RESEARCH ARTICLE

Exploring the comorbidity mechanism of Chaihu Jia Longgu Muli Decoction in the treatment of vertigo and anxiety disorder based on network pharmacology and molecular docking

Hanshuo Dong¹, Bin Zhang², Xin Teng², Li Sun^{1,*}

¹Dizziness Clinic, Jilin Provincial Academy of Chinese Medicine Sciences, Changchun, Jilin, China. ²Changchun University of Chinese Medicine, Changchun, Jilin, China.

Received: July 4, 2024; accepted: October 15, 2024.

The incidence of vertigo with anxiety has been increasing year by year. Vertigo with anxiety significantly affects the physical and mental health of patients and reduces their quality of life. Therefore, how to effectively treat this condition has attracted widespread attention. This study investigated the mechanism of Chaihu Jia Longgu Muli Decoction (CLMD) in treating the co-morbidities of vertigo and anxiety utilizing network pharmacology and molecular docking technology. The active ingredients and action targets of CLMD were obtained from the TCMSP, BATMAN-TCM, HERB databases. The disease targets for vertigo disease and anxiety disorder were acquired using Genecard, OMIM, and DRUGBANK databases. These data sources were integrated and analyzed to identify the key action targets for the co-treatment of heterogeneous diseases by CLMD. The network visualization and STRING mapping of the protein interaction network were performed using Cytoscape v3.8.2. Additionally, Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis were conducted using Metascape platform. The molecular docking was verified using AutoDock. A total of 100 effective active ingredients were obtained from CLMD. Among these, 262 potential targets were predicted with 101 key targets being identified as exerting therapeutic effects. The notable targets included AKT1, IL6, TNF, VEGFA, IL1B, and others. The GO and KEGG databases were primarily utilized to investigate the involvement of these active ingredients and targets in various signaling pathways including 5-hydroxytryptaminergic synapses, dopaminergic neural synapses, cAMP signaling pathways, calcium signaling pathways. The molecular docking analysis revealed a strong binding affinity between the active ingredients and the crucial target molecules. Network pharmacological analysis further elucidated that CLMD exerted its therapeutic effects on the co-occurrence of vertigo and anxiety through diverse biological processes and associated signaling pathways. These findings contributed valuable insights into the underlying mechanism of CLMD in the treatment of vertigo and anxiety comorbidities.

Keywords: vertigo; anxiety disorders; Chaihu Jia Longgu Muli Decoction; network pharmacology.

*Corresponding author: Li Sun, Dizziness Clinic, Jilin Provincial Academy of Chinese Medicine Sciences, Changchun 130000, Jilin, China. Email: <u>18946584555@163.com</u>.

Introduction

Vertigo is a form of movement illusion resulting from a spatial orientation disorder within the human body with a potential lifetime prevalence reaching up to 10% [1]. In conjunction with vertigo symptoms, a considerable number of patients also experience comorbidities such as anxiety, depression, and other psychological ailments [2]. Anxiety disorder is one of the most common accompanying symptoms of vertigo, seen in 18% of these patients [3]. The intricate association between vertigo and anxiety engenders a reciprocal causation, resulting in a detrimental cycle that significantly impacts patients' quality of life. The advancement of psychosomatic medicine has prompted an increasing number of scholars to recognize the significance of psychological factors in disease pathogenesis, consequently making vertigo accompanied by anxiety disorder a prominent subject of research both domestically and internationally.

Traditional Chinese medicine (TCM) has a long history of treating diseases and has formed its unique treatment system during thousands of years of clinical practice. One of the most important elements of TCM is to treat different diseases with the same treatment. Chaihu Jia Longgu Muli Decoction (CLMD) is a classic TCM formula, which is first recorded in the "Treatise on Febrile Diseases" and has the effect of reconciling heat, calming, and tranquilizing [4]. Clinical treatment of vertigo with anxiety disorder shows that CLMD has a remarkable effect on anxiety disorder [5]. Related studies have confirmed that CLMD treats mental and nervous system diseases bv regulating brain-derived monoamine transmitters, neurotrophic factors, and anti-apoptosis [4-7]. In extensive clinical experience, CLMD has been found that it is effective in treating vertigo with anxiety. However, it is important to note that the composition of this formula is complex, which makes it difficult to explain the mechanism of action using a single clinical study. Notably, there is a dearth of scholarly exploration regarding the effectiveness and underlying mechanism of action for these two concurrent conditions. Network pharmacology, encompassing various interdisciplinary fields such as systems biology, pharmacology, and bioinformatics, enables the comprehensive analysis of compounds and diseases through the exploration of diseasegene-target-drug interaction networks. This

approach offers notable advantages in elucidating the targets and mechanisms underlying drug treatment for various diseases.

This study employed network pharmacology and molecular docking techniques to investigate the underlying mechanism of CLMD in treating the co-occurrence of vertigo and anxiety. The research would offer insights for the clinical utilization of CLMD in managing vertigo patients with comorbid anxiety.

Materials and methods

Screening of related ingredients and targets of CLMD

The chemical constituents of CLMD included Radxi bupleuri, Rheum officinale, Pinellia ternate, Scutellaria baicalensis, Ginseng, Cassia twig, Ginger, Poria cocos, Long Gu, Conchaostreae, and Fructus Zlziphi Jujubae and were identified through the utilization of TCMSP (http://tcmspw.com/tcmsp.php), BATMAN-TCM (http://bionet.ncpsb.org.cn/batman-tcm/), and the HERB database (http://herb.ac.cn/). The TCMSP database was screened using constraints of oral bioavailability (OB) \geq 30% and druglikeness (DL) \geq 0.18. The potential active components of BATMAN-TCM database were obtained by applying a score cutoff of \geq 20 and a P value less than 0.05. The active ingredients and targets were supplemented using the HERB, Swiss Target Prediction database (http://swisstargetprediction.ch/), and relevant literatures, and then unified, sorted, and removed duplicates to establish a target database for core prescriptions. Standardized naming was achieved through the utilization of the Uniprot (https://www.uniprot.org/) database.

Disease target screening

Vertigo and anxiety disorder related genes were identified from the databases of Genecard (<u>http://www.genecards.org/</u>), OMIM (<u>http://www.omim.org/</u>), and DRUGBANK (<u>https://go.drugbank.com/</u>). The Genecard database was assessed based on the median value of its "relevance score". Following the integration of the three databases, redundant targets were excluded to establish a comprehensive disease target database.

Looking for the target of CLMD in the treatment of vertigo with anxiety

The Venny 2.1 (https://bioinfogp.cnb.csic.es/tools/venny/) was employed to combine the target of CLMD with the target of vertigo and anxiety disorder. The common target of CLMD was a potential target for the treatment of comorbid vertigo and anxiety.

Construction of PPI network and TCMcomponent-target-disease network

The drug-disease common targets were entered into the String database (<u>https://string-db.org/</u>) with the species specified as "Homo sapiens" and the confidence level of 0.4. The protein-protein interaction (PPI) network was employed. Cytoscape 3.8.2 (<u>http://www.Cytoscape.org/</u>) was used to further visualize the results of the PPI network. The common targets were imported into Cytoscape 3.8.2 to construct "TCMcomponent-target-disease" network. The network diagram was visualized and analyzed.

Gene ontology (GO) functional enrichment analysis and Kyoto encyclopedia of genes and genomes (KEGG) pathway enrichment analysis The Metascape database (<u>https://metascape.org/gp/index.html</u>) was used for enrichment of the core target with *P* value

less than 0.01. The top 20 biological processes and signaling pathways were screened out.

Molecular docking

To assess the affinity between the active ingredients and targets, the molecular docking of active ingredients of CLMD and core targets was conducted using the AutoDock Vina software (<u>https://vina.scripps.edu/</u>). The 3D structures of ingredients and targets were obtained from PubChem (<u>https://pubchem.ncbi.nlm.nih.gov/</u>) and PDB databases (<u>https://www.rcsb.org/</u>). The

proteins were processed using PyMol (<u>https://www.pymol.org/</u>) and AutoDock Vina software and stored in qdbqt format. Following molecular docking with AutoDock Vina, PyMol was used to visualize and analyze the complex of the core target protein and the ligand.

Results

CLMD active ingredient target prediction

A total of 120 active ingredients of CLMD were identified through database screening. There were 13 ingredients in Radxi bupleuri, 32 in Scutellaria baicalensis, 11 in Pinellia ternate, 4 in Ginger, 16 in Ginseng, 6 in Cassia twig, 6 in Poria cocos, 7 in Rheum officinale, 2 in Long Gu, 5 in Conchaostreae, 18 in Fructus Zlziphi Jujubae. After removing duplicates, 100 potential active ingredients were obtained (Table 1). Meanwhile, 262 drug targets were obtained from Swiss target prediction database through duplication.

Disease related genes

A total of 5,340 genes related to vertigo and 1,645 genes related to anxiety disorder were obtained from Genecard, OMIM, and DRUGBANK databases. The data were aggregated, and duplicates were removed, resulting in the identification of 2,573 targets for vertigo and 1,474 targets for anxiety disorder.

Potential targets of CLMD in treating vertigo with anxiety disorder

The possible targets of CLMD for the treatment of vertigo with anxiety disorder were shown in Figure 1. A total of 101 common targets between the CLMD active ingredients targets and vertigo with anxiety disorder related targets were identified.

Key targets protein-protein interaction (PPI) analysis

The PPI network map of 101 common targets for CLMD treatment of vertigo with anxiety disorder was constructed (Figure 2). Targets that were situated closer to the center in the PPI map exhibited a higher degree of correlation with

Table 1. Active ingredients of CLMD.

