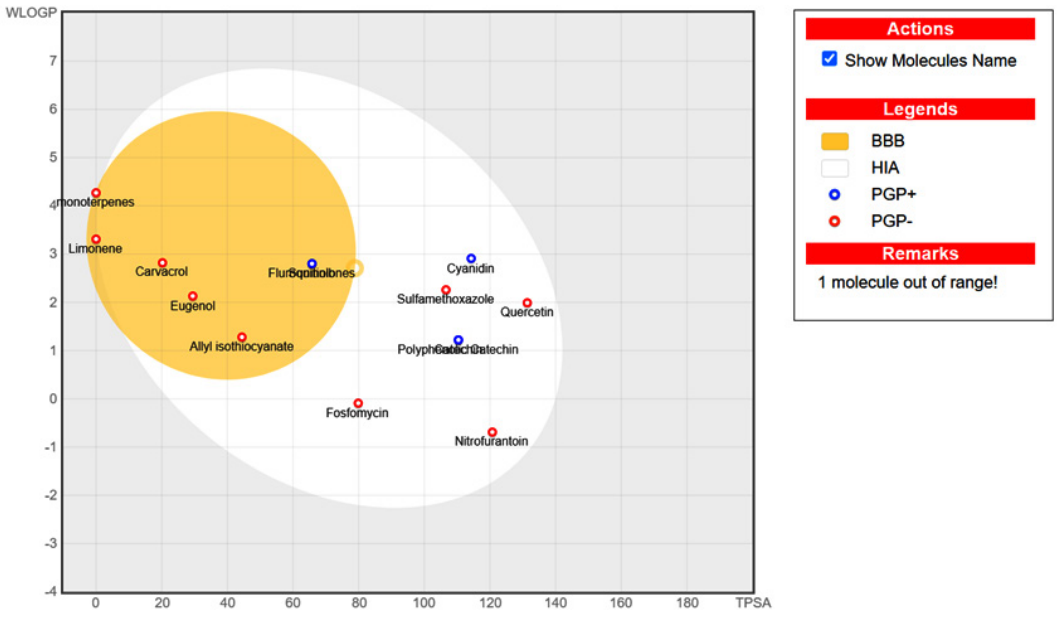

Fig. 1. Graphical information: here two fraction yellow shows the compound with probability to enter in brain and white shows the compound probability of absorption in GI tract

Table 8. Dru Map prediction

name	fa_human	papp_ human_ caco2	d_sol74	fe_human	cr_type_ human	clr_ human	fu_p_ human_ class	fu_p_ human_ value	clint_ human
Allyl isothiocyanate	High	High	Low	Medium-High	Secretion	0.0909	Medium	0.2565	Stable
Cyanidin	High	Low	Low	Low	Secretion	0.016734	Low	0.0519	Stable
Quercetin	High	Low	Low	Low	Intermediate	0.009642	Low	0.0594	Stable
Limonene	High	Low	High	Low	Intermediate	0.025338	High	0.1421	Stable
Catechin	Medium	Low	Low	Medium-High	Secretion	0.046878	Low	0.1172	Stable
Carvacrol	High	High	High	Low	Reabsorption	0.002976	High	0.2511	Moderate
Eugenol	High	High	High	Low	Reabsorption	0.005664	High	0.4016	Moderate
oils	Low	Low	Low	Low	Intermediate	0.008076	Low	0.048	Stable
Polyphenolic Catechin	Medium	Low	Low	Medium-High	Secretion	0.046878	Low	0.1172	Stable
monoterpenes	Medium	Low	High	Medium-High	Intermediate	0.022734	Low	0.1002	Stable
Sulfamethoxazole	High	High	High	Low	Reabsorption	0.002646	High	0.1821	Moderate
Nitrofurantoin	High	Low	High	Low	Reabsorption	0.008688	High	0.4411	Stable
Fosfomycin	Medium	Low	High	Medium-High	Intermediate	0.104166	High	0.5539	Stable
Fluroquinolones	Medium	Low	High	Low	Reabsorption	0.004746	Low	0.0778	Stable
Sunitinib	Medium	Low	High	Low	Reabsorption	0.004746	Low	0.0778	Stable

egg, an elliptical region occupied by well-absorbed molecules.

The drug likeness rule score is displayed in Table 7. According to Lipisnki's guidelines, constituent shown in table exhibited druglikeness. The Lipinski filter (Pfizer) is the first of five specifications that specifies small molecules through their physicochemical parameter profiles, comprising Molecular Weight (MW) < 500, MLOGP d" 4.15, N or O d" 10, and NH or OH d" 5.

Boiled Egg

The yellow region (yolk) on this graphical user interface indicates a high probability of brain penetration. A white area indicates that the gastrointestinal tract is likely to absorb it passively. There is no differentiation between the white and yolk regions. If a spot is determined to be a non-substrate of P-gp (PGP—), it is colored red; if it is determined that P-gp successfully releases it, it is colored blue (PGP+).

Fluroquinolone and Sunitinib are predicted to passively cross the blood-brain barrier (in the yolk) but pump out from the brain (blue dot), while polyphenolic catechin and cyanidin are predicted to be well-absorbed but not access the brain (in the white) and PGP+ (blue dot). It is expected that monoterpenes, limonene, carvacrol, eugenol, and allyl isothiocyanate will penetrate the brain (in the yolk) and not be released actively (red dot). It is anticipated that nitrofurantoin, quercetin, fosfomycin, and sulfamethoxazole will be effectively absorbed but not prone to active release. Since it is outside the plot's range, one molecule oil should not be absorbed or BBB permeant.

CONCLUSION

Antimicrobial, antioxidant, anti-candida, anti-inflammatory and antibacterial are the potential biological activities of the phytoconstituents taken for the study. The findings of the ADME research suggested that medicinal plant containing Allyl isothiocyanate, Cyanidin, Quercetin, Limonene, Catechin from cranberry, Carvacrol and Eugenol from Coleus Aromaticus and Ocimum Sanctum, oils from *Syzygium aromaticum* and *Cymbopogon citratus*, Polyphenolic Catechin from *Camellia sinensis* and monoterpenes from *Ocimum suave* have the potential for drug development study. Dru MAP results also confirms stability of compound calculated by Swiss ADME. Our research may serve as the foundation for further in vitro and in vivo research of Phyto drug from these phytoconstituents.

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Ethics Statement

This research did not involve human participants, animal subjects, or any material that requires ethical approval.

Informed Consent Statement

This study did not involve human participants, and therefore, informed consent was not required.

Clinical Trial Registration

This research does not involve any clinical trials**.**

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Not Applicable.

Author Contributions

Nisha Mehlawat: Conceptualization, Methodology, Writing – Original Draft; Jinny Tomar: Supervision, Analysis, Review & Editing, final Approval; Ravi Datta Sharma: Supervision, Analysis, Review & Editing, final Approval; Deepak Chand Sharma: Supervision, Analysis.

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