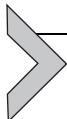Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Understanding the activating mechanism of the immune system against COVID-19 by Traditional Indian Medicine: Network pharmacology approach

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Contents

Abstract

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) transmissions are occurring rapidly; it is raising the alarm around the globe. Though vaccines are currently available, the evolution and mutations in the SARS-CoV-2 threaten available vaccines' significance. The drugs are still undergoing clinical trials, and certain medications are approved for "emergency use" or as an "off-label" drug during the pandemic. These drugs have been effective yet accommodating side effects, which also can be lethal. Complementary and alternative medicine is highly demanded since it embraces a holistic approach. Since ancient times, natural products have been used as drugs to treat various diseases in the medical field and are still widely practiced. Medicinal plants contain many active compounds that serve as the key to an effective drug design. The Kabasura kudineer and Nilavembu kudineer are the two most widely approved formulations to treat COVID-19. However, the mechanism of these formulations is not well known. The proposed study used a network pharmacology approach to understand the immune-boosting mechanism by the Kabasura kudineer, Nilavembu kudineer, and JACOM in treating COVID-19. The plants and phytochemical chemical compounds in the Kabasura kudineer, Nilavembu kudineer, and JACOM were obtained from the literature. The Swiss target prediction algorithm was used to predict the targets for these phytochemical compounds. The common genes for the COVID-19 infection and the drug targets were identified. The gene–gene interaction network was constructed to understand the interactions between these common genes and enrichment analyses to determine the biological process, molecular functions, cellular functions, pathways involved, *etc.* Finally, virtual screening and molecular docking studies were performed to identify the most potential targets and significant phytochemical compounds to treat the COVID-19. The present study identified potential targets as ACE, Cathepsin L, Cathepsin B, Cathepsin K, DPP4, EGFR, HDAC2, IL6, RIPK1, and VEGFA. Similarly, betulinic acid, 5″-(2″″-Hydroxybenzyl) uvarinol, antofine, (S)-1'-methyloctyl caffeate, (Z)-3-phenyl-2-propenal, 7-oxo-10α-cucurbitadienol, and PLX-4720 collectively to be potential treatment agents for COVID-19.

Abbreviations

ACE	angiotensin–converting enzyme
COVID-19	coronavirus disease 2019
CTSB	Cathepsin B
CTSL	Cathepsin L
DPP4	dipeptidyl peptidase–4
EGFR	epidermal growth factor receptor

HDAC2	histone deacetylase 2
IL–6	interleukin 6
PABPC1	poly(A)-binding protein C1
POLA	polymerase I
RIPK1	receptor-interacting serine/threonine-protein kinase 1
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SIGMAR1	Sigma non-opioid intracellular receptor 1
TCM	Traditional Chinese Medicine
TIM	Traditional Indian Medicine
VEGFA	vascular endothelial growth factor A
WHO	World Health Organization

1. Introduction

SARS-CoV-2 is a genetic variant of coronavirus known to cause respiratory illness and was reported as a global pandemic on March 11th, 2020 (Cucinotta & Vanelli, 2020). RT-PCR performed detects the infection and predicts the presence of Coronavirus. The virus has a close genetic resemblance with bat coronavirus, implying that it might have arisen from a bat-borne virus. This protocol has been published by World Health Organization (WHO) and used as a guideline for detecting the disease (Corman et al., 2020). Rapidly the viral infection begun to spread, increasing the number of cases in China and various parts of the world resulting from human-to-human transmission through close contact and primarily *via* respiratory droplets produced *via* coughs and sneezes (Dhand & Li, 2020). Currently, India stands behind the USA in the second position in the total number of people infected by COVID-19 (Kumar, Kumar, Christopher, & Doss, 2020; Kumar, Kumar, Siva, & Doss, 2020). As of September 6th, 2021, the reported cases are more than 220,563,227, and at least 4,565,483 people have died. The infection begins with the SARS-CoV-2 attaching to the enzyme called ACE2, which again is expressed in cells of various tissues and organs but is particularly abundant in type 2 lung pneumocytes. The people involved are frequently asymptomatic throughout the early stages of incubation, as well as the type I interferon response slows viral replication. With active replication and dissemination of SARS-CoV-2, the disease advances from mild to moderate symptoms such as sore throat, tear, fiber, and muscle pains, leading by both virus-associated respiratory tissue damage and antiviral activity (Cain & Cidlowski, 2020).