| NOL020714 bacalelin 33.52 0.21 NOL020058 betra-strostrenol 36.51 0.75 NOL0200570 Cavidine 35.64 0.81 NOL0200579 Casidine 35.64 0.81 NOL020579 Cavidine 35.64 0.81 NOL020579 Casidine 30.7 0.2 NOL020579 Casidine 30.7 0.2 NOL020570 Casidine 30.7 0.2 NOL020570 Casidine 30.7 0.2 NOL020571 Detail-Difformancide, santhine-9 44.72 0.21 NOL020578 Cycloartenol 38.69 0.76 NOL020578 Cycloartenol 38.69 0.76 NOL020578 Cycloartenol 38.69 0.76 NOL020578 Cycloartenol 38.69 0.76 NOL020579 Detailon 43.59470 0.556 NOL020570 Asternitin Asternitin 43.694270 0.396 NOL020571 Castenonalin 43.694270 0 | Mol ID | Molecule name | OB (%) | DL |
|--|------------|--|-------------|---------|
| MOL00038 beta-storer ASI 0 0.76 MOL000470 Cavidie ASI 0 0.76 MOL000570 Cavidie ASI 0 0.32 MOL000571 Cavidie ASI 0 0.72 MOL000575 Cavidie ASI 0 0.72 MOL000575 Cavidie/Molest-de-Asi-ane ASI 0 0.72 MOL000587 Deta-Dhibotranoide, anthine-9 4.82 0.72 MOL000587 Deta-Dhibotranoide, anthine-9 4.82 0.23 MOL000587 Cavidie Arrapilia 4.834510 0.2305 MOL000581 Cavidie Arrapilia 4.8045072 0.2406 MOL000593 Astenterin 4.8045072 0.4334 MOL000593 Astenterin 4.80545072 0.6398 MOL000593 Astenterin 4.8045072 0.6398 MOL000593 Astenterin 4.903525 0.4394 MOL000593 Astenterin 4.903525 0.5639 MOL000593 Astenterin 4.913555 0.5529 MOL000513 | MOL002714 | baicalein | 33.52 | 0.21 |
| NOL000499 Sigmastere 33.8 0.76 NOL000519 Cavidne 35.4 0.81 NOL000519 Cavidne 35.4 0.81 NOL000519 (35.65)-3-(bent)/(-C/+/pdrox)bent)/(paratine 2,5-quinone 46.89 0.72 NOL000575 24-Ethylcholast-4-en-3-one 36.6 0.76 NOL000576 0.13-etosadienoit 39.9 0.2 NOL000578 Gavidne 39.9 0.2 NOL000578 0.27 5.2 0.27 NOL000578 Quicotation 44.27 0.2 NOL000578 Quicotation 44.832/852 0.438 NOL00058 Quicotation 44.832/852 0.438 NOL000452 Kaempferoi 48.943705 0.386 NOL000453 S.5.6.7-tetamethosychenyl chronone 19.7495927 0.59317 NOL000453 Quicotatia 44.033401 0.5561 NOL000471 Balcalain 42.1007623 0.59317 NOL000471 Balcalain 42.2939655 0.75633 NOL00 | MOL000358 | beta-sitosterol | 36.91 | 0.75 |
| NOL202270 Cavidne S.6.4 0.82 NOL200597 (35.65)-3-(berxyl)-6(4+rydrxyberxyl) piperane-2.5-quinone 36.08 0.76 NOL2005930 (35.65)-3-(berxyl)-6(4+rydrxyberxyl) piperane-2.5-quinone 36.08 0.76 NOL2005930 Berndonic acid 39.99 0.22 NOL200597 beta-D-Ribdranoside, xanthine-9 44.82 0.21 NOL200597 Cycloartenol 38.69 0.27 NOL200598 Quercetin 44.8222495 0.236 NOL200592 Akaempferol 44.8222495 0.2465 NOL200593 Guercetin 44.8222495 0.2465 NOL200594 Areapilinh 45.8944 0.2476 NOL2004538 3.5,6,7-tetramethory-24.3,4,5-trimethoryhenyl chromone 3.948927 0.53817 NOL2004539 G.5,6,7-tetramethory-24.3,4,5-trimethoryhenyl chromone 3.948 0.30712 NOL200453 Mol200453 Guercetin 0.6388 0.3681 NOL200453 Linely Lanethory 0.558 0.558 0.558 NOL200453 Linely Lanethory | MOL000449 | Stigmasterol | 43.83 | 0.76 |
| NOCL000535 Caniferin 31.11 0.32 NOCL000575 (35.65)-3(heprit)/(e-t-d-yoo)noene acid 30.6 0.72 NOCL000530 genda caid 30.7 0.2 NOCL000537 24-Ethycholes-4-en-3-one 30.7 0.2 NOCL000537 Deta D-Thibdramoside, axinthine 9 44.72 0.21 NOCL000537 Deta D-Thibdramoside, axinthine 9 44.72 0.21 NOCL000537 Genda Calde, axinthine 9 44.72 0.22 NOCL00054 querceruin 64.6333421 0.275 NOCL00054 querceruin 64.64334421 0.2405 NOCL00054 querceruin 45.60437072 0.336 NOCL000543 Genda Areapillin 45.0534070 0.5566 NOCL000543 Cubebin 51.75 0.5566 NOCL000543 Longlisurin A 47.27214894 0.5301 NOCL000543 EUPATIN 49.83 0.24 NOCL000574 Baicalin 41.93362 0.7564 NOCL000775 Baicalin 41.60 0.42 <td>MOL002670</td> <td>Cavidine</td> <td>35.64</td> <td>0.81</td> | MOL002670 | Cavidine | 35.64 | 0.81 |
| NOCL00997 (35,65)-3-(barxy)-6-(4-bytaxyberxy) piperame-2.5-quinome 46.89 0.72 NOCL00753 24-Ethylcholest-4-one-3-one 36.80 0.76 NOCL009697 beta-D-Ribdruranside, xanthine-9 44.72 0.21 NOCL009697 beta-D-Ribdruranside, xanthine-9 44.812 0.725 NOCL009697 beta-D-Ribdruranside, xanthine-9 44.8124246 0.220 NOCL000988 quercetin 45.812420 0.235 NOCL000989 quercetin 45.812420 0.235 NOCL000989 3.5.6.7-tetramethoxy-23.4.5-trimethoxyphenyl) chromone 31.919927 0.53317 NOCL00663 (+) Anomalin 45.913927 0.53317 NOCL00663 (+) Anomalin 40.1026623 0.8488 NOCL00671 Sale 0.768 0.3988 NOCL00672 Baicalin 40.1326926 0.5588 NOCL00673 Cubehin 57.824 0.5898 NOCL00775 Baicalin 40.1230696 0.769 NOCL00279 Duacosterol qt 35.80 0.724 NOCL0027 | MOL000519 | coniferin | 31.11 | 0.32 |
| NOLD01755 Constraints 30.08 0.75 NOLD05535 0.13-inicisadienoic 30.7 0.2 NOLD05535 0.13-inicisadienoic 30.7 0.2 NOLD05537 beta-0-Ribdrarnsoids extintine-9 44.72 0.21 NOLD05537 beta-0-Ribdrarnsoids extintine-9 44.72 0.275 NOLD05537 deta-30.81 0.275 0.356 NOLD05537 deta-30.81 0.275 0.356 NOLD05538 association 44.823.422551 0.206 NOL000542 kaempftrol 44.833.422 0.356 NOL000543 3.5.6.7-tetramethory-2 (3.4.5 trimethoxyphenyl) chromone 31.97495237 0.53917 NOL000545 Linoleyl actrate 42.1070623 0.8986 NOL000547 Linoleyl actrate 42.3733552 0.3564 NOL000573 Peado-spinasterol 42.973552 0.3564 NOL00071 aloe-emodin 83.88 0.24 NOL000225 EUPATN 50.8 0.36 NOL000226 Torlatchen 41.60 | MOI 006957 | (35.65)-3-(benzyl)-6-(4-bydroxybenzyl) piperazine-2.5-quinone | 46.89 | 0.27 |
| NOLD05303 C. gondoi acid 39.9 0.2 NOLD05637 beta-0-Ribdirancis(c, xanthine-9 34.9 0.2 NOLD05637 beta-0-Ribdirancis(c, xanthine-9 34.9 0.7 NOLD0538 Cycloarton 46.83705 0.36 NOLD0539 Quercetin 44.822496 0.24 NOLD0539 Kaempferol 41.822496 0.24 NOL006588 3.5,6,7-tetramethory-24.34,5-trimethoxyphenyl chromone 31.9745527 0.366 NOL006633 (+) Anomalin 40.0534075 0.65360 NOL006633 (+) Anomalin 40.077623 0.38415 NOL00674 Liongisaurin A 47.7212498 0.3838 NOL00675 Baicarin 40.132607623 0.78633 NOL006741 aleo-emodin 8.38 0.24 NOL000713 Baicarin 40.13260763 0.7824 NOL000226 (+) Cratechin 46.66 0.24 NOL00227 Daucosterol, qt 35.89 0.77 NOL00228 Thein 45.94 0.44 <td>MOI 001755</td> <td>24-Fthylcholest-4-en-3-one</td> <td>36.08</td> <td>0.76</td> | MOI 001755 | 24-Fthylcholest-4-en-3-one | 36.08 | 0.76 |
| MOL00693F 10.13-icosadienoic 39.99 0.2 MOL00693F beta-D.Ribofranoská xanthine-9 44.72 0.21 MOL00597 Cycloartenal 38.69 0.78 MOL00602 kaempferol 44.8322057 0.20065 MOL00402 kaempferol 44.8822057 0.41384 MOL004058 3,5,6,7-tetramethoxy-24,4,5-trimethoxyhenyl) chromone 31.9749527 0.41394 MOL004053 (.), A,5,6,7-tetramethoxy-24,6,2-trimethoxyhenyl) chromone 31.9749527 0.41384 MOL004053 (.), A,5,6,7-tetramethoxy-24,6,2-trimethoxyhenyl) chromone 31.9749527 0.435804 0.30112 MOL004053 (.), A,5,6,7-tetramethoxy-24,6,2-trimethoxyhenyl) chromone 31.28 0.6368 MOL013137 (.), Cubebin 31.08 0.41 0.3045 MOL010415 (.), Anomalin 40.125.60059 0.752.41 0.508 MOL010471 abore modin 40.125.60059 0.752.41 0.508 MOL010471 abore modin 41.212.007605 0.7863 0.74 MOL010471 abore modin 41.22.07 | MOL005030 | gondoic acid | 30.7 | 0.70 |
| MOL006967 beta-D-Riberanoside, xanthine-9 44.72 0.21 MOL0030378 Cycloartenol 36.6 0.75 MOL00422 kaempferol 46.43334812 0.27525 MOL00403 Arcepalin 45.043370 0.3066 MOL004059 Arcepalin 45.0643707 0.41394 MOL004059 3.5.6.7-tetramethory-2/2/4.5-trimethoxyhenyl) chromone 13.97492370 0.3012 MOL004053 3.5.6.7-tetramethory-2/2/4.5-trimethoxyhenyl) chromone 13.97492370 0.3012 MOL004053 Cubekin 42.0370562 0.56961 MOL004054 Longikaurin A 42.0730552 0.55951 MOL004052 Longikaurin A 42.0730552 0.55951 MOL00471 alae-emodin 43.8 0.24 MOL002235 EUPATIN 50.8 0.71 MOL002237 Daucosterol at 32.69 0.73 MOL002238 Toralatone 42.03 0.84 MOL002237 Daucosterol at 32.69 0.24 MOL002238 LipArtechin 45.63< | MOL006936 | 10 13-eicosadienoic | 39.99 | 0.2 |
| Noncostor Deck of Note National Science Part 1 Construction NOCL000358 Quercetin 48.66.333.4812 0.27325 NOCL000354 Quercetin 48.66.4333.4812 0.27325 NOCL000458 3.5,6.7-tetramethory.24.3,5 trimethoryphenyl chromone 13.97495927 0.29317 NOCL004588 3.5,6.7-tetramethory.24.3,5 trimethoryphenyl chromone 13.97495927 0.29317 NOCL004653 (H)-Anomalin 3.04.65.53005 0.5556 NOCL004653 (H)-Anomalin 42.02076623 0.19845 NOCL00454 (Longikurin A 47.221.98 0.53981 NOCL004718 Pseudo-spinasterol 42.10076623 0.19845 NOCL004713 Pseudo-spinasterol 42.0107663 0.19845 NOCL00275 Baicalin 40.123.60076 0.7254 NOCL002718 EVPATN So.8 0.41 NOCL002728 Trafactone 46.64 0.24 NOCL00228 Trafactone 45.85 0.78 NOCL00228 Jujubasaponin V_qt 32.69 0.78 < | MOL006967 | hata-D-Rihofuranoside vanthine-9 | 14 72 | 0.2 |
| MOLID0006 Classical querestion 46.4338.121 0.279.55 MOLID00422 k.aempferol 46.4338.121 0.279.55 MOLID00423 k.aempferol 45.061.770 0.306 MOLID00469 Arcapilin 45.061.770 0.3167 MOLID0458 3.5.6.7-tetramethxy-2/2.4.5.4-trimethxypheryl) chromone 13.794.927 0.5391.70 MOLID0453 (-).Anomalin 46.053.307 0.6398.8 MOLID0454 Longikaurin A 42.070.762.30 3.948.70 MOLID04624 Longikaurin A 42.073.752.50 2.756.93 MOLID04624 Longikaurin A 42.073.652.00 2.752.41 MOLID0471 albe-emodin 83.83 0.24 MOLID02235 EUPATIN 50.8 0.41 MOLID02245 Chrein 47.07 0.28 MOLID02235 Toralactone 42.073.052.0 0.34 MOLID02245 LipArtin P 32.69 0.62 MOLID02326 Toralactone 42.83 0.24 MOLID0231 Stepharine 33.8 | MOL003578 | Cycloartenol | 38.69 | 0.21 |
| Noncoords Landstand 118221451 0.13406 MOL0000354 isorhannetin 49.60437705 0.366 MOL0004988 3,5,6,7-tetramethory-2(3,4,5-trimethoxyphenyl) chromone 31.9749527 0.53317 MOL004533 (-)-Anomalin 40.60534007 0.63988 MOL00453 (-)-Anomalin 40.0553407 0.63988 MOL00453 (-)-Anomalin 40.0553407 0.63988 MOL004543 Lioneleyl acetate 42.077512488 0.53015 MOL004713 Pseudo-spinasterol 43.38 0.24 MOL004713 Pseudo-spinasterol 43.38 0.24 MOL000471 aloe-emodin 43.38 0.74 MOL000228 (-)-catechin 49.68 0.41 MOL000228 Torialactone 46.65 0.24 MOL00228 Torialactone 42.97 0.28 MOL012920 Mauritine D 89.31 0.45 MOL012921 Stepharine 31.55 0.33 MOL012924 Jubasaponin / qqt 36.98 0.75 | MOI 000098 | quercetin | 16 1333/812 | 0.75 |
