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in silico ADMET Screening of Compounds Present in *Cyanthillium cinereum* (L.) H. Rob.

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Drug development involves assessment of absorption, distribution, metabolism, excretion and toxicity (ADMET) increasingly earlier in the discovery process. *in silico* ADMET studies are expected to reduce the risk of late-stage attrition of drug development and to optimize screening and testing by looking at only the promising compounds. To this end, several *in silico* approaches for predicting ADMET properties of compounds from their chemical structure have been developed, ranging from data-based approaches. In this study, ADMET prediction has been done for 20 compounds from the plant *Cyanthillium cinereum* extracts. Some of the compounds were predicted to be non-toxic.

Keywords: ADMET, *Cyanthillium cinereum*, Lipinski rule.

INTRODUCTION

Medicinal plants have been used for a long time to treat disease all over the world [1]. They are used as a source of drugs in traditional system of medicine like Ayurveda, Unani, *etc*. and known to offer cure for various diseases. Knowledge of medicinal chemistry involves a thorough understanding of the relationship between chemical structure and biological properties. Most promising drug molecules often failed due to the unsatisfactory ADMET properties. It is more important to improve the rate of success in drug development by applying new technologies. The ADMET evaluation is used to minimize cost, time and labour of intensive screening and testing. The goal of *in silico* ADMET is to predict the compound's worse behaviour in the whole body by assembling all kinetic processes in one model.

Researchers have taken interest in the characterization and analysis of plant constituents [2]. Therapeutic values have been found in a large number of such compounds and are used in drug developments [3]. *Cyanthillium cinereum* (Asteraceae) is an annual herbaceous plant, distributed throughout India identified as a weed [4]. A number of disorders including fever, inflammation, worms, pain, diuresis, abortion and various gastrointestinal disorders are treated with this herb [5]. Decoction or infusion of the whole herb is used to treat fever and eye infections. It is also used in a remedy for urinary bladder spasms and strangury.

Cyanthillium cinereum contains sesquiterpene lactones like vernolide-A, vernolide-B [6]; β-amyrin, lupeol and their acetates; β-sitosterol, stigmasterol, α-spinasterol and phenolic resin. The roots contain δ-amyrin acetate, α-amyrin acetate, β-amyrin acetate, β-amyrin and α-amyrin [7] and the leaves contain urticifolene (new polyene), lutein (carotenoid) and sitosterol (triterpenoid). The stem, bark and leaves contain lupeol, 12-oleanen-3-ol-3β-acetate and stigmasterol [8-10]. Abundant opportunities have been provided by natural products for novel drug formulation. In present study, *in silico* ADMET predictions of some compounds were discussed with emphasis on structure pattern recognition that was developed recently. The *in silico* ADMET, pharmacokinetics, drug-likeness and toxicity prediction were discussed in details and the computational data could be used for prediction in drug discovery and hazard risk assessment.

EXPERIMENTAL

Chemical constituents from *Cyanthillium cinereum* which have been reported (20 numbers) from our laboratory to be gallic acid, apigenin, 12-oleanen 3-ol-3β acetate, α-amyrin acetate, α-spinasterol, apigenin, caffeic acid, chrysoeriol, dotriacontanoic acid, ethyl caffeate, ferulic acid, lupeol, lupeol

acetate, quercetin, luteolin, rutin, β-sitosterol, stigmasterol, vernolide A, vernolide B and vernolide C were considered and their chemical structures were obtained from Chem Draw. The drug-likeness properties were studied using Swiss ADME and Mol inspiration software available in the open web.

***in silico* ADMET screening:** In the present study, the relevant pharmacological properties of the compounds and consequential descriptors of drug-likeness like mutagenicity and toxicity were predicted using online tool Swiss ADME [11]. Using the pharmacokinetics parameters the ADMET properties were determined. From the Log P and S prediction programs, integrating the results of lipophilicity and hydrophilicity of these molecules has been obtained. Lipophilicity were predicted by using five different models namely XLOGP3 (atomistic method/knowledge based library), WLOGP (atomistic method/ Wildman and Crippen), MLOGP (topological method), SILICOS-IT (hybrid method) and iLOGP (in-house physics-based method). The arithmetic mean was calculated to arrive at a consensus value of log $P_{o/w}$. Water solubility was predicted using two topological methods ESOL model and the other from Ali *et. al*. method [12].