Several variants of concern (VOC) have appeared worldwide and seem to pose a significant threat to public health due to enhanced transmissibility or infectivity (Kumar, Shaikh, Kumar, Doss, & Zayed, 2021). Despite efficient vaccines, the coronavirus pandemic elicits widespread concern about discovering critical new variants from California, South Africa, UK, and Brazil (Plante et al., 2021). SARS-CoV-2 variants raise concerns about higher transmission and escaping on both vaccine and natural infection protection, especially in light of concerns about a specific mink strain, which triggered a person's illnesses and the possibility for future alterations. While most mutations are insignificant, the virus occasionally obtains a mutation that offers it an edge over other strains. The virus uses the spike protein to penetrate living cells through the ACE2 receptor. The spike protein's receptor-binding domain (RBD) is the most changeable component of the coronavirus genome (Tai et al., 2020). Mutations in viruses may lead to immune suppression in the host that the host antibodies initiate, necessitating their identification and monitoring for antibody therapy efficacy. The N439K, N440K, Q493K, and E484K spike mutations were prone to immunological escape, and this recent discovery is drawing attention (Srivastava, Banu, Singh, Sowpati, & Mishra, 2021). These mutations have given rise to several lineages. In the absence of direct drugs for the treatment, many efforts have been directed towards developing vaccines against COVID-19. Live attenuated or inactivated viruses, virus-like particles (VLP), protein subunits, viral vector (non-replicating and replicating), DNA, RNA, and nanoparticles, among additional vaccinations, are used in the conduit, each with its own set of advantages and disadvantages. According to the WHO report, these vaccines could only be 50% effective (What Is COVID-19 Vaccine Efficacy? |WHO| Regional Office for Africa, 2021a).

Complementary and alternative medicine is in high demand since it embraces a holistic approach. Since ancient times, natural products have been used as drugs in medical treatment and are still widely practiced. Medicinal plants contain many active compounds, which serve as the key to an effective drug design. Herbal medicine is achieving attention because of its extensive therapeutics like potent antiviral, immunomodulatory, anti–inflammatory, and anti–oxidant properties (Ross, 2009). Traditional Indian Medicine (TIM)—AYUSH and Traditional Chinese medicine (TCM) are ancient yet living traditions. These two traditional medicines are very philosophical and based on experiments, and they seem to be very effective in combatting viral diseases. Using these drugs from their natural origin is the main root of therapy (Patwardhan, Warude, Pushpangadan, & Bhatt, 2005).

Pharmaceutical companies have re-established their policies in favor of natural product drug development and discovery. China has effectively endorsed its therapies over the world with a scientific approach. The emerging popularity of TCM can be verified by the rapid upsurge in licensed Chinese medicine providers in the United States. Constant efforts in advancing these therapies in China have set TCM creditable (Youns, Hoheisel, & Efferth, 2010). Worldwide, Siddha is recognized and emerging, and there has been an increase in demand for medicinal plants in India. The growing use of traditional therapies requires more scientific evidence for the principles behind treatments and the effectiveness of medicines. Latest developments in the biological sciences, genomics, and proteomics can justify these therapies (Rathinam et al., 2020).

Several medicines mentioned by Ministry AYUSH, India have been in practice for viral diseases like Chikungunya and Dengue for the past two decades. Herbal formulations such as Kabasura kudineer and Nilavembu kudineer are widely used to treat phlegmatic and hemorrhagic fevers and are approved by the Siddha medicine (Jain et al., 2020; Natarajan et al., 2020). Decoding using *in silico* studies in Nilavembu kudineer against SARS-CoV-2 spike protein showcases that these medicines can be recognized as a valuable drug to combat COVID-19. Nilavembu kudineer interacts with ACE2 receptor, which serves as the pathogen entrance, and in the outcome, the pathogen cannot enter into the host body. Kabasura kudineer or choornam possesses antiviral solid, anti-bacterial, and immunomodulatory properties. Numerous studies have unveiled the anti-inflammatory properties of Kabasura kudineer. This herbal formulation became reasonably recognized during times of flu due to its therapeutic qualities. *In silico* docking was performed using Kabasura kudineer against SARS-CoV-2 spike protein. Its rich active Phyto-constituents revealed a favorable outcome that prevented the merging of viral replication binding with viral proteins and inhibited host receptors' binding. This verifies that Kabasura kudineer could be a potential herbal formulation to combat COVID-19 if proven with further preclinical and clinical confirmatory studies (Natarajan et al., 2020).

In our study, medicinal plants used in herbal formulations of Nilavembu kudineer were our primary focus to understand their drug inhibitory potential against SARS-CoV-2. In comparison to modern medicine, Siddha medicine's approach is more holistic. Hence, investigating and ameliorating the effectiveness of Siddha medicine to obtain the solution with the most negligible side effects on immune-compromised patients and the patients with co-morbid conditions (Kiran et al., 2020).
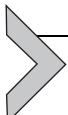
2. Materials and methods

2.1 Genes responsible for COVID-19

The human genes responsible for the COVID-19 disease were collected from the GeneCards database (Rebhan, Chalifa-Caspi, Prilusky, & Lancet, 1997). This database summarizes the current accessible biomedical information, including the human genes, proteins, and relevant diseases. The term "COVID-19" was used as the search term.

2.2 Siddha formulation as the supplement

The standard Siddha formulations such as Kabasura kudineer, Nilavembu kudineer, and JACOM that showed promising treatment results were chosen for this study (Jain et al., 2020; Kiran et al., 2020; Natarajan et al., 2020). The plant sources for these formulations were taken from the previous literature. The list of phytochemical compounds in these plant sources was obtained from the Chemical Entities of Biological Interest (ChEBI) database. This database provides an ontology of molecular entities focused on 'small' chemical compounds (Hastings et al., 2013).