| NCL00022 Nates in preside 11.8024/37/30 0.366 MOLD04609 Arraspillin 48.9643502 0.3366 MOLD04609 Arraspillin 48.9643502 0.41394 MOLD04609 \$5,6,7-tetramethory-24,4,5,4-trimethoxyphenyl) chromone 31.9749527 0.59317 MOLD0453 (+)-Anomalin 46.0533076 0.6566 MOLD0454 Liongikaurin A 47.72214984 0.53015 MOLD04642 Longikaurin A 47.72214984 0.53015 MOLD04642 Longikaurin A 40.12360996 0.7524 MOLD00452 EUPATIN 50.8 0.41 MOLD00276 Baicalin 40.1236099 0.7524 MOLD00277 Baicalin 46.66 0.24 MOLD00278 EUPATIN 50.8 0.41 MOLD02280 rhein 47.07 0.28 MOLD02281 Toralactone 46.66 0.24 MOLD02281 Toralactone 36.56 0.78 MOLD02281 Karaspoini L _q t 32.69 0.62 | MOL000038 | kaomnforol | 40.45554612 | 0.27525 |
| Inclucious Samaniterim Samaniterim <thsamaniterim< th=""> <thsamaniterim< th=""></thsamaniterim<></thsamaniterim<> | MOL000422 | icorhampatin | 41.88224934 | 0.24000 |
| INCLOUCIDD Integral | MOL000334 | Aroapillin | 49.00437703 | 0.300 |
| MOLD04335 5,5,0,7+tetrainteutoxypreny (Linolitore) 21.57,3227 0.33712 MOLD04653 (+).Anomalin 46.05534076 0.6566 MOLD04653 (-).Ebebin 57.1281280 0.63988 MOLD04654 Linoleyl acetate 42.10076623 0.19845 MOL004718 Pseudo-spinasterol 42.97936552 0.75693 MOL000471 aloe-emodin 83.38 0.24 MOL000471 aloe-emodin 83.38 0.24 MOL000276 Batcalin 40.12360986 0.41 MOL002281 EUPATIN 50.8 0.41 MOL002281 Toralactone 46.46 0.24 MOL002281 rbein 47.07 0.28 MOL002297 Daucosterol_qt 35.99 0.73 MOL012296 rbein/rite 36.49 0.43 MOL012976 cournestrol 36.49 0.43 MOL012986 Jujubasaponin V_at 36.99 0.63 MOL012976 cournestrol 36.45 0.78 MOL012986 | MOL004609 | Aredpillin 2 E 6 7 totramothowy 2 /2 4 E trimothowynhonyd) chromono | 46.90455072 | 0.41594 |
| MOL000400 Defunition 40.05333047 0.30712 MOL001653 (H)-Anomalin 46.05534077 0.6566 MOL001645 Linoleyi scetate 47.72214984 0.13945 MOL001645 Linoleyi scetate 47.72214984 0.13945 MOL004624 Longikaurin A 47.72214984 0.53015 MOL004718 Pseudo-spinasterol 42.29736552 0.75693 MOL0002776 Baicalin 40.13260996 0.75264 MOL0002255 EUPATIN 50.8 0.41 MOL000266 (-)-catechin 49.68 0.24 MOL002277 Daucosterol.qt 35.89 0.7 MOL012221 ztepharine 31.55 0.33 MOL012291 stepharine 31.55 0.33 MOL012926 Jujubasaponin V_qt 36.89 0.63 MOL012927 Occlaurine 42.35 0.24 MOL012928 Mairin 55.38 0.78 MOL012929 Mairine 56.20 0.4 MOL01000277 Et | NOL004398 | 5,5,6,7-tetramethoxy-2-(5,4,5-trimethoxyphenyi) tillomone | 31.97495927 | 0.39317 |
| MOLDAGS3 (PANDMAIN) 4-00334/07 0.03988 MOLD013187 Cubebin 57.1281289 0.19845 MOLD04718 Pseudo-spinasterol 42.9793652 0.75924 MOLD04718 Pseudo-spinasterol 42.9793652 0.75924 MOLD0275 Baicalin 40.1236098 0.41 MOLD02235 EUPATIN 50.8 0.41 MOLD02236 rhein 47.07 0.28 MOLD02276 Baicalin 40.126098 0.41 MOLD02281 Toralactone 46.46 0.24 MOLD02297 Daucosterol qt 35.89 0.7 MOLD02298 rhein 47.07 0.33 MOLD02297 Daucosterol qt 32.69 0.63 MOLD02298 Jujubasponin V_qt 36.89 0.7 MOLD01294 Auritine D 89.13 0.45 MOLD01292 Mauritine D 89.13 0.45 MOLD01454 Derberine 53.88 0.78 MOLD000713 Ruverside_qt 36.12 | NOL00490 | | 30.04553904 | 0.30712 |
| MOLD1318/ CLUBEDIM 57.1812429 0.03986 MOLD01645 Linoley lactate 42.10076622 0.19845 MOLD01716 Pseudo-spinsterol 42.27936552 0.75593 MOLD02776 Baicalin 40.12360996 0.75264 MOLD02235 EUPATIN 50.8 0.41 MOLD02266 (-)-catechin 46.66 0.24 MOLD02267 Daucsterol_qt 35.89 0.7 MOLD02268 Toralactone 46.66 0.24 MOLD02277 Daucsterol_qt 35.89 0.7 MOLD02264 zizyphs saponin / qt 35.89 0.7 MOLD02277 Daucsterol_qt 31.55 0.33 MOLD02286 jujubasaponin / qt 36.69 0.62 MOLD12946 zizyphs saponin / qt 36.99 0.63 MOLD0292 Mauritine D 89.13 0.45 MOLD02136 Ruvoide_qt 4.35 0.24 MOLD02137 Moldo213 6.83 0.24 MOLD02773 beta-carotene | NOL04053 | (+)-Anomain Cubakin | 40.05534070 | 0.0500 |
| MOUD01045 Lindiely actate 42.1007/06.3 0.13943 MOUD04718 Pseudo-spinasterol 42.97316552 0.75593 MOUD04717 aboe-modin 83.38 0.24 MOUD0471 aboe-modin 83.38 0.24 MOUD0225 EUPATIN 50.8 0.41 MOUD02281 Toralactone 49.68 0.24 MOUD02297 Daucosterol_qt 35.89 0.7 MOUD02291 stepharine 31.55 0.33 MOUD12946 zizyphus saponin Lqt 32.69 0.62 MOUD0297 Daucosterol_qt 36.99 0.63 MOUD12976 coumestrol 32.49 0.34 MOUD12976 coumestrol 32.49 0.34 MOUD12976 Jujubasaponin Lqt 36.99 0.63 MOUD01297 Mauritne D 36.81 0.74 MOUD0451 berberine 36.80 0.78 MOUD0452 (\$1/catechin 34.31 0.54 MOUD00452 Ruveside_qt 31.10 | NOL013187 | | 57.1281289 | 0.03988 |
| MCLU04624 LongikaLIM A 47.2214958 0.33015 MOL004718 Pseudo-spinasterol 42.9736552 0.75594 MOL002235 EUPATIN 83.38 0.24 MOL002241 Toralactone 46.46 0.24 MOL002268 rhein 47.07 0.28 MOL002277 Daucosterol_qt 33.89 0.7 MOL002268 rhein 47.07 0.28 MOL002277 Daucosterol_qt 32.69 0.62 MOL012921 stepharine 32.69 0.62 MOL012926 Jujubasaponin Lqt 32.69 0.63 MOL012927 Cournestrol 32.49 0.34 MOL012926 Mauritine D 89.13 0.45 MOL012929 Mauritine C 83.81 0.24 MOL00211 Malrin 55.38 0.78 MOL000273 Stepholidine 33.11 0.54 MOL000273 Stepholidine 33.11 0.54 MOL000273 Stepholidine 36.61 0.75 | MOL001645 | Linoieyi acetate | 42.10076623 | 0.19845 |
| NULLUA718 Pseudo-spinateroi 42.973e5.22 0.75934 NOLD02775 Baicalin 40.1230095 0.75264 NOLD0275 EUPATIN 50.8 0.41 NOLD02281 Toralactone 46.46 0.24 NOLD02286 ntein 4.0.07 0.28 NOLD02297 Daucosterol_qt 33.59 0.7 NOLD02297 Daucosterol_qt 33.59 0.7 NOLD02297 Daucosterol_qt 32.69 0.52 NOLD02297 coumestrol 32.49 0.34 NOLD01296 coumestrol 32.49 0.34 NOLD01296 coumestrol 32.49 0.34 NOLD01296 Jujubasaponin L.qt 36.69 0.75 NOLD01292 Mauritine D 89.13 0.64 NOLD01454 berberine 36.69 0.75 NOLD004350 Ruvoside_qt 31.11 0.54 NOLD00427 Stepholidine 33.11 0.54 NOLD00273 beta-arotene 37.18 0.9 | MOL004624 | Longikaurin A | 47.72214984 | 0.53015 |
| MOLD02776 Barcain 40.12.50096 0.75.46 MOLD002215 EUPATIN 50.8 0.41 MOLD002281 Toralactone 46.46 0.24 MOLD022081 Toralactone 46.46 0.24 MOL002207 Daucosterol_qt 35.89 0.77 MOL012921 Stepharine 31.55 0.33 MOL012926 Coursectorl_qt 32.49 0.44 MOL012926 Mauritine D 36.99 0.63 MOL012920 Mauritine D 36.86 0.78 MOL00211 Mairin 55.38 0.78 MOL000211 Mairin 55.38 0.78 MOL00042 (+)-catechin 34.43 0.42 MOL000421 Stepholidine 31.11 0.54 MOL000213 Nuciferin 34.31 0.45 MOL000273 Stepholidine 34.43 0.4 MOL000273 C2R)-2-[(35,5R,105,13R,14R,16R,17R)-3,16-dthydrox-44,10,13,14-pentamethyl- 2,3,5,6,12,15,16,17-octahydro1H-cyclopental_alphenanthren-17-yl-6-methylhept-s-encic aci 0.77 | MOL004718 | Pseudo-spinasterol | 42.97936552 | 0.75693 |
| MOL000471 aloe-enodin 88.38 0.24 MOL002255 EUPATIN 50.8 0.41 MOL002281 Toralactone 46.46 0.24 MOL002286 rhein 47.07 0.28 MOL002297 Daucosterol_qt 35.89 0.7 MOL012946 zizyphus saponin l_qt 32.69 0.62 MOL012976 coumestrol 32.49 0.34 MOL012986 Jujubasaponin V_qt 36.99 0.63 MOL012986 Jujubasaponin V_qt 36.99 0.63 MOL001297 Mauritine D 89.13 0.45 MOL001292 Mauritine D 89.13 0.45 MOL001430 Ruvoside_qt 36.12 0.76 MOL00430 Ruvoside qt 36.12 0.76 MOL00430 Ruvoside qt 31.1 0.54 MOL000727 Stepholidine 33.1 0.54 MOL000727 beta-carotene 37.8 0.58 MOL000727 beta-carotene 38.71 0.84 | MOL002776 | Baicalin | 40.12360996 | 0.75264 |
| MCI0002255 EUPA IN 50.8 0.41 MCI000256 -(catechin 46.66 0.24 MCI002268 rhein 47.07 0.28 MCI002277 Daucosterol_gt 35.89 0.7 MCI012921 stepharine 31.55 0.33 MCI012946 2izyphus saponin l_qt 32.49 0.34 MCI012952 Mauritine D 89.13 0.45 MCI012929 Mauritine D 89.13 0.45 MCI001529 Mauritine D 89.13 0.24 MCI001522 (S)-Coclaurine 42.35 0.24 MCI000152 (S)-Coclaurine 36.12 0.78 MCI000211 Mairin 55.84 0.78 MCI000277 Fumarine 59.6 0.83 MCI000277 Fumarine 59.6 0.83 MCI000278 Fumarine 59.6 0.77 MCI000277 Fumarine 59.6 0.79 MCI000273 C28,51,318,148,168,178,-316-dihydroxy-4,41,01,31,4-pentamethyl- 0.75 <td>MOL000471</td> <td>aloe-emodin</td> <td>83.38</td> <td>0.24</td> | MOL000471 | aloe-emodin | 83.38 | 0.24 |
| MOL000096 (-)-catechin 49.68 0.24 MOL002281 Toralactone 46.46 0.24 MOL002285 rhein 47.07 0.28 MOL01297 Daucosterol_qt 35.89 0.7 MOL012921 stepharine 31.55 0.33 MOL012976 coumestrol 32.49 0.34 MOL012986 Jujubasaponin V_qt 36.89 0.63 MOL012976 Coumestrol 89.13 0.45 MOL001292 Mauritine D 89.13 0.45 MOL001522 (S)-Coclaurine 42.35 0.24 MOL00452 (+)-catechin 55.38 0.78 MOL004350 Ruvoside_qt 31.11 0.54 MOL00432 (+)-catechin 34.32 0.42 MOL000427 Stepholidine 33.11 0.54 MOL000273 beta-carotene 37.18 0.58 MOL000274 Fumarine 59.26 0.83 MOL000275 trametenolic acid 38.71 0.8 </td <td>MOL002235</td> <td>EUPATIN</td> <td>50.8</td> <td>0.41</td> | MOL002235 | EUPATIN | 50.8 | 0.41 |
| M01002281 Toralactone 46.46 0.24 M01002285 rhein 47.07 0.28 M01002297 Daucosterol_qt 35.89 0.7 M01012921 stepharine 31.55 0.33 M01012926 Ztepharine 32.69 0.62 M01012976 cournestrol 32.49 0.43 M01012986 Jujubasaponin V_qt 36.99 0.63 M01001292 Mauritine D 89.13 0.45 M01000152 (5)-Coclaurine 42.35 0.24 M01000211 Mairin 55.38 0.78 M01000273 Ruvoside_qt 36.12 0.76 M010007213 Nuciferin 34.43 0.4 M01000773 Furmarine 59.26 0.83 M01000275 Caryl-2-f(35.5R,105,13R,14R,16R,17R)-3,16-dihydroxy-4,4,10,13,14-pentamethyl- 0.93 0.81 M01000275 Caryl-2-f(35.5R,105,13R,14R,16R,17R)-3,16-dihydroxy-4,4,10,13,14-pentamethyl- 0.36 0.77 M01000273 Caryl-14-cycopentalalphenanthren-17-yl-6-methylhept-5-enoic acid | MOL000096 | (-)-catechin | 49.68 | 0.24 |
| M0L002268 rhein 47.07 0.28 M0L002297 Daucosterol_qt 35.89 0.7 M0L012946 zizyphus saponin l_qt 32.69 0.62 M0L012976 coumestrol 32.49 0.34 M0L012986 Jujubasaponin V_qt 36.99 0.63 M0L012992 Mauritine D 89.13 0.45 M0L001522 (S)-Coclaurine 42.35 0.24 M0L002011 Mairin 55.38 0.78 M0L00452 (+)-catechin 36.12 0.76 M0L000452 (+)-catechin 36.13 0.24 M0L000627 Stepholidine 33.11 0.54 M0L000773 beta-carotene 37.18 0.58 M0L000273 (2R)-2-[(35,5R,105,13R,14R,16R,17R)-3,16-dihydroxy-4,4,10,13,14-pentamethyl- 2,3,5,5,6,12,15,16,17-octahydro-1H-cyclopenta[a]phenathren-17-yl]-6-methylhept-5-enoic acid 38.71 0.88 M0L000273 (2R)-2-[(35,5R,105,13R,14R,16R,17R)-3,16-dihydroxy-4,4,10,13,14-pentamethyl- 2,3,5,5,6,12,15,16,17-octahydro-1H-cyclopenta[a]phenathren-17-yl]-6-methylhept-5-enoic acid 38.71 0.8 M0L000275 | MOL002281 | Toralactone | 46.46 | 0.24 |