Simple molecular and physico-chemical descriptors were computed using Open Babel version 2.3.0. The topological polar surface area was calculated by the fragmental technique. Topological polar surface area was calculated using the polar atoms such as sulphur and phosphorus. Multiple linear regressions adapted from Potts and Guy was used to predict skin permeability coefficient. Drug-likeness is given through filters such as Lipinski (Pfizer), The Ghose (Amgen) [13], Veber (GSK) [14], Egan (Pharmacia) [15] and Muegge (Bayer). Toxicity parameters like AMES toxicity (mutagenicity) and cardiotoxicity (hERG-I & II inhibition) [16] were predicted using pkCSM web server. The Bioavailability score was implemented without changes from Martin [17] and it is similar but seeks to predict the probability of a compound to have at least 10% oral bioavailability in rat or measurable Caco-2 permeability.

RESULTS AND DISCUSSION

A drug is said to be effective, when it attains its target inside the human body in adequate concentration and stays long enough for the expected biological events to occur in a bioactive form. The "drug-likeness" of compounds was assessed by the molecular properties such as molecular weight (m.w.), calculated lipophilicity (Alog P), polar surface area (PSA), number of hydrogen bond acceptors (HBA) and number of hydrogen bond donors (HBD). These properties help to analyze novel compounds without wasting time on lead molecules that would be toxic or metabolized by the body into an inactive form that is unable to cross membranes.

Physico-chemical properties: Lipinski rule of 5 was used to predict rapidly the drug likeliness of the compounds as reported in Table-1. The molecular weight, number of H-bond donors and number of H-bond acceptors are considered in the Lipinski rule. The molecular weight plays an important role and the compounds lying between 170 and 480 will be optimum for a drug-like molecule. It is obvious that when the molecular weight increases the bulkiness of the molecules also increases, which affects the drug action. In present study, except rutin all compounds are well within the limits of Lipinski rule of 5.

Total prostate-specific antigen (tPSA) is another parameter and used to predict transport properties of drugs. Compounds with lower tPSA were favourable for drug-like property than those with high tPSA because they were better substrates of *p*-glycoprotein which is responsible for drug efflux from the cell. In the present study, the TPSA value range between 20 and 131.36 (Table-1), suggested a good cell permeability and drug-like property. With respect to the number of rotatable bonds

TABLE-1
PHYSICO-CHEMICAL PROPERTIES OF THE COMPOUNDS OF *C. cinereum*

Compound name	m.f.	m.w. (g/mol) (< 500 g)	No. of heavy atoms	No. of aromatic heavy atoms	Fraction CsP3 (0.25-1)	No. of rotatable bonds ≤ 15	No. of H-bond acceptor ≤ 10	No. of H-bond donor ≤ 5	MR (40-130)	TPSA (70-140 Å^2)
Gallic acid	$C_7H_6O_5$	170.12	12	6	0.00	1	5	4	39.47	97.99
12-Oleanen 3-ol-3β acetate	$C_{32}H_{52}O_2$	468.75	34	0	0.91	2	2	0	144.62	26.3
α-Amyrin acetate	$C_{30}H_{50}O$	426.72	31	0	0.93	0	1	1	134.88	20.23
α-Spinasterol	$C_{29}H_{48}O$	412.69	30	0	0.86	5	1	1	132.75	20.23
Apigenin	$C_{15}H_{10}O_5$	270.24	20	16	0	1	5	3	73.99	90.9
Caffeic acid	$C_9H_8O_4$	180.16	13	6	0	2	4	3	47.16	77.76
Chrysoeriol	$C_{16}H_{12}O_6$	300.26	22	16	0.06	2	66	3	80.48	100.13
Dotriacontanoic acid	$C_{32}H_{64}O_2$	480.85	34	0	0.97	30	2	1	157.71	37.30
Ethyl caffeate	$C_{11}H_{12}O_4$	208.21	15	6	0.18	4	4	2	56.29	66.76
Ferulic acid	$C_{10}H_{10}O_4$	194.18	14	6	0.10	3	4	2	51.63	66.76
Lupeol acetate	$C_{32}H_{52}O_2$	468.75	34	0	0.91	3	2	0	144.88	26.3
Lupeol	$C_{30}H_{50}O$	426.72	31	0	0.93	1	1	1	135.14	20.23
Luteolin	$C_{15}H_{10}O_6$	286.24	21	16	0	1	6	4	76.01	111.13
Quercetin	$C_{15}H_{10}O_7$	302.24	22	16	0	1	7	5	78.03	131.36
Rutin	$C_{27}H_{30}O_{16}$	610.52	43	16	0.44	6	16	10	141.38	269.43
β-Sitosterol	$C_{29}H_{50}O$	414.71	30	0	0.93	6	1	1	133.23	20.23
Stigmasterol	$C_{29}H_{48}O$	412.69	30	0	0.86	5	1	1	132.75	20.23
Vernolide A	$C_{21}H_{28}O_7$	392.44	28	0	0.62	5	7	1	101.27	91.29
Vernolide B	$C_{23}H_{30}O_8$	434.48	31	0	0.61	7	8	0	111.01	97.36
Vernolide C	$C_{19}H_{22}O_7$	362.37	26	0	0.58	3	7	1	89.51	94.59