2.3 Druglikeness of phytochemical compounds

The drug-likeness of the phytochemical compounds was evaluated using the SwissADME server (Daina, Michielin, & Zoete, 2017). The canonical SMILES format of phytochemical compounds was given as the input in SwissADME. We have considered the number of Lipinski violations given for each compound. The compounds with one or less than one Lipinski violations were selected for further analysis.

2.4 Target prediction for the phytochemical compounds

The various human protein targets for each phytochemical compound were identified using the SwissTargetPrediction (Gfeller et al., 2014). This server predicts bioactive molecules (query molecule) targets based on a blend of 2D and 3D resemblance procedures with known ligands. The top-ranking targets obtained for each phytochemical compound, with a probability of more than 0 was chosen for further analysis. The canonical SMILES format of phytochemical compounds was given as the input in SwissTargetPrediction.

2.5 Common target identification

A Venn diagram was created to find the expected targets for the identified phytochemical compounds and COVID-19 (genes affected by COVID-19). This was achieved using an online tool named Bioinformatics & Evolutionary Genomics. Using the Venn diagram, we identified the targets of phytochemical compounds with the same target as COVID-19 infection. Thus, the typical targets were used for further studies.

2.6 Enrichment analysis

The enrichment analysis was executed using the FunRich (Pathan et al., 2015). FunRich is a standalone package primarily utilized for the enrichment and interaction network analysis of proteins and genes. Enrichment analysis can be performed for biological process (BP), cellular process (CC), biological pathways, and molecular function (MF).

2.7 Pathway analysis

The pathway analysis was performed using the Reactome. Reactome is a comprehensive and well-annotated library of human molecular pathways and reactions (Fabregat et al., 2016).

2.8 Gene–gene interaction analysis

The standard targets obtained from the Venn diagram were subjected to a network analysis study. This was performed using the STRING database with default parameters (Szklarczyk et al., 2019). The STRING database aims to gather, score, and integrate all openly accessible protein–protein interaction information sources and complement these with computational predictions. Thus, this network analysis explains how these genes are biologically linked or overlapped through different pathways and functions.

2.9 Virtual screening and molecular interaction analysis

Several identified targets mapped in the gene–gene interaction have been targeted for more than one phytochemical compound. The virtual screening was performed using the AutoDock Vina plugin of the PyRx with the default parameter (Dallakyan & Olson, 2015; Trott & Olson, 2010). The protein structures with PDB IDs 6H5W, 2XU1, 6AY2, 2QT9, 4WKQ, 6WBW, 1ALU, 4ITJ, and 3QTK were taken for the proteins ACE, Cathepsin L, Cathepsin B, Cathepsin K, DPP4, EGFR, HDAC2, IL6, RIPK1, and VEGFA respectively. The compound showing the best affinity was taken

for docking using the AutoDock standalone package (Morris et al., 2009). Blind docking protocol was performed using the Lamarckian Genetic Algorithm (Morris et al., 1998). The amino acid interaction with the compounds was visualized using the Discovery Studio.

3. Results and discussions
3.1 Genes responsible for COVID-19

Human genes that are involved in response to any disease are numerous and highly diverse within the genome. A total of 339 genes were obtained. A set of genes were retrieved from the GeneCards database with the keyword COVID. The detailed table with external identifiers is provided in Table 1.

3.2 Siddha formulation as the supplement

The list of plants involved in the formulation of Kabasura kudineer, Nilavembu kudineer, and JACOM were identified from the literature source. A total of 25 plants were identified in the formulation (Table 2). Further, a list of phytochemical compounds from the identified 25 plants was obtained from the ChEBI database. Three hundred and fourteen phytochemical compounds were identified in these 25 plants overall (Table 3).

3.3 Drug likeliness of phytochemical compounds

For a compound to persuade as a drug, the compound must satisfy a set of parameters that will prove its compatibility, efficiency, and toxicity. Lipinski's "rule of five" highlights possible bioavailability problems if two or more properties were violated. The SwissADME server was used to identify the Lipinski rule of 5 violations. The overall results from the SwissADME are tabulated in Table 4. The list of 285 compounds that satisfy the Lipinski rule of 5 is tabulated in Table 5.

3.4 Target prediction for the phytochemical compounds

The SwissTagetPrediction was used to find the target of the compounds that satisfied the Lipinski rule of 5. The overall 24,843 targets were predicted for the 285 compounds (Supplementary Table 1 in the online version at https://doi.org/10.1016/bs.apcsb.2021.11.007). The probability score will be provided for each of the targets. Considering the confidence level, the targets with a probability score of more than 0 were considered for further research (Supplementary Table 2 in the online version at https://doi.org/10.1016/bs.apcsb.2021.11.007).

Table 1 The list of genes responsible for the COVID-19 with the identifiers obtained from GeneCards database.