| M0L002297 Daucosterol_qt 35.89 0.7 M0L012921 stepharine 31.55 0.33 M0L012976 coumestrol 32.69 0.62 M0L012976 coumestrol 36.99 0.63 M0L012986 Jujubasaponin V_qt 36.99 0.63 M0L012992 Mauritine D 83.89 0.78 M0L001522 (5)-Coclaurine 42.35 0.24 M0L000211 Mairin 55.38 0.78 M0L000522 (+)-catechin 54.83 0.24 M0L000521 Stepholidine 33.11 0.54 M0L000737 Fumarine 59.26 0.83 M0L00273 beta-carotene 37.18 0.58 M0L00273 CR)-2-[(35,5R,105,13R,14R,16R,17R),316-dihydroxy-4,410,13,14-pentamethyl- 30.93 0.81 M0L000273 Cerevisterol 36.91 0.75 M0L000273 Cerevisterol 37.96 0.77 M0L000273 Cerevisterol 36.91 0.75 M0L000273 ergosta- | MOL002268 | rhein | 47.07 | 0.28 |
| M01012921 stepharine 31.55 0.33 M01012946 zizyphus saponin Lqt 32.69 0.62 M01012976 cournestrol 32.49 0.34 M01012986 Jujubasaponin V_qt 36.69 0.63 M01001592 Mauritine D 89.13 0.45 M01001522 (S)-Coclaurine 42.35 0.24 M01001522 (S)-Coclaurine 43.61 0.76 M01000452 (+)-catechin 55.38 0.78 M010004350 Ruvoside_qt 36.12 0.76 M01000273 Stepholidine 33.11 0.54 M01000273 beta-carotene 37.18 0.58 M01000273 beta-carotene 37.18 0.58 M01000275 trametenolic acid 38.71 0.81 M01000275 trametenolic acid 36.91 0.75 M01000275 trametenolic acid 36.91 0.75 M01000275 trametenolic acid 36.91 0.75 M01000273 ergostar 7.22-cien-sbeta | MOL002297 | Daucosterol_qt | 35.89 | 0.7 |
| M0L012946 zizyphus saponin Lqt 32.69 0.62 M0L012976 coumestrol 32.49 0.34 M0L012986 Jujubasaponin V_qt 36.99 0.63 M0L012992 Mauritine D 89.13 0.45 M0L001521 (S)-Coclaurine 42.35 0.24 M0L000152 (S)-Coclaurine 42.35 0.24 M0L000211 Mairin 55.38 0.78 M0L000492 (+)-catechin 54.83 0.24 M0L000527 Stepholidine 33.11 0.54 M0L000773 Nuciferin 34.43 0.44 M0L000773 beta-carotene 37.18 0.58 M0L000275 fumarine 59.26 0.83 M0L000773 beta-carotene 37.18 0.58 M0L000275 trametenolic acid 38.71 0.75 M0L000275 trametenolic acid 38.71 0.81 M0L000275 trametenolic acid 36.91 0.75 M0L000282 ergosta-7,22E-dien-3beta-ol 36.91 0.72 M0L000275 trametenolic acid 36.91 0.75 M0L000276 trametenolic acid 36.91 0.75 M0L000275 strofinin 5.21 0. | MOL012921 | stepharine | 31.55 | 0.33 |
| M0L012976 coumestrol 32.49 0.34 M0L012986 Jujubasaponin V_qt 36.99 0.63 M0L012992 Mauritine D 88.13 0.45 M0L001522 (S)-Coclaurine 42.35 0.24 M0L00455 Molto01522 (S)-Coclaurine 42.35 0.24 M0L00450 Musoide_qt 36.12 0.76 M0L00452 Ruvoside_qt 36.12 0.76 M0L000627 Stepholidine 31.11 0.54 M0L000737 Fumarine 52.6 0.83 M0L000273 beta-carotene 37.18 0.58 M0L000273 beta-carotene 37.18 0.58 M0L000275 trametenolic acid 38.71 0.75 M0L000275 trametenolic acid 38.71 0.72 M0L000275 ergosta-7,22E-dien-3beta-ol 36.91 0.72 M0L000275 ergosta-7,22E-dien-3beta-ol 36.91 0.72 M0L000275 ergosta-7,22E-dien-3beta-ol 36.91 0.72 M0L000 | MOL012946 | zizyphus saponin I_qt | 32.69 | 0.62 |
| M0L012986 Jujubasaponin V_qt 36.99 0.63 M0L012992 Mauritine D 89.13 0.45 M0L001522 (S)-Coclaurine 42.35 0.24 M0L000211 Mairitine D 42.35 0.24 M0L000452 (S)-Coclaurine 42.35 0.78 M0L0004350 Ruvoside_qt 36.12 0.76 M0L000492 (+)-catechin 54.83 0.24 M0L0007713 Nuciferin 34.43 0.4 M0L0007713 Nuciferin 34.43 0.4 M0L000773 beta-carotene 37.18 0.58 M0L000773 2,3,5,6,12,15,16,17-octahydro-1H-cyclopenta[a]phenanthren-17-y]-6-methylhept-5-enoic acid 38.71 0.8 M0L000279 Cerevisterol 37.96 0.77 M0L000273 Caterosterol 36.91 0.75 M0L000273 Cerevisterol 37.96 0.77 M0L000273 Cerevisterol 36.91 0.75 M0L000273 Ergosterol peroxide 40.36 0.81 | MOL012976 | coumestrol | 32.49 | 0.34 |
| MDI012992 Mauritine D 89.13 0.45 MOL001454 berberine 36.86 0.78 MOL001522 (5)-Coclaurine 42.35 0.24 MOL000211 Mairin 55.38 0.78 MOL000450 Ruvoside_qt 36.12 0.76 MOL000492 (+)-catechin 54.83 0.24 MOL000627 Stepholidine 33.11 0.54 MOL000713 Nuciferin 34.43 0.4 MOL0002773 beta-carotene 59.26 0.83 MOL0002773 beta-carotene 36.91 0.75 MOL000275 (2R)-2-[(35,5R,105,137,14R,16R,17R)-3,16-41/motry-4,4,10,13,14-pentamethyl- 30.93 0.81 MOL000279 Cerevisterol 36.91 0.75 MOL000279 Cerevisterol 35.1 0.72 MOL000279 Cerevisterol 35.1 0.72 MOL000270 ergosterol peroxide 40.36 0.81 MOL000273 ergosterol peroxide 40.36 0.24 MOL000359 | MOL012986 | Jujubasaponin V_qt | 36.99 | 0.63 |
| MOL001454 berberine 36.86 0.78 MOL001522 (S)-Coclaurine 42.35 0.24 MOL000330 Ruvoside_qt 36.12 0.76 MOL000430 Ruvoside_qt 36.12 0.76 MOL000492 (+)-catechin 54.83 0.24 MOL000527 Stepholidine 33.11 0.54 MOL000731 Nuciferin 34.43 0.4 MOL0002773 beta-carotene 59.26 0.83 MOL000273 beta-carotene 36.91 0.75 MOL000273 (2R)-2-[(35,5R,105,13R,14R,15R,17N)-3,16-dihydroxy-4,4,10,13,14-pentamethyl- 2,3,5,6,12,15,16,17-octahydro-1H-cyclopenta[a]phenanthren-17-y]-6-methylhept-5-enoic acid 30.93 0.81 MOL000275 trametenolic acid 36.91 0.75 MOL000279 Cerevisterol 37.96 0.77 MOL000283 ergosta-7,22E-dien-3beta-ol 43.51 0.78 MOL0004576 taxifolin 57.84 0.27 MOL00073 ent-Ergosterol peroxide 44.03 0.81 MOL0004576 <t< td=""><td>MOL012992</td><td>Mauritine D</td><td>89.13</td><td>0.45</td></t<> | MOL012992 | Mauritine D | 89.13 | 0.45 |
| MOL001522 (\$)-Coclaurine 42.35 0.24 MOL000211 Mairin 55.38 0.78 MOL004350 Ruvoside_qt 36.12 0.76 MOL000627 Stepholidine 33.11 0.54 MOL007213 Nuciferin 34.43 0.4 MOL000277 Eumarine 50.26 0.83 MOL000273 beta-carotene 37.18 0.58 MOL000273 beta-carotene 36.91 0.75 MOL000275 trametenolic acid 38.71 0.81 MOL000275 trametenolic acid 38.71 0.73 MOL000275 cerevisterol 37.96 0.77 MOL000275 trametenolic acid 38.71 0.78 MOL000275 trametenolic acid 38.71 0.72 MOL000275 trametenolic acid 38.71 0.72 MOL000276 cerevisterol 37.96 0.77 MOL000275 trametenolic acid 38.71 0.78 MOL000282 ergosta-7,22E-dien-3beta-ol | MOL001454 | berberine | 36.86 | 0.78 |
| MOL000211 Mairin 55.38 0.78 MOL000430 Ruvoside_qt 36.12 0.76 MOL000492 (+)-catechin 54.83 0.24 MOL000273 Stepholidine 33.11 0.54 MOL000273 Nuciferin 34.43 0.4 MOL000273 beta-carotene 37.18 0.58 MOL000273 beta-carotene 30.93 0.81 MOL000273 (2R)-2-[(35,5R,105,13R,14R,15R,17R)-3,16-dihydroxy-4,4,10,13,14-pentamethyl- 2,3,5,6,12,15,16,17-octahydro-1H-cyclopenta[a]phenanthren-17-yl]-6-methylhept-5-enoic acid 38.71 0.81 MOL000275 trametenolic acid 38.71 0.72 MOL000282 ergosta-7,22E-dien-3beta-ol 43.51 0.72 MOL000283 Ergosterol peroxide 40.36 0.81 MOL00073 ergosta-7,22E-dien-3beta-ol 43.51 0.72 MOL000282 ergosta-7,22E-dien-3beta-ol 43.51 0.75 MOL000283 Ergosterol peroxide 40.36 0.24 MOL00073 ergosta-7,22E-dien-3beta-ol 43.51 0.75 <t< td=""><td>MOL001522</td><td>(S)-Coclaurine</td><td>42.35</td><td>0.24</td></t<> | MOL001522 | (S)-Coclaurine | 42.35 | 0.24 |
| M0L004350 Ruvoside_qt 36.12 0.76 M0L000492 (+)-catechin 54.83 0.24 M0L00067 Stepholidine 33.11 0.54 M0L000731 Nuciferin 34.43 0.4 M0L000787 Fumarine 59.26 0.83 M0L00273 beta-carotene 37.18 0.58 M0L000273 (2R)-2-[(35,5R,105,13R,14R,16R,17R)-3,16-dihydroxy-4,4,10,13,14-pentamethyl- 30.93 0.81 M0L000273 (2R)-2-[(35,5R,105,13R,14R,16R,17R)-3,16-dihydroxy-4,4,10,13,14-pentamethyl- 30.93 0.81 M0L000279 Cerevisterol 38.71 0.8 0.77 M0L000279 Cerevisterol 37.6 0.77 M0L00028 ergosta-7,22E-dien-3beta-ol 43.51 0.72 M0L00028 ergostar-7,22E-dien-3beta-ol 43.51 0.72 M0L000276 caxifolin 57.84 0.24 M0L00035 sitosterol 36.91 0.75 M0L000173 ent-Epicatechin 48.96 0.24 M0L00173 oroxyli a | MOL000211 | Mairin | 55.38 | 0.78 |
| MOL000492 (+)-catechin 54.83 0.24 MOL000677 Stepholidine 33.11 0.54 MOL007213 Nuciferin 34.43 0.4 MOL000787 Fumarine 59.26 0.83 MOL000276 beta-carotene 37.18 0.58 MOL000276 hederagenin 36.91 0.75 MOL000273 (2R)-2-[(35,5R,105,13R,14R,16R,17R)-3,16-dihydroxy-4,4,10,13,14-pentamethyl- 2,3,5,6,12,15,16,17-octahydro-1H-cyclopenta[a]phenanthren-17-yl]-6-methylhept-5-enoic acid 38.71 0.8 MOL000279 Cerevisterol 37.96 0.77 MOL000282 ergosta-7,22E-dien-3beta-ol 43.51 0.72 MOL000283 Ergosterol peroxide 40.36 0.81 MOL000359 sitosterol 36.91 0.75 MOL00073 ent-Epicatechin 48.96 0.24 MOL00073 ent-Epicatechin 48.96 0.24 MOL00073 oroxylin a 30.68 0.23 MOL00073 acacetin 34.97 0.24 MOL00173 oroxylin a | MOL004350 | Ruvoside_qt | 36.12 | 0.76 |
| MOL000627 Stepholidine 33.11 0.54 MOL007213 Nuciferin 34.43 0.4 MOL000787 Fumarine 59.26 0.83 MOL0002773 beta-carotene 37.18 0.58 MOL000273 (2R)-2-[(3S,5R,10S,13R,14R,16R,17R)-3,16-dihydroxy-4,4,10,13,14-pentamethyl- 2,3,5,6,12,15,16,17-octahydro-1H-cyclopenta]a]phenanthren-17-yl]-6-methylhept-5-enoic acid 38.71 0.81 MOL000279 Cerevisterol 37.96 0.77 MOL000279 Cerevisterol 37.96 0.77 MOL000279 Cerevisterol 37.96 0.77 MOL000283 ergosta-7,22E-dien-3beta-ol 43.51 0.72 MOL000276 cerevisterol 36.91 0.75 MOL000283 ergosta-7,22E-dien-3beta-ol 43.51 0.72 MOL000359 sitosterol peroxide 40.36 0.81 MOL00073 ent-Epicatechin 48.96 0.24 MOL00073 ent-Epicatechin 30.68 0.23 MOL000173 wogonin 30.68 0.23 MOL00173 < | MOL000492 | (+)-catechin | 54.83 | 0.24 |
| MOL007213 Nuciferin 34.43 0.4 MOL000787 Fumarine 59.26 0.83 MOL000273 beta-carotene 37.18 0.58 MOL00029 hederagenin 36.91 0.75 MOL000273 (2R)-2-[(35,5R,105,13R,14R,16R,17R)-3,16-dihydroxy-4,4,10,13,14-pentamethyl- 2,3,5,6,12,15,16,17-octahydro-1H-cyclopenta[a]phenanthren-17-yl]-6-methylhept-5-enoic acid 30.93 0.81 MOL000275 trametenolic acid 38.71 0.83 MOL000276 cerevisterol 37.96 0.77 MOL000282 ergosta-7,22E-dien-3beta-ol 43.51 0.72 MOL000283 Ergosterol peroxide 40.36 0.81 MOL000359 sitosterol 36.91 0.75 MOL000359 ent-Ejcatechin 48.96 0.24 MOL00073 ent-Ejcatechin 48.96 0.24 MOL00073 ent-Ejcatechin 48.96 0.24 MOL00073 acacetin 34.97 0.24 MOL00073 acacetin 34.97 0.24 MOL00282 (2R)-7-hydroxy-5- | MOL000627 | Stepholidine | 33.11 | 0.54 |
| MOL000787 Fumarine 59.26 0.83 MOL002773 beta-carotene 37.18 0.58 MOL000296 hederagenin 36.91 0.75 MOL000273 (2R)-2-[(35,5R,105,13R,14R,15R,17R)-3,16-dihydroxy-4,4,10,13,14-pentamethyl- 2,3,5,6,12,15,16,17-octahydro-1H-cyclopenta[a]phenanthren-17-yl]-6-methylhept-5-enoic acid 38.71 0.81 MOL000275 trametenolic acid 38.71 0.81 MOL000282 ergosta-7,22E-dien-3beta-ol 43.51 0.72 MOL000283 Ergosterol peroxide 40.36 0.81 MOL000284 ergosta-7,22E-dien-3beta-ol 35.91 0.75 MOL000285 Ergosterol peroxide 40.36 0.81 MOL000276 taxifolin 57.84 0.27 MOL000359 sitosterol 36.91 0.75 MOL0001736 (-1-taxifolin 60.51 0.27 MOL000173 acacetin 34.97 0.24 MOL001736 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL002928 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 | MOL007213 | Nuciferin | 34.43 | 0.4 |