except dotriacontanoic acid, all other compounds obey the limits.

Pharmacokinetics: The gastrointestinal (GI) absorption of a drug is the process of passing of drug in the bloodstream, once it is administrated. It affects the bioavailability of a drug and determines how quickly and how much of the drug reaches the intended place of action. In the present study, only ten compounds *viz*. galic acid, epigenin, caffeic acid, chrysoeriol, luteolin, quercetin, ethyl caffeate, ferulic acid, vernolide A, vernolide B and vernolide C have high absorption in the gastro intestinal track. When studied for blood-brain barrier (BBB) permeation property, Table-2 shows that only two compounds namely, ethyl caffeate, ferulic acid can pass through the barrier suggested that all the other compounds were safe to be developed as drugs.

In an attempt to know whether these compounds were non-substrates of the glycoprotein (P-gp) permeability, Table-2 suggested that except dotriacontanoic acid, rutin and vernolide A, all other compounds did not inhibit P-gp and become P-gp substrates. The major purpose of P-gp is to shield the central nervous system from xenobiotics by active efflux of these compounds through biological membranes.

It is necessary to understand the interaction of molecules with cytochromes P450 (CYP). It is said to be CYP enzymes

TABLE-2
PHARMACOKINETIC PROPERTIES OF THE COMPOUNDS OF *C. cinereum*

Compound name	GI absorption	BBB permeant	P-gp substrate	Inhibitor					log K_p (skin permeation) cm/s
				CYP1A2	CYP2C19	CYP2C9	CYP2D6	CYP3A4	
Gallic acid	High	No	No	No	No	No	No	Yes	-6.84
12-Oleanen 3-ol-3β acetate	Low	No	No	No	No	No	No	No	-2.25
α-Amyrin acetate	Low	No	No	No	No	No	No	No	-2.41
α-Spinasterol	Low	No	No	No	No	No	No	No	-2.92
Apigenin	High	No	No	yes	No	No	Yes	Yes	-5.8
Caffeic acid	High	No	No	No	No	No	No	No	-6.58
Chrysoeriol	High	No	No	yes	No	Yes	Yes	Yes	-5.93
Dotriacontanoic acid	Low	No	Yes	No	No	No	No	No	-1.98
Ethyl caffeate	High	Yes	No	No	No	No	No	No	-5.75
Ferulic acid	High	Yes	No	No	No	No	No	No	-6.41
Lupeol acetate	Low	No	No	No	No	No	No	No	-1.74
Lupeol	Low	No	No	No	No	No	No	No	-1.9
Luteolin	High	No	No	yes	No	No	Yes	Yes	-6.25
Quercetin	High	No	No	yes	No	No	Yes	Yes	-7.05
Rutin	Low	No	Yes	No	No	No	No	No	-10.26
β-Sitosterol	Low	No	No	No	No	No	No	No	-2.2
Stigmasterol	Low	No	No	No	No	yes	No	No	-2.74
Vernolide A	High	No	Yes	No	No	No	No	No	-7.23
Vernolide B	High	No	No	No	No	No	No	No	-7.47
Vernolide C	High	No	No	No	No	No	No	No	-7.85