Input term	Symbol	Ensembl	HGNC	NCBI Entrez gene	OMIM	UniProtKB/Swiss-Prot
AKAP8	AKAP8	ENSG00000105127	378	10270	604692	O43823
AKAP8L	AKAP8L	ENSG00000011243	29857	26993	609475	Q9ULX6
AKAP9	AKAP9	ENSG00000127914	379	10142	604001	Q99996
GGCX	GGCX	ENSG00000115486	4247	2677	137167	P38435
MDN1	MDN1	ENSG00000112159	18302	23195	618200	Q9NU22
MAT2B	MAT2B	ENSG00000038274	6905	27430	605527	Q9NZL9
GDF15	GDF15	ENSG00000130513	30142	9518	605312	Q99988
GCC1	GCC1	ENSG00000179562	19095	79571	607418	Q96CN9
GCC2	GCC2	ENSG00000135968	23218	9648	612711	Q8IWJ2
MIPOL1	MIPOL1	ENSG00000151338	21460	145282	606850	Q8TD10
MIB1	MIB1	ENSG00000101752	21086	57534	608677	Q86YT6
GOLGA2	GOLGA2	ENSG00000167110	4425	2801	602580	Q08379
GOLGA3	GOLGA3	ENSG00000090615	4426	2802	602581	Q08378
GNB1	GNB1	ENSG00000078369	4396	2782	139380	P62873
GNG5	GNG5	ENSG00000174021	4408	2787	600874	P63218
GOLGB1	GOLGB1	ENSG00000173230	4429	2804	602500	Q14789

Continued

Table 1 The list of genes responsible for the COVID-19 with the identifiers obtained from GeneCards database.—cont'd

Input term	Symbol	Ensembl	HGNC	NCBI Entrez gene	OMIM	UniProtKB/Swiss-Prot
GORASP1	GORASP1	ENSG00000114745	16769	64689	606867	Q9BQQ3
CD14	CD14	ENSG00000170458	1628	929	158120	P08571
CCDC86	CCDC86	ENSG00000110104	28359	79080	611293	Q9H6F5
MAP7D1	MAP7D1	ENSG00000116871	25514	55700	NA	Q3KQU3
FBXL12	FBXL12	ENSG00000127452	13611	54850	609079	Q9NXK8
ATE1	ATE1	ENSG00000107669	782	11101	607103	O95260
FAM162A	FAM162A	ENSG00000114023	17865	26355	608017	Q96A26
EXOSC2	EXOSC2	ENSG00000130713	17097	23404	602238	Q13868
EXOSC3	EXOSC3	ENSG00000107371	17944	51010	606489	Q9NQT5
EXOSC5	EXOSC5	ENSG00000077348	24662	56915	606492	Q9NQT4
EXOSC8	EXOSC8	ENSG00000120699	17035	11340	606019	Q96B26
EZH2	EZH2	ENSG00000106462	3527	2146	601573	Q15910
AP2A2	AP2A2	ENSG00000183020	562	161	607242	O94973
AP2M1	AP2M1	ENSG00000161203	564	1173	601024	Q96CW1
AP3B1	AP3B1	ENSG00000132842	566	8546	603401	O00203
ARL6IP6	ARL6IP6	ENSG00000177917	24048	151188	616495	Q8N6S5
ARF6	ARF6	ENSG00000165527	659	382	600464	P62330

ATP13A3	ATP13A3	ENSG00000133657	24113	79572	610232	Q9H7F0
ATP1B1	ATP1B1	ENSG00000143153	804	481	182330	P05026
ATP6AP1	ATP6AP1	ENSG00000071553	868	537	300197	Q15904
ATP6V1A	ATP6V1A	ENSG00000114573	851	523	607027	P38606
FBLN5	FBLN5	ENSG00000140092	3602	10516	604580	Q9UBX5
FBN1	FBN1	ENSG00000166147	3603	2200	134797	P35555
FBN2	FBN2	ENSG00000138829	3604	2201	612570	P35556
FAM8A1	FAM8A1	ENSG00000137414	16372	51439	618409	Q9UBU6
FAM98A	FAM98A	ENSG00000119812	24520	25940	NA	Q8NCA5
ERC1	ERC1	ENSG00000082805	17072	23085	607127	Q8IUD2
ALG11	ALG11	ENSG00000253710	32456	440138	613666	Q2TAA5
ALG5	ALG5	ENSG00000120697	20266	29880	604565	Q9Y673
AGTR2	AGTR2	ENSG00000180772	338	186	300034	P50052
ERGIC1	ERGIC1	ENSG00000113719	29205	57222	617946	Q969X5
LOC117134593	LOC117134593	NA	NA	117134593	NA	NA
LOC117134604	LOC117134604	NA	NA	117134604	NA	NA
LOC117134605	LOC117134605	NA	NA	117134605	NA	NA
LOC117134606	LOC117134606	NA	NA	117134606	NA	NA

Table 1 The list of genes responsible for the COVID-19 with the identifiers obtained from GeneCards database.—cont'd