| MOL002773 beta-carotene 37.18 0.58 MOL000296 hederagenin 36.91 0.75 MOL000273 (2R)-2-[(35,5R,105,13R,14R,16R,17R)-3,16-dihydroxy-4,4,10,13,14-pentamethyl- 2,3,5,6,12,15,16,17-octahydro-1H-cyclopenta[a]phenanthren-17-yl]-6-methylhept-5-enoic acid 30.93 0.81 MOL000275 trametenolic acid 38.71 0.8 MOL000282 ergosta-7,22E-dien-3beta-ol 43.51 0.72 MOL000283 Ergosterol peroxide 40.36 0.81 MOL000276 taxifolin 57.84 0.27 MOL000283 Ergosterol peroxide 40.36 0.81 MOL000359 sitosterol 60.51 0.27 MOL000173 ent-Epicatechin 48.96 0.24 MOL000173 wogonin 30.68 0.23 MOL000173 acacetin 44.97 0.27 MOL000284 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL000293 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL002934 MEOBAICALEIN 104.34 0.44< | MOL000787 | Fumarine | 59.26 | 0.83 |
| MOL000296 hederagenin 36.91 0.75 MOL000273 (2R)-2-[(3S,5R,10S,13R,14R,16R,17R)-3,16-dihydroxy-4,4,10,13,14-pentamethyl- 2,3,5,6,12,15,16,17-octahydro-1H-cyclopenta[a]phenanthren-17-yl]-6-methylhept-5-enoic acid 30.93 0.81 MOL000275 trametenolic acid 38.71 0.87 MOL000279 Cerevisterol 37.96 0.77 MOL000282 ergosta-7,22E-dien-3beta-ol 43.51 0.72 MOL000359 Ergosterol peroxide 40.36 0.81 MOL00073 ent-Epicatechin 36.91 0.75 MOL00073 ent-Epicatechin 48.96 0.24 MOL00073 ent-Epicatechin 48.96 0.24 MOL000173 wogonin 30.68 0.23 MOL000173 wogonin 30.68 0.23 MOL000282 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL000292 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL002934 NEOBAICALEIN 104.34 0.44 MOL002934 NEOBAICALEIN 37.94 0.37< | MOL002773 | beta-carotene | 37.18 | 0.58 |
| MOL000273 (2R)-2-[(3S,5R,10S,13R,14R,16R,17R)-3,16-dihydroxy-4,4,10,13,14-pentamethyl- 2,3,5,6,12,15,16,17-octahydro-1H-cyclopenta[a]phenanthren-17-yl]-6-methylhept-5-enoic acid 30.93 0.81 MOL000275 trametenolic acid 38.71 0.8 MOL000279 Cerevisterol 37.96 0.77 MOL000282 ergosta-7,22E-dien-3beta-ol 43.51 0.72 MOL000283 Ergosterol peroxide 40.36 0.81 MOL000359 sitosterol 36.91 0.75 MOL0001736 (-)-taxifolin 57.84 0.27 MOL0001736 (-)-taxifolin 60.51 0.27 MOL000173 wogonin 30.68 0.23 MOL000173 oroxylin a 0.24 0.24 MOL0012928 oroxylin a 0.23 0.24 MOL0022928 oroxylin a 41.37 0.23 MOL0022934 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL0022934 Moslosooflavone 44.09 0.25 MOL0022934 Moslosoflavone 44.09 0.37 | MOL000296 | hederagenin | 36.91 | 0.75 |
| MOL000273 2,3,5,6,12,15,16,17-octahydro-1H-cyclopenta[a]phenanthren-17-yl]-6-methylhept-5-enoic acid 30.93 0.81 MOL000275 trametenolic acid 38.71 0.8 MOL000279 Cerewisterol 37.96 0.77 MOL000282 ergosta-7,22E-dien-3beta-ol 43.51 0.72 MOL000283 Ergosterol peroxide 40.36 0.81 MOL000359 sitosterol 36.91 0.75 MOL000073 ent-Epicatechin 48.96 0.24 MOL0001736 (-)-taxifolin 60.51 0.27 MOL0002928 oroxylin a 31.97 0.24 MOL002928 oroxylin a 41.37 0.23 MOL002928 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL002924 Moslosooflavone 44.09 0.25 MOL002934 NEOBAICALEIN 104.34 0.44 MOL0022927 Skullcapflavone II 69.51 0.44 MOL00252 5,2'-Dihydroxy-6,7,8-trimethoxyflavone 31.71 0.35 | MOI 000272 | (2R)-2-[(3S,5R,10S,13R,14R,16R,17R)-3,16-dihydroxy-4,4,10,13,14-pentamethyl- | 20.02 | 0.01 |
| MOL000275 trametenolic acid 38.71 0.8 MOL000279 Cerevisterol 37.96 0.77 MOL000282 ergosta-7,22E-dien-3beta-ol 43.51 0.72 MOL000283 Ergosterol peroxide 40.36 0.81 MOL004576 taxifolin 57.84 0.27 MOL000359 sitosterol 36.91 0.75 MOL00073 ent-Epicatechin 48.96 0.24 MOL001736 (-)-taxifolin 60.51 0.27 MOL00173 wogonin 30.68 0.23 MOL00228 oroxylin a 34.97 0.24 MOL00228 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL00228 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL0022934 NEOBAICALEIN 104.34 0.44 MOL002934 NEOBAICALEIN 104.34 0.44 MOL002927 Skullcapflavone II 69.51 0.44 MOL00552 5,2'-Dihydroxy-6,7,8-trimethoxyflavone 31.71 0.35 < | 1010100275 | 2,3,5,6,12,15,16,17-octahydro-1H-cyclopenta[a]phenanthren-17-yl]-6-methylhept-5-enoic acid | 50.95 | 0.81 |
| MOL000279 Cerevisterol 37.96 0.77 MOL000282 ergosta-7,22E-dien-3beta-ol 43.51 0.72 MOL000283 Ergosterol peroxide 40.36 0.81 MOL0004576 taxifolin 57.84 0.27 MOL000359 sitosterol 36.91 0.75 MOL00073 ent-Epicatechin 48.96 0.24 MOL0001736 (-)-taxifolin 60.51 0.27 MOL000173 wogonin 30.68 0.23 MOL00028 oroxylin a 41.37 0.24 MOL002928 oroxylin a 41.37 0.23 MOL002934 Moslosooflavone 44.09 0.25 MOL002934 NEOBAICALEIN 104.34 0.44 MOL002927 Skullcapflavone II 69.51 0.44 MOL000552 5,2'-Dihydroxy-6,7,8-trimethoxyflavone 31.71 0.35 | MOL000275 | trametenolic acid | 38.71 | 0.8 |
| MOL000282 ergosta-7,22E-dien-3beta-ol 43.51 0.72 MOL000283 Ergosterol peroxide 40.36 0.81 MOL004576 taxifolin 57.84 0.27 MOL000359 sitosterol 36.91 0.75 MOL00073 ent-Epicatechin 48.96 0.24 MOL001736 (-)-taxifolin 60.51 0.27 MOL000173 wogonin 30.68 0.23 MOL001689 acacetin 34.97 0.24 MOL00228 0roxylin a 41.37 0.23 MOL00228 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL002934 NEOBAICALEIN 104.34 0.44 MOL002927 Skullcapflavone II 69.51 0.44 MOL000552 5,2'-Dihydroxy-6,7,8-trimethoxyflavone 31.71 0.35 | MOL000279 | Cerevisterol | 37.96 | 0.77 |
| MOL000283 Ergosterol peroxide 40.36 0.81 MOL004576 taxifolin 57.84 0.27 MOL000359 sitosterol 36.91 0.75 MOL00073 ent-Epicatechin 48.96 0.24 MOL0001736 (-)-taxifolin 60.51 0.27 MOL000173 wogonin 30.68 0.23 MOL001689 acacetin 34.97 0.24 MOL00228 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL00228 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL00228 MOslosooflavone 44.09 0.25 MOL002934 NEOBAICALEIN 104.34 0.44 MOL002927 Skullcapflavone II 69.51 0.44 MOL000552 5,2'-Dihydroxy-6,7,8-trimethoxyflavone 31.71 0.35 | MOL000282 | ergosta-7,22E-dien-3beta-ol | 43.51 | 0.72 |
| MOL004576 taxifolin 57.84 0.27 MOL000359 sitosterol 36.91 0.75 MOL000073 ent-Epicatechin 48.96 0.24 MOL001736 (-)-taxifolin 60.51 0.27 MOL000173 wogonin 30.68 0.23 MOL001689 acacetin 34.97 0.24 MOL002928 oroxylin a 41.37 0.23 MOL00228 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL002934 MEOBAICALEIN 104.34 0.44 MOL002927 Skullcapflavone II 69.51 0.44 MOL000552 5,2'-Dihydroxy-6,7,8-trimethoxyflavone 31.71 0.35 | MOL000283 | Ergosterol peroxide | 40.36 | 0.81 |
| MOL000359 sitosterol 36.91 0.75 MOL000073 ent-Epicatechin 48.96 0.24 MOL001736 (-)-taxifolin 60.51 0.27 MOL000173 wogonin 30.68 0.23 MOL0001689 acacetin 34.97 0.24 MOL002928 oroxylin a 41.37 0.23 MOL000228 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL002934 Moslosooflavone 44.09 0.25 MOL002934 NEOBAICALEIN 104.34 0.44 MOL002927 Skullcapflavone II 69.51 0.44 MOL000552 5,2'-Dihydroxy-6,7,8-trimethoxyflavone 31.71 0.35 | MOL004576 | taxifolin | 57.84 | 0.27 |
| MOL000073 ent-Epicatechin 48.96 0.24 MOL001736 (-)-taxifolin 60.51 0.27 MOL000173 wogonin 30.68 0.23 MOL001689 acacetin 34.97 0.24 MOL002928 oroxylin a 41.37 0.23 MOL000228 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL008206 Moslosooflavone 44.09 0.25 MOL002934 NEOBAICALEIN 104.34 0.44 MOL002927 Skullcapflavone II 69.51 0.44 MOL000552 5,2'-Dihydroxy-6,7,8-trimethoxyflavone 31.71 0.35 | MOL000359 | sitosterol | 36.91 | 0.75 |
| MOL001736 (-)-taxifolin 60.51 0.27 MOL000173 wogonin 30.68 0.23 MOL001689 acacetin 34.97 0.24 MOL002928 oroxylin a 41.37 0.23 MOL000228 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL008206 Moslosooflavone 44.09 0.25 MOL002934 NEOBAICALEIN 104.34 0.44 MOL002927 Skullcapflavone II 69.51 0.44 MOL000552 5,2'-Dihydroxy-6,7,8-trimethoxyflavone 31.71 0.35 | MOL000073 | ent-Epicatechin | 48.96 | 0.24 |
| MOL000173 wogonin 30.68 0.23 MOL001689 acacetin 34.97 0.24 MOL002928 oroxylin a 41.37 0.23 MOL000228 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL008206 Moslosooflavone 44.09 0.25 MOL002934 NEOBAICALEIN 104.34 0.44 MOL012266 rivularin 37.94 0.37 MOL002927 Skullcapflavone II 69.51 0.44 MOL000552 5,2'-Dihydroxy-6,7,8-trimethoxyflavone 31.71 0.35 | MOL001736 | (-)-taxifolin | 60.51 | 0.27 |
| MOL001689 acacetin 34.97 0.24 MOL002928 oroxylin a 41.37 0.23 MOL000228 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL008206 Moslosooflavone 44.09 0.25 MOL002934 NEOBAICALEIN 104.34 0.44 MOL012266 rivularin 37.94 0.37 MOL002927 Skullcapflavone II 69.51 0.44 MOL000552 5,2'-Dihydroxy-6,7,8-trimethoxyflavone 31.71 0.35 | MOL000173 | wogonin | 30.68 | 0.23 |
| MOL002928 oroxylin a 41.37 0.23 MOL000228 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL008206 Moslosooflavone 44.09 0.25 MOL002934 NEOBAICALEIN 104.34 0.44 MOL012266 rivularin 37.94 0.37 MOL002927 Skullcapflavone II 69.51 0.44 MOL000552 5,2'-Dihydroxy-6,7,8-trimethoxyflavone 31.71 0.35 | MOL001689 | acacetin | 34.97 | 0.24 |
| MOL000228 (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one 55.23 0.2 MOL008206 Moslosooflavone 44.09 0.25 MOL002934 NEOBAICALEIN 104.34 0.44 MOL012266 rivularin 37.94 0.37 MOL002927 Skullcapflavone II 69.51 0.44 MOL000552 5,2'-Dihydroxy-6,7,8-trimethoxyflavone 31.71 0.35 | MOL002928 | oroxylin a | 41.37 | 0.23 |
| MOL008206 Moslosooflavone 44.09 0.25 MOL002934 NEOBAICALEIN 104.34 0.44 MOL012266 rivularin 37.94 0.37 MOL002927 Skullcapflavone II 69.51 0.44 MOL000552 5,2'-Dihydroxy-6,7,8-trimethoxyflavone 31.71 0.35 | MOL000228 | (2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one | 55.23 | 0.2 |
| MOL002934 NEOBAICALEIN 104.34 0.44 MOL012266 rivularin 37.94 0.37 MOL002927 Skullcapflavone II 69.51 0.44 MOL000552 5,2'-Dihydroxy-6,7,8-trimethoxyflavone 31.71 0.35 | MOL008206 | Moslosooflavone | 44.09 | 0.25 |
| MOL012266 rivularin 37.94 0.37 MOL002927 Skullcapflavone II 69.51 0.44 MOL000552 5,2'-Dihydroxy-6,7,8-trimethoxyflavone 31.71 0.35 | MOL002934 | NEOBAICALEIN | 104.34 | 0.44 |
| MOL002927 Skullcapflavone II 69.51 0.44 MOL000552 5,2'-Dihydroxy-6,7,8-trimethoxyflavone 31.71 0.35 | MOL012266 | rivularin | 37.94 | 0.37 |
| MOL000552 5,2'-Dihydroxy-6,7,8-trimethoxyflavone 31.71 0.35 | MOL002927 | Skullcapflavone II | 69.51 | 0.44 |
| | MOL000552 | 5,2'-Dihydroxy-6,7,8-trimethoxyflavone | 31.71 | 0.35 |