TABLE-3
DRUG-LIKENESS PROPERTIES OF THE COMPOUNDS OF *C. cinereum*

Compound name	Lipinski	Ghose	Veber	Egan	Muegge	Bioavailability score
Gallic acid	Yes	No; 2*	Yes	Yes	No; 1*	0.56
12-Oleanen 3-ol-3β acetate	No; 1*	No; 3*	Yes	No; 1*	No; 1*	0.55
α-Amyrin acetate	No; 1*	No; 3*	Yes	No; 1*	No; 2*	0.55
α-Spinasterol	No; 1*	No; 3*	Yes	No; 1*	No; 2*	0.55
Apigenin	Yes	Yes	Yes	Yes	Yes	0.55
Caffeic acid	Yes	Yes	Yes	Yes	No; 1*	0.56
Chrysoeriol	Yes	Yes	Yes	Yes	Yes	0.55
Dotriacontanoic acid	Yes	No; 4*	No; 1*	No; 1*	No; 2*	0.56
Ethyl caffeate	Yes	Yes	Yes	Yes	Yes	0.55
Ferulic acid	Yes	Yes	Yes	Yes	No; 1*	0.56
Lupeol acetate	No; 1*	No; 3*	Yes	No; 1*	No; 1*	0.55
Lupeol	No; 1*	No; 3*	Yes	No; 1*	No; 2*	0.55
Luteolin	Yes	Yes	Yes	Yes	Yes	0.55
Quercetin	Yes	Yes	Yes	Yes	Yes	0.55
Rutin	No; 3*	No; 4*	No; 1*	No; 1*	No; 4*	0.17
β-Sitosterol	No; 1*	No; 3*	Yes	No; 1*	No; 2*	0.55
Stigmasterol	No; 1*	No; 3*	Yes	No; 1*	No; 2*	0.55
Vernolide A	Yes	Yes	Yes	Yes	Yes	0.55
Vernolide B	Yes	Yes	Yes	Yes	Yes	0.55
Vernolide C	Yes	Yes	Yes	Yes	Yes	0.55

*Violation

and plays a key role in the elimination of drugs through metabolic biotransformation. It acts synergistically with P-gp to eliminate the xenobiotics from the tissues. In this super family of isoenzymes CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP-3A4 were found to be more important. These isoenzymes' inhibition is certainly one of the major causes of pharmacokinetics related drug-drug interactions leading to unwanted adverse effects due to the lower clearance and accumulation of the drug or its metabolites. In this study, gallic acid, epigenin, luteolin, chrysoeriol and stigmasterol inhibited at least one of these isoenzymes. With respect to the skin permeability coefficient, which is expressed in log units and a more negative log Kp value corresponds to a less skin permeant molecule.

Drug likeness: A drug absorbed in required time and distributed well into the system for its effective metabolism and action is said to be a good drug. Higher clog P value signifies lower hydrophilicity, poor absorption and permeation. A drug that is administered intravenously has 100% bioavailability. Compounds luteolin, apigenin, chrysoeriol, ethyl caffeate, quercetin, vernolide A, vernolide B, vernolide C showed 0 violations and obeyed 'Rule of 5', whereas compound rutin violated 3 properties.

Most of the compounds were rejected with three or four violations in the screening process with Ghose rule. However, with Veber rules, all the compounds meet the criteria of drug-likeness assessment. Dotriacontanoic acid and rutin were rejected with one violation are shown in Table-3.

Medicinal properties: Medicinal chemistry deals with the problematic fragments such as toxic, chemically reactive, metabolically unstable, aggregator, dye or other perturbation of assays. There are two complementary filters; Brenk [18] speaks of structural alert of the compounds, whereas PAINS [19] is about pan assay interference compounds from screening. Apigenin and chrysoeriol were the compounds with no violations of the rules and stood as lead-like compound (Table-4).

TABLE-4
MEDICINAL PROPERTIES OF THE COMPOUNDS OF *C. cinereum*

Compound name	PAINS	Brenk	Lead likeness	Synthetic accessibility
Gallic acid	1#	1#	No; 1*	1.22
12-Oleanen-3-ol-3β acetate	0#	1#	No; 2*	5.98
α-Amyrin acetate	0#	1#	No; 2*	6.04
α-Spinasterol	0#	1#	No; 2*	6.09
Apigenin	0#	0#	Yes; 0*	2.96
Caffeic acid	1#	2#	No; 1*	1.81
Chrysoeriol	0#	0#	Yes; 0*	3.06
Dotriacontanoic acid	0#	0#	No; 3*	4.24
Ethyl caffeate	1#	2#	No; 1*	2.20
Ferulic acid	0#	1#	No; 1*	1.93
Lupeol acetate	0#	1#	No; 2*	5.66
Lupeol	0#	1#	No; 2*	5.49
Luteolin	1#	1#	Yes; 0*	3.02
Quercetin	1#	1#	Yes; 0*	3.23
Rutin	1#	1#	No; 1*	6.52
β-Sitosterol	0#	1#	No; 2*	6.3
Stigmasterol	0#	1#	No; 2*	6.21
Vernolide A	0#	2#	No; 1*	6.67
Vernolide B	0#	2#	No; 1*	6.87
Vernolide C	0#	4#	No; 1*	6.52