Input term	Symbol	Ensembl	HGNC	NCBI Entrez gene	OMIM	UniProtKB/Swiss-Prot
LOC117134607	LOC117134607	NA	NA	117134607	NA	NA
LOC117134608	LOC117134608	NA	NA	117134608	NA	NA
LOC117134611	LOC117134611	NA	NA	117134611	NA	NA
LOC117135104	LOC117135104	NA	NA	117135104	NA	NA
LOC117135105	LOC117135105	NA	NA	117135105	NA	NA
LOC117135106	LOC117135106	NA	NA	117135106	NA	NA
ERLEC1	ERLEC1	ENSG00000068912	25222	27248	611229	Q96DZ1
LOC117152610	LOC117152610	NA	NA	117152610	NA	NA
LOC117152611	LOC117152611	NA	NA	117152611	NA	NA
LOC117204000	LOC117204000	NA	NA	117204000	NA	NA
LOC117204001	LOC117204001	NA	NA	117204001	NA	NA
LOC117600004	LOC117600004	NA	NA	117600004	NA	NA
LOC117693187	LOC117693187	NA	NA	117693187	NA	NA
ERO1B	ERO1B	ENSG00000086619	14355	56605	615437	Q86YB8
ERP44	ERP44	ENSG00000023318	18311	23071	609170	Q9BS26
AGPS	AGPS	ENSG00000018510	327	8540	603051	O00116
FKBP10	FKBP10	ENSG00000141756	18169	60681	607063	Q96AY3

FKBP15	FKBP15	ENSG00000119321	23397	23307	617398	Q5T1M5
MEPCE	MEPCE	ENSG00000146834	20247	56257	611478	Q7L2J0
FKBP7	FKBP7	ENSG00000079150	3723	51661	607062	Q9Y680
BCKDK	BCKDK	ENSG00000103507	16902	10295	614901	O14874
ACE	ACE	ENSG00000159640	2707	1636	106180	P12821
ACE2	ACE2	ENSG00000130234	13557	59272	300335	Q9BYF1
ADAM9	ADAM9	ENSG00000168615	216	8754	602713	Q13443
ADAMTS1	ADAMTS1	ENSG00000154734	217	9510	605174	Q9UHI8
AAR2	AAR2	ENSG00000131043	15886	25980	617365	Q9Y312
AASS	AASS	ENSG00000008311	17366	10157	605113	Q9UDR5
AATF	AATF	ENSG00000275700	19235	26574	608463	Q9NY61
ACSL3	ACSL3	ENSG00000123983	3570	2181	602371	O95573
ACADM	ACADM	ENSG00000117054	89	34	607008	P11310
BSG	BSG	ENSG00000172270	1116	682	109480	P35613
FYCO1	FYCO1	ENSG00000163820	14673	79443	607182	Q9BQS8
G3BP1	G3BP1	ENSG00000145907	30292	10146	608431	Q13283
G3BP2	G3BP2	ENSG00000138757	30291	9908	NA	Q9UN86
BRD2	BRD2	ENSG00000204256	1103	6046	601540	P25440

Table 1 The list of genes responsible for the COVID-19 with the identifiers obtained from GeneCards database.—cont'd

Input term	Symbol	Ensembl	HGNC	NCBI Entrez gene	OMIM	UniProtKB/Swiss-Prot
BRD4	BRD4	ENSG00000141867	13575	23476	608749	O60885
MFGE8	MFGE8	ENSG00000140545	7036	4240	602281	Q08431
BZW2	BZW2	ENSG00000136261	18808	28969	NA	Q9Y6E2
FOXRED2	FOXRED2	ENSG00000100350	26264	80020	613777	Q8IWF2
FURIN	FURIN	ENSG00000140564	8568	5045	136950	P09958
C1ORF50	C1orf50	ENSG00000164008	28795	79078	NA	Q9BV19
LOX	LOX	ENSG00000113083	6664	4015	153455	P28300
FASTKD5	FASTKD5	ENSG00000215251	25790	60493	614272	Q7L8L6
ATP5MG	ATP5MG	ENSG00000167283	14247	10632	617473	O75964
CWC27	CWC27	ENSG00000153015	10664	10283	617170	Q6UX04
CYB5B	CYB5B	ENSG00000103018	24374	80777	611964	O43169
CYB5R3	CYB5R3	ENSG00000100243	2873	1727	613213	P00387
HS2ST1	HS2ST1	ENSG00000153936	5193	9653	604844	Q7LGA3
HS6ST2	HS6ST2	ENSG00000171004	19133	90161	300545	Q96MM7
CTSB	CTSB	ENSG00000164733	2527	1508	116810	P07858
CTSL	CTSL	ENSG00000135047	2537	1514	116880	P07711
CRP	CRP	ENSG00000132693	2367	1401	123260	P02741

HOOK1	HOOK1	ENSG00000134709	19884	51361	607820	Q9UJC3
HEATR3	HEATR3	ENSG00000155393	26087	55027	614951	Q7Z4Q2
HECTD1	HECTD1	ENSG00000092148	20157	25831	618649	Q9ULT8
GLA	GLA	ENSG00000102393	4296	2717	300644	P06280
GIGYF2	GIGYF2	ENSG00000204120	11960	26058	612003	Q6Y7W6
GFER	GFER	ENSG00000127554	4236	2671	600924	P55789
ETFA	ETFA	ENSG00000140374	3481	2108	608053	P13804
ANO6	ANO6	ENSG00000177119	25240	196527	608663	Q4KMQ2
GRPEL1	GRPEL1	ENSG00000109519	19696	80273	606173	Q9HAV7
CDK5RAP2	CDK5RAP2	ENSG00000136861	18672	55755	608201	Q96SN8
GTF2F2	GTF2F2	ENSG00000188342	4653	2963	189969	P13984
CEP112	CEP112	ENSG00000154240	28514	201134	NA	Q8N8E3
CEP135	CEP135	ENSG00000174799	29086	9662	611423	Q66GS9
CEP250	CEP250	ENSG00000126001	1859	11190	609689	Q9BV73
CEP350	CEP350	ENSG00000135837	24238	9857	617870	Q5VT06
CEP43	CEP43	ENSG00000213066	17012	11116	605392	O95684
CEP68	CEP68	ENSG00000011523	29076	23177	616889	Q76N32
CENPF	CENPF	ENSG00000117724	1857	1063	600236	P49454