| MOL002015 | Calvinania | 40.07 | 0.22 |
|-----------|--|-------|------|
| MOL002915 | Savigenin | 49.07 | 0.33 |
| MOL002933 | 5,7,4'-Trihydroxy-8-methoxyflavone | 36.56 | 0.27 |
| MOL002917 | 5,2',6'-Trihydroxy-7,8-dimethoxyflavone | 45.05 | 0.33 |
| MOL002932 | Panicolin | 76.26 | 0.29 |
| MOL002897 | epiberberine | 43.09 | 0.78 |
| MOL002937 | DIHYDROOROXYLIN | 66.06 | 0.23 |
| MOL001458 | coptisine | 30.67 | 0.86 |
| MOL002909 | 5,7,2,5-tetrahydroxy-8,6-dimethoxyflavone | 33.82 | 0.45 |
| MOL000525 | Norwogonin | 39.4 | 0.21 |
| MOL002914 | Eriodyctiol (flavanone) | 41.35 | 0.24 |
| MOL002925 | 5,7,2',6'-Tetrahydroxyflavone | 37.01 | 0.24 |
| MOL002879 | Diop | 43.59 | 0.39 |
| MOL012245 | 5,7,4'-trihydroxy-6-methoxyflavanone | 36.63 | 0.27 |
| MOL012246 | 5,7,4'-trihydroxy-8-methoxyflavanone | 74.24 | 0.26 |
| MOL002910 | Carthamidin | 41.15 | 0.24 |
| MOL002913 | Dihydrobaicalin_qt | 40.04 | 0.21 |
| MOL001490 | bis[(2S)-2-ethylhexyl] benzene-1,2-dicarboxylate | 43.59 | 0.35 |
| MOL010415 | 11,13-Eicosadienoic acid, methyl ester | 39.28 | 0.23 |
| | Calcium Phosphate | | |
| | Calcium Carbonate | | |
| | Aluminum | | |
| | Calcium Sulphate | | |
| | Silicon | | |
| MOL003648 | Inermin | 65.83 | 0.54 |
| MOL005344 | ginsenoside rh2 | 36.32 | 0.56 |
| MOL005384 | suchilactone | 57.52 | 0.56 |
| MOL005321 | Frutinone A | 65.9 | 0.34 |
| MOL005308 | Aposiopolamine | 66.65 | 0.22 |
| MOL005356 | Girinimbin | 61.22 | 0.31 |
| MOL005320 | arachidonate | 45.57 | 0.2 |
| MOL005317 | Deoxyharringtonine | 39.27 | 0.81 |
| MOL005318 | Dianthramine | 40.45 | 0.2 |
| MOL005348 | Ginsenoside-Rh4_qt | 31.11 | 0.78 |
| MOL005376 | Panaxadiol | 33.09 | 0.79 |
| MOL005399 | alexandrin_qt | 36.91 | 0.75 |
| MOL006129 | 6-methylgingediacetate2 | 48.73 | 0.32 |
| MOL001771 | poriferast-5-en-3beta-ol | 36.91 | 0.75 |
| MOL008698 | Dihydrocapsaicin | 47.07 | 0.19 |