*Violation; #Alert

Lipophilicity: Lipophilicity (log P) of compounds takes place in a significant position in the membrane transport of the compounds thereby determining the drug's action. So, it is advisable to have the Log P value within the optimal range to improve the compound's quality and likelihood of its success in therapeutics. If the lipophilicity is too low, a drug will exhibit a poor ADMET property [20]. Log P value of these compounds was determined by computational methods which were freely available to predict *n*-octanol/water partition coefficient (log $P_{o/w}$) values and are presented in Table-5. It was interesting to

TABLE-5
LIPOPHILICITY PROPERTIES OF THE COMPOUNDS OF *C. cinereum*

Compound name	log $P_{o/w}$ (iLOGP)	log $P_{o/w}$ (XLOGP3) (-0.7 to +5.0)	log $P_{o/w}$ (WLOGP)	log $P_{o/w}$ (MLOGP)	log $P_{o/w}$ (SILICOS-IT)	Consensus log $P_{o/w}$
Gallic acid	0.21	0.70	0.50	-0.16	-0.20	0.21
12-Oleanen-3-ol-3β acetate	5.19	9.73	8.74	7.08	7.42	7.63
α-Amyrin acetate	4.76	9.15	8.17	6.92	6.92	7.18
α-Spinasterol	5.11	8.3	7.8	6.62	6.86	6.94
Apigenin	1.89	3.02	2.58	0.52	2.52	2.11
Caffeic acid	0.97	1.15	1.09	0.70	0.75	0.93
Chrysoeriol	2.44	3.1	2.59	0.22	2.55	2.18
Dotriacontanoic acid	7.37	15.79	11.79	7.58	12.30	10.97
Ethyl caffeate	2.04	2.56	1.57	1.30	1.64	1.82
Ferulic acid	1.62	1.51	1.39	1.00	1.26	1.36
Lupeol acetate	5.17	10.45	8.6	7.08	7.33	7.72
Lupeol	4.76	9.87	8.02	6.92	6.82	7.28
Luteolin	1.86	2.53	2.28	-0.03	2.03	1.73
Quercetin	1.63	1.54	1.99	-0.56	1.54	1.23
Rutin	2.43	-0.33	-1.69	-3.89	-2.11	-1.12
β-Sitosterol	5.05	9.34	8.02	6.73	7.04	7.24
Stigmasterol	5.08	8.56	7.8	6.62	6.86	6.98
Vernolide A	3.07	2.06	2.55	1.63	2.8	2.42
Vernolide B	3.92	2.08	3.12	2	3.32	2.89
Vernolide C	2.45	0.93	1.17	1.18	1.85	1.52

note that log P values of some compounds are more than 5. The compounds with values below 5 were gallic acid, apigenin, caffeic acid, chrysoeriol, ethyl caffeate, ferulic acid, luteolin, quercetin, vernolide A, vernolide B and vernolide C.

Water solubility: Water solubility is similar to lipophilicity, the method of multiple predictive and the results are showed in Table-6. It is one of important factors determining oral bioavailability. In general, solubility increases with increasing HBD and HBA count, PSA and the fraction of the bonds that can freely rotate, but is negatively influenced by increasing log P, log D and the number of aromatic rings [21]. In the present study, gallic acid, apigenin, caffeic acid, ethyl caffeate, ferulic acid, quercetin, vernolide A, vernolide B and vernolide C have very good solubility.

Toxicity: *in silico* Toxicity risk was performed and the risk parameters are shown in Table-7. The toxicity parameters include irritant, tumourigenic, mutagenicity and reproductive effect property. In the present study most of the compounds are non-toxic in nature.