Continued

Table 1 The list of genes responsible for the COVID-19 with the identifiers obtained from GeneCards database.—cont'd

Input term	Symbol	Ensembl	HGNC	NCBI Entrez gene	OMIM	UniProtKB/Swiss-Prot
GOLGA7	GOLGA7	ENSG00000147533	24876	51125	609453	Q7Z5G4
HLA-A	HLA-A	ENSG00000206503	4931	3105	142800	P04439
RHOA	RHOA	ENSG00000067560	667	387	165390	P61586
HMOX1	HMOX1	ENSG00000100292	5013	3162	141250	P09601
COQ8B	COQ8B	ENSG00000123815	19041	79934	615567	Q96D53
CLIP4	CLIP4	ENSG00000115295	26108	79745	NA	Q8N3C7
HLA-DRB1	HLA-DRB1	ENSG00000196126	4948	3123	142857	P01911
CISD3	CISD3	ENSG00000277972	27578	284106	611933	P0C7P0
CIT	CIT	ENSG00000122966	1985	11113	605629	O14578
CLCC1	CLCC1	ENSG00000121940	29675	23155	617539	Q96S66
RIPK1	RIPK1	ENSG00000137275	10019	8737	603453	Q13546
COLGALT1	COLGALT1	ENSG00000130309	26182	79709	617531	Q8NBJ5
COMT	COMT	ENSG00000093010	2228	1312	116790	P21964
HDAC2	HDAC2	ENSG00000196591	4853	3066	605164	Q92769
CHPF	CHPF	ENSG00000123989	24291	79586	610405	Q8IZ52
CHPF2	CHPF2	ENSG00000033100	29270	54480	608037	Q9P2E5
DNAJC11	DNAJC11	ENSG00000007923	25570	55735	614827	Q9NVH1

DNAJC19	DNAJC19	ENSG00000205981	30528	131118	608977	Q96DA6
DNMT1	DNMT1	ENSG00000130816	2976	1786	126375	P26358
MRPS2	MRPS2	ENSG00000122140	14495	51116	611971	Q9Y399
MRPS25	MRPS25	ENSG00000131368	14511	64432	611987	P82663
MRPS27	MRPS27	ENSG00000113048	14512	23107	611989	Q92552
MRPS5	MRPS5	ENSG00000144029	14498	64969	611972	P82675
DPP4	DPP4	ENSG00000197635	3009	1803	102720	P27487
MTCH1	MTCH1	ENSG00000137409	17586	23787	610449	Q9NZJ7
MTARC1	MTARC1	ENSG00000186205	26189	64757	614126	Q5VT66
EDEM3	EDEM3	ENSG00000116406	16787	80267	610214	Q9BZQ6
CD8A	CD8A	ENSG00000153563	1706	925	186910	P01732
GPT	GPT	ENSG00000167701	4552	2875	138200	P24298
GPX1	GPX1	ENSG00000233276	4553	2876	138320	P07203
CD209	CD209	ENSG00000090659	1641	30835	604672	Q9NNX6
GRIPAP1	GRIPAP1	ENSG00000068400	18706	56850	300408	Q4V328
GGH	GGH	ENSG00000137563	4248	8836	601509	Q92820
MOV10	MOV10	ENSG00000155363	7200	4343	610742	Q9HCE1
MPHOSPH10	MPHOSPH10	ENSG00000124383	7213	10199	605503	O00566

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Table 1 The list of genes responsible for the COVID-19 with the identifiers obtained from GeneCards database.—cont'd

Input term	Symbol	Ensembl	HGNC	NCBI Entrez gene	OMIM	UniProtKB/Swiss-Prot
DDX10	DDX10	ENSG00000178105	2735	1662	601235	Q13206
DDX21	DDX21	ENSG00000165732	2744	9188	606357	Q9NR30
RNF41	RNF41	ENSG00000181852	18,401	10193	NA	Q9H4P4
COL6A1	COL6A1	ENSG00000142156	2211	1291	120220	P12109
DCAF7	DCAF7	ENSG00000136485	30915	10238	605973	P61962
DCAKD	DCAKD	ENSG00000172992	26238	79877	NA	Q8WVC6
NDUFAF2	NDUFAF2	ENSG00000164182	28086	91942	609653	Q8N183
EIF4E2	EIF4E2	ENSG00000135930	3293	9470	605895	O60573
EIF4H	EIF4H	ENSG00000106682	12741	7458	603431	Q15056
ELOB	ELOB	ENSG00000103363	11619	6923	600787	Q15370
ELOC	ELOC	ENSG00000154582	11617	6921	600788	Q15369
EMC1	EMC1	ENSG00000127463	28957	23065	616846	Q8N766
NEU1	NEU1	ENSG00000204386	7758	4758	608272	Q99519
NEK9	NEK9	ENSG00000119638	18591	91754	609798	Q8TD19
CSNK2A2	CSNK2A2	ENSG00000070770	2459	1459	115442	P19784
CSNK2B	CSNK2B	ENSG00000204435	2460	1460	115441	P67870
CRTC3	CRTC3	ENSG00000140577	26148	64784	608986	Q6UUV7