Notes: DL: Drug-like properties. OB: Oral bioavailability.



Figure 1. Venny diagram of the targets of CLMD and the targets of vertigo with anxiety disorder.



Figure 2. PPI network of the 101 targets of CLMD for the treatment of vertigo with anxiety disorder.

| Uniprot | Gene | Protein | Degree |
|---------|-------|---|--------|
| P31749 | AKT1 | RAC-alpha serine/threonine-protein kinase | 65 |
| P05231 | IL6 | Interleukin-6 | 63 |
| P01375 | TNF | Tumor necrosis factor | 59 |
| P15692 | VEGFA | Vascular endothelial growth factor A | 58 |
| P01584 | IL1B | Interleukin-1 beta | 57 |
| P04637 | TP53 | Cellular tumor antigen p53 | 56 |
| P01100 | FOS | Protein c-Fos | 54 |
| P42574 | CASP3 | Caspase-3 | 54 |
| P01133 | EGF | Pro-epidermal growth factor | 53 |
| P03372 | ESR | Estrogen receptor | 52 |

 Table 2. Core targets of CLMD for treating vertigo with anxiety disorder.

other targets, suggesting their potential significance in the treatment of vertigo with anxiety by CLMD. There were 101 nodes and 1,363 dges, the average node degree was 27, an average local clustering coefficient of 0.64, and *P* < 1.0e-16. The obtained PPI network data were imported into Cytoscape v3.8.2 software and arranged according to the value of degree. The higher the degree value was, the more important it might be in the treatment of vertigo with anxiety with CLMD. The top 10 targets in degree ranking were *AKT1*, *IL6*, *TNF*, *VEGFA*, *IL1B*, *TP53*, *FOS*, *CASP3*, *EGF*, *ESR*. These targets might be the key to treating vertigo and anxiety comorbidity with CLMD (Table 2).

CLMD-compound-target-disease network map

The active ingredients and targets of CLMD were imported into the Cytoscape v3.8.2 to construct the CLMD-compound-target-disease network, which could more intuitively reflect the characteristics of multi-components and multitargets of CLMD in the treatment of vertigo and anxiety comorbidities (Figure 3). The degree values were calculated through the Network Analysis plug-in. The top ingredients were determined as quercetin, beta-sitosterol, stigmasterol, kaempferol, and baicalein. The results indicated that these ingredients might be the key active ingredients for the simultaneous treatment of different diseases in CLMD.

GO functional enrichment analysis



Figure 3. Network of TCM-component-target-disease of CLMD treating vertigo with anxiety. Green: compounds. Red: targets. Yellow: disease. Blue: drug.

The common targets of drugs and diseases were introduced into the Metascape platform for GO functional enrichment analysis. The results showed that these genes were engaged in 440 biological processes (BP), 150 molecular functions (MF), and 113 cellular components (CC). The 10 paths with the highest *P* values for each part were selected (Figure 4). The BP of top 10 paths mainly included cellular responses to organic cyclic compound, inorganic substance, nitrogen compound, and xenobiotic stimulus, *etc.* The top MF mainly included kinase binding, signaling receptor regulator activity, protein homodimerization activity, protein domain specific binding, and heme binding, *etc.* The



Figure 4. GO functional enrichment analysis.