One of the toxicity parameter given much attention is cardio-toxicity due to which few marketed TZD were withdrawn from the market. The human ether a go-go related gene (hERG) cause sudden death (prolongation of QT interval) of patient when non-antiarrhythmic drugs administered is a major pharmacological safety issue. Hence, early stage evaluation of hERG blocking effect of the molecules provides safe drugs in drug discovery. All the molecules do not inhibit hERG -I but eight molecules inhibit hERG-II. Gallic acid, caffeic acid, chrysoeriol, lupeol, quercetin, ethyl caffeate, ferulic acid, vernolide A, vernolide B and vernolide C were predicted to be devoid of toxicity.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

TABLE-6
WATER SOLUBILITY OF THE COMPOUNDS OF *C. cinereum*

Compound name	ESOL log S (0-6)	Ali log S	SILICOS-IT log S
Gallic acid	-1.64	-2.34	-0.04
12-Oleanen-3-ol-3β acetate	-8.74	-10.2	-7.77
α-Amyrin acetate	-8.25	-9.47	-7.16
α-Spinasterol	-7.3	-8.59	-5.47
Apigenin	-3.94	-4.59	-4.4
Caffeic acid	-1.89	-2.38	-0.71
Chrysoeriol	-4.06	-4.87	-4.52
Dotriacontanoic acid	-10.79	-16.72	-11.63
Ethyl caffeate	-2.78	-3.61	-1.82
Ferulic acid	-2.11	-2.52	-1.42
Lupeol acetate	-9.13	-10.95	-7.35
Lupeol	-8.64	-10.22	-6.74
Luteolin	-3.71	-4.51	-3.82
Quercetin	-3.16	-3.91	-3.24
Rutin	-3.3	-4.87	-0.29
β-Sitosterol	-7.9	-9.67	-6.19
Stigmasterol	-7.46	-8.86	-5.47
Vernolide A	3.24	-3.61	-3.03
Vernolide B	-3.38	-3.75	-3.64
Vernolide C	-2.47	-2.5	-1.74

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TABLE-7
TOXICITY PARAMETER OF THE COMPOUNDS OF *C. cinereum*

Compound name	Maximum tolerated dose (human)	Inhibitor		Toxicity						Skin sensiti-zation
		hERG I	hERG II	AMES	Oral rat acute	Oral rat chronic	Hepato	*T. pyriformis*	Minnow	
Gallic acid	0.611	No	No	No	1.911	2.85	No	0.087	2.187	No
12-Oleanen-3-ol-3β acetate	-0.485	No	Yes	No	2.25	2.039	No	0.359	-1.996	No
α-Amyrin acetate	-0.571	No	Yes	No	2.467	0.856	No	0.384	-1.309	No
α-Spinasterol	-0.664	No	Yes	No	2.54	0.872	No	0.433	-1.675	No
Apigenin	0.713	No	Yes	No	2.327	1.671	No	0.458	0.95	No
Caffeic acid	0.828	No	No	Yes	2.018	1.846	No	0.064	-1.728	No
Chrysoeriol	0.672	No	No	No	2.463	1.509	No	0.338	1.248	No
Dotriacontanoic acid	-0.298	No	No	No	1.806	4.416	Yes	0.285	-4.937	Yes
Ethyl caffeate	0.916	No	No	No	1.888	1.781	No	0.686	1.014	No
Ferulic acid	1.087	No	No	No	2.558	1.939	No	0.201	2.294	No
Lupeol acetate	0.316	No	Yes	No	2.671	2.185	No	0.308	-4.847	No
Lupeol	0.042	No	No	No	2.925	1.756	No	0.346	-2.413	No
Luteolin	0.982	No	Yes	No	2.178	2.259	No	0.352	0.97	No
Quercetin	1.147	no	no	Yes	2.2	3.063	no	0.3	1.343	No
Rutin	0.427	No	Yes	Yes	2.445	5.414	No	0.285	2.682	No
β-Sitosterol	-0.341	No	Yes	No	2.854	1.085	No	0.477	-2.079	No
Stigmasterol	-0.664	No	Yes	No	2.54	0.872	No	0.433	-1.675	No
Vernolide A	-0.274	No	No	No	2.567	1.313	No	0.304	2.667	No
Vernolide B	-0.112	No	No	No	2.756	1.398	No	0.281	2.647	No
Vernolide C	-0.324	No	No	No	3.467	1.107	No	0.295	3.007	No

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