PCSK6	PCSK6	ENSG00000140479	8569	5046	167405	P29122
IL17A	IL17A	ENSG00000112115	5981	3605	603149	Q16552
IL17RA	IL17RA	ENSG00000177663	5985	23765	605461	Q96F46
IL10	IL10	ENSG00000136634	5962	3586	124092	P22301
IL2RA	IL2RA	ENSG00000134460	6008	3559	147730	P01589
SPART	SPART	ENSG00000133104	18514	23111	607111	Q8N0X7
PDZD11	PDZD11	ENSG00000120509	28034	51248	300632	Q5EBL8
PRRC2B	PRRC2B	ENSG00000130723	28121	84726	NA	Q5JSZ5
NPTX1	NPTX1	ENSG00000171246	7952	4884	602367	Q15818
SELENOS	SELENOS	ENSG00000131871	30396	55829	607918	Q9BQE4
NPC2	NPC2	ENSG00000119655	14537	10577	601015	P61916
PABPC1	PABPC1	ENSG00000070756	8554	26986	604679	P11940
PABPC4	PABPC4	ENSG00000090621	8557	8761	603407	Q13310
IDE	IDE	ENSG00000119912	5381	3416	146680	P14735
PRKACA	PRKACA	ENSG00000072062	9380	5566	601639	P17612
PCNT	PCNT	ENSG00000160299	16068	5116	605925	O95613
PRKAR2A	PRKAR2A	ENSG00000114302	9391	5576	176910	P13861
PDE4DIP	PDE4DIP	ENSG00000178104	15580	9659	608117	Q5VU43

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Table 1 The list of genes responsible for the COVID-19 with the identifiers obtained from GeneCards database.—cont'd

Input term	Symbol	Ensembl	HGNC	NCBI Entrez gene	OMIM	UniProtKB/Swiss-Prot
SAAL1	SAAL1	ENSG00000166788	25158	113174	NA	Q96ER3
SCARB1	SCARB1	ENSG00000073060	1664	949	601040	Q8WTV0
SCCPDH	SCCPDH	ENSG00000143653	24275	51097	NA	Q8NBX0
SDF2	SDF2	ENSG00000132581	10675	6388	602934	Q99470
RRP9	RRP9	ENSG00000114767	16829	9136	NA	O43818
SBNO1	SBNO1	ENSG00000139697	22973	55206	614274	A3KN83
RTN4	RTN4	ENSG00000115310	14085	57142	604475	Q9NQC3
EGFR	EGFR	ENSG00000146648	3236	1956	131550	P00533
RPL36	RPL36	ENSG00000130255	13631	25873	617893	Q9Y3U8
ENPEP	ENPEP	ENSG00000138792	3355	2028	138297	Q07075
NGDN	NGDN	ENSG00000129460	20271	25983	610777	Q8NEJ9
NGLY1	NGLY1	ENSG00000151092	17646	55768	610661	Q96IV0
NIN	NIN	ENSG00000100503	14906	51199	608684	Q8N4C6
NINL	NINL	ENSG00000101004	29163	22981	609580	Q9Y2I6
SLC44A2	SLC44A2	ENSG00000129353	17292	57153	606106	Q8IWA5
NUP210	NUP210	ENSG00000132182	30052	23225	607703	Q8TEM1
NUP214	NUP214	ENSG00000126883	8064	8021	114350	P35658

SLC6A19	SLC6A19	ENSG00000174358	27960	340024	608893	Q695T7
SMOC1	SMOC1	ENSG00000198732	20318	64093	608488	Q9H4F8
PKP2	PKP2	ENSG00000057294	9024	5318	602861	Q99959
SLU7	SLU7	ENSG00000164609	16939	10569	605974	O95391
PITRM1	PITRM1	ENSG00000107959	17663	10531	618211	Q5JRX3
HSBP1	HSBP1	ENSG00000230989	5203	3281	604553	O75506
OS9	OS9	ENSG00000135506	16994	10956	609677	Q13438
POFUT1	POFUT1	ENSG00000101346	14988	23509	607491	Q9H488
POGLUT2	POGLUT2	ENSG00000134901	19350	79070	611613	Q6UW63
POGLUT3	POGLUT3	ENSG00000178202	28496	143888	618503	Q7Z4H8
POLA1	POLA1	ENSG00000101868	9173	5422	312040	P09884
POLA2	POLA2	ENSG00000014138	30073	23649	NA	Q14181
PLOD2	PLOD2	ENSG00000152952	9082	5352	601865	O00469
SNIP1	SNIP1	ENSG00000163877	30587	79753	608241	Q8TAD8
PLD3	PLD3	ENSG00000105223	17158	23646	615698	Q8IV08
PLEKHA5	PLEKHA5	ENSG00000052126	30036	54477	607770	Q9HAU0
PLEKHF2	PLEKHF2	ENSG00000175895	20757	79666	615208	Q9H8W4
SIRT5	SIRT5	ENSG00000124523	14933	23408	604483	Q9NXA8