Top 20 KEGG of Enrichment

Figure 5. KEGG pathway enrichment analysis.

| | | Core targets | |
|------------------|-------------|--------------|-------------|
| Ligand molecules | CASP3 (mol) | VEGFA (mol) | STAT3 (mol) |
| quercetin | -7.6 (A) | -7.5 (B) | -7.3 (C) |
| baicalein | -7.5 (D) | -7.3 (E) | -7.5 (F) |
| kaempferol | -7.7 (G) | -7.6 (H) | -7.4 (1) |

Table 3. Core targets of CLMD for treating vertigo with anxiety disorder.



Figure 6. The docking outcomes between the primary target and the active component visualized utilizing PyMol software.

enriched CC evolved dendrite, membrane raft, plasma membrane protein complex, neuronal cell body vesicle lumen, distal axon, and lytic vacuole, *etc*.

KEGG pathway enrichment analysis

A total of 312 KEGG pathways were identified from the Metascape platform. The first 20 pathways were visualized in Figure 5. The KEGG analysis mainly evolved AGE-RAGE signaling pathway in diabetic complications, serotonergic synapse, dopaminergic synapse, cAMP signaling pathway, calcium signaling pathway, *etc*.

Molecular docking

The compounds exhibiting elevated degree values of quercetin, baicalein, and kaempferol in

CLMD were subjected to molecular docking analysis with core targets *CASP3*, *VEGFA*, and *STAT3*, respectively. The molecular docking results were shown in Table 3. Binding energy indicated that the two could bind freely. The lower the binding capacity is, the stronger the affinity between receptor and ligand is, and the possibility of interaction between the two is high. The docking outcomes between the primary target and the active component were visualized utilizing Pymol software (Figure 6).

Discussion

Vertigo with anxiety is one of the most common complaints of clinical patients. At present,

conventional Western medicine treatment uses selective serotonin reuptake inhibitors, which exerts side effects such as nausea, ataxia, and even an increased risk of anxiety and depression [8, 9]. Therefore, it is difficult to achieve satisfactory treatment effects, leading to poor compliance. CLMD is one of the classic TCM formulas for treating vertigo with anxiety. However, the mechanism and target of CLMD in the treatment of vertigo with anxiety have not been clarified, which cannot provide sufficient theoretical support for clinical research and application. This study investigated the mechanism by which CLMD might alleviate vertigo with anxiety disorder based on network pharmacology. A total of 100 active ingredients of CLMD were collected through databases including quercetin, beta-sitosterol, stigmasterol, baicalein, and other key active ingredients. Quercetin has against oxidative stress and neuroinflammation, which is the possible therapeutic choice for neurological disorder [10]. Previous study showed that guercetin could improve HPA axis dysregulation and lower the expression of corticosterone and adrenocorticotropic hormones to achieve therapeutic effect against anxiety disorders [11]. Meanwhile, quercetin could inhibit the apoptosis of nerve cells and play a neuroprotective role, and then improve brain blood flow, reduce the vertigo symptoms [12]. Baicalein, a flavonoid, has shown promising results in treating anxiety [13]. Many studies showed that baicalein improved anxiety by regulating GABA receptor [14, 15]. Kaempferol can regulate the levels of NO and NOS and protect endothelial cells from oxidative damage, playing a role in treating vertigo and headache [16].

PPI network analysis suggested that CLMD exerted therapeutic effects on vertigo with anxiety disorder by regulating 101 targets such as *AKT1, IL6, TNF, VEGFA,* and *CASP3.* KEGG enrichment analysis suggested that mechanism of CLMD for vertigo with anxiety treatment was closely correlated with serotonergic synapse, dopaminergic synapse, cAMP signaling pathway, and calcium signaling pathway. Among them, serotonergic synapse and dopaminergic synapse were directly related to vertigo with anxiety. Prior research has indicated that the coexistence of vertigo and anxiety can be attributed to the existence of neural connections between the vestibular nucleus and the nucleus associated with emotions. These connections facilitate interaction between the two nuclei, mediated by neurotransmitters such as serotonin (5-HT) and dopamine (DA) [17-19]. The molecular docking results showed that CASP3, VEGFA, STAT3 were the core targets in CLMD. Among them, CASP3 is involved in the mechanism of apoptosis [20]. Regulating the expression of CASP3 in vestibular nucleus can effectively improve the vestibular blood supply and alleviate vertigo symptoms [21]. Past studies showed that anxiety disorder was positively correlated with VEGFA, which reduced oxidative stress and inflammatory processes by regulating the TLR4/Myd8/NF-B signaling pathway, thus improving anxiety [22, 23]. Those targets could be well attached to the protein, indicating that the target of CLMD was highly related to the disease gene.

This study verified the multi-pathways and multitargets mechanism of CLMD in the treatment of vertigo with anxiety through the combination of network pharmacology and molecular docking. The results suggested that CLMD might regulate serotonergic synapse and dopaminergic synapse pathways by acting on key targets such as VEGFA, CASP3, and STAT3 through quercetin, kaempferol, and baicalein, thereby improving symptoms of vertigo and anxiety. These findings provided novel insight into the mechanism of the action of CLMD on vertigo with anxiety disorder.

Acknowledgements

This research was supported by Jilin Science and Technology Development Program Project (Grant No. YDZJ202301ZYTS430).

References

- Murdin L, Schilder AG. 2015. Epidemiology of balance symptoms and disorders in the community: A systematic review. Otol Neurotol. 36(3):387-392.
- Peluso ÉT, Quintana MI, Ganança FF. 2016. Anxiety and depressive disorders in elderly with chronic dizziness of vestibular origin. Braz J Otorhinolaryngol. 82(2):209-214.
- Kim SK, Kim YB, Park IS, Hong SJ, Kim H, Hong SM. 2016. Clinical analysis of dizzy patients with high levels of depression and anxiety. J Audiol Otol. 20(3):174-178.
- Liu Y, Ma S , Qu R. 2010. SCLM, total saponins extracted from Chaihu-jia-longgu-muli-tang, reduces chronic mild stressinduced apoptosis in the hippocampus in mice. Pharm Biol. 48(8):840-848.
- Li Z, Qi Y, Liu K, Cao Y, Zhang H, Song C, *et al*. 2023. Clinical application of Chaihu Jia Longgu Muli Decoction based on modern pathophysiology mechanism. Zhongguo Zhong Yao Za Zhi. 48(10):2620-2624.
- Li Z, Qi Y, Liu K, Cao Y, Zhang H, Song C, et al. 2021. Effect of Chaihu-jia-Longgu-Muli decoction on withdrawal symptoms in rats with methamphetamine-induced conditioned place preference. Biosci Rep. 41(8):BSR20211376.
- Wang X, Chen J, Zhang H, Huang Z, Zou Z, Chen Y, et al. 2019. Immediate and persistent antidepressant-like effects of Chaihujia-Longgu-Muli-tang are associated with instantly up-regulated BDNF in the hippocampus of mice. Biosci Rep. 39(1):BSR20181539.
- Hain TC, Uddin M. 2003. Pharmacological treatment of vertigo. CNS Drugs 17(2):85-100.
- Simon NM, Parker SW, Wernick-Robinson M, Oppenheimer JE, Hoge EA, Worthington JJ, *et al.* 2005. Fluoxetine for vestibular dysfunction and anxiety: A prospective pilot study. Psychosomatics. 46(4):334-339.
- Agrawal K, Chakraborty P, Dewanjee S, Arfin S, Das SS, Dey A, et al. 2023. Neuropharmacological interventions of quercetin and its derivatives in neurological and psychological disorders. Neurosci Biobehav Rev. 144:104955.
- Kosari-Nasab M, Shokouhi G, Ghorbanihaghjo A, Mesgari-Abbasi M, Salari AA. 2019. Quercetin mitigates anxiety-like behavior and normalizes hypothalamus-pituitary-adrenal axis function in a mouse model of mild traumatic brain injury. Behav Pharmacol. 30(2 and 3-Spec Issue):282-289.
- Kosari-Nasab M, Shokouhi G, Ghorbanihaghjo A, Mesgari-Abbasi M, Salari AA. 2020. Quercetin protects against cerebral ischemia/reperfusion and oxygen glucose deprivation/reoxygenation neurotoxicity. J Nutr Biochem. 83:108436.
- Ruan L, Guan K, Wang Y, Gu M, Chen Y, Cai L, et al. 2023. Baicalein exerts anxiolytic and antinociceptive effects in a mouse model of posttraumatic stress disorder: Involvement of the serotonergic system and spinal delta-opioid receptors. Prog. Neuropsychopharmacol Biol Psychiatry. 122:110689.
- Awad R, Arnason JT, Trudeau V, Bergeron C, Budzinski JW, Foster BC, et al. 2003. Phytochemical and biological analysis of skullcap (*Scutellaria lateriflora* L.): A medicinal plant with anxiolytic properties. Phytomedicine. 10(8):640-649.
- de Carvalho RS, Duarte FS, de Lima TC. 2011. Involvement of GABAergic non-benzodiazepine sites in the anxiolytic-like and

sedative effects of the flavonoid baicalein in mice. Behav Brain Res. 221(1):75-82.

- Liu M, Fan G, Zhang D, Zhu M, Zhang H. 2021. Study on mechanism of Jiawei Chaiqin Wendan Decoction in treatment of vestibular migraine based on network pharmacology and molecular docking technology. Evid Based Complement Alternat Med. 2021:5528403.
- Staab JP, Ruckenstein MJ, Solomon D, Shepard NT. 2002. Serotonin reuptake inhibitors for dizziness with psychiatric symptoms. Arch Otolaryngol Head Neck Surg. 128(5):554-560.
- Balaban CD, Thayer JF. 2001. Neurological bases for balanceanxiety links. J Anxiety Disord. 15(1-2):53-79.
- Balaban CD. 2002. Neural substrates linking balance control and anxiety. Physiol Behav. 77(4-5):469-475.
- Broughton BR, Reutens DC, Sobey CG. 2009. Apoptotic mechanisms after cerebral ischemia. Stroke. 40(5):e331-e339.
- Dong YS, Xing SL, Zhou HY, Zhang W, Sun W, Fan JM. 2020. Effects of fast-twisting long-retaining acupuncture therapy on apoptosis and expression of related proteins in vestibular nucleus in rats with vertigo induced by posterior circulation ischemia. Zhongguo Zhen Jiu. 40(2):179-184.
- Sundberg I, Rasmusson AJ, Ramklint M, Just D, Ekselius L, Cunningham JL. 2020. Daytime melatonin levels in saliva are associated with inflammatory markers and anxiety disorders. Psychoneuroendocrinology. 112:104514.
- Abdelzaher WY, Mohammed HH, Welson NN, Batiha GE, Baty RS, Abdel-Aziz AM. 2021. Rivaroxaban modulates TLR4/Myd88/NF-Kβ signaling pathway in a dose-dependent manner with suppression of oxidative stress and inflammation in an experimental model of depression. Front Pharmacol. 12:715354.