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Table 1 The list of genes responsible for the COVID-19 with the identifiers obtained from GeneCards database.—cont'd

Input term	Symbol	Ensembl	HGNC	NCBI Entrez gene	OMIM	UniProtKB/Swiss-Prot
SLC27A2	SLC27A2	ENSG00000140284	10996	11001	603247	O14975
SLC30A7	SLC30A7	ENSG00000162695	19306	148867	611149	Q8NEW0
SLC30A9	SLC30A9	ENSG00000014824	1329	10463	604604	Q6PML9
NUP54	NUP54	ENSG00000138750	17359	53371	607607	Q7Z3B4
NUP58	NUP58	ENSG00000139496	20261	9818	607615	Q9BVL2
NUP62	NUP62	ENSG00000213024	8066	23636	605815	P37198
NUP88	NUP88	ENSG00000108559	8067	4927	602552	Q99567
NUP98	NUP98	ENSG00000110713	8068	4928	601021	P52948
NUTF2	NUTF2	ENSG00000102898	13722	10204	605813	P61970
SLC25A21	SLC25A21	ENSG00000183032	14411	89874	607571	Q9BQT8
NSD2	NSD2	ENSG00000109685	12766	7468	602952	O96028
SEPSECS	SEPSECS	ENSG00000109618	30605	51091	613009	Q9HD40
SIGMAR1	SIGMAR1	ENSG00000147955	8157	10280	601978	Q99720
SIL1	SIL1	ENSG00000120725	24624	64374	608005	Q9H173
SRP19	SRP19	ENSG00000153037	11300	6728	182175	P09132
SRP54	SRP54	ENSG00000100883	11301	6729	604857	P61011
INS	INS	ENSG00000254647	6081	3630	176730	P01308

SRP72	SRP72	ENSG00000174780	11303	6731	602122	O76094
IMPDH2	IMPDH2	ENSG00000178035	6053	3615	146691	P12268
PTGES2	PTGES2	ENSG00000148334	17822	80142	608152	Q9H7Z7
INHBE	INHBE	ENSG00000139269	24029	83729	612031	P58166
PSMD8	PSMD8	ENSG00000099341	9566	5714	617844	P48556
INTS4	INTS4	ENSG00000149262	25048	92105	611348	Q96HW7
TOR1A	TOR1A	ENSG00000136827	3098	1861	605204	O14656
TOR1AIP1	TOR1AIP1	ENSG00000143337	29456	26092	614512	Q5JTV8
LARP1	LARP1	ENSG00000155506	29531	23367	612059	Q6PKG0
LARP4B	LARP4B	ENSG00000107929	28987	23185	616513	Q92615
LARP7	LARP7	ENSG00000174720	24912	51574	612026	Q4G0J3
TUBGCP2	TUBGCP2	ENSG00000130640	18599	10844	617817	Q9BSJ2
TUBGCP3	TUBGCP3	ENSG00000126216	18598	10426	617818	Q96CW5
UGGT2	UGGT2	ENSG00000102595	15664	55757	605898	Q9NYU1
TRIM59	TRIM59	ENSG00000213186	30834	286827	616148	Q8IWR1
UBAP2	UBAP2	ENSG00000137073	14185	55833	NA	Q5T6F2
TYSND1	TYSND1	ENSG00000156521	28531	219743	611017	Q2T9J0
UBAP2L	UBAP2L	ENSG00000143569	29877	9898	616472	Q14157

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Table 1 The list of genes responsible for the COVID-19 with the identifiers obtained from GeneCards database.—cont'd

Input term	Symbol	Ensembl	HGNC	NCBI Entrez gene	OMIM	UniProtKB/Swiss-Prot
UPF1	UPF1	ENSG00000005007	9962	5976	601430	Q92900
ITGB1	ITGB1	ENSG00000150093	6153	3688	135630	P05556
PUSL1	PUSL1	ENSG00000169972	26914	126789	NA	Q8N0Z8
PVR	PVR	ENSG00000073008	9705	5817	173850	P15151
RAB2A	RAB2A	ENSG00000104388	9763	5862	179509	P61019
RAP1GDS1	RAP1GDS1	ENSG00000138698	9859	5910	179502	P52306
KNG1	KNG1	ENSG00000113889	6383	3827	612358	P01042
TCF12	TCF12	ENSG00000140262	11623	6938	600480	Q99081
TARS2	TARS2	ENSG00000143374	30740	80222	612805	Q9BW92
REEP5	REEP5	ENSG00000129625	30077	7905	125265	Q00765
REEP6	REEP6	ENSG00000115255	30078	92840	609346	Q96HR9
TBK1	TBK1	ENSG00000183735	11584	29110	604834	Q9UHD2
TBKBP1	TBKBP1	ENSG00000198933	30140	9755	608476	A7MCY6
RBX1	RBX1	ENSG00000100387	9928	9978	603814	P62877
RBM41	RBM41	ENSG00000089682	25617	55285	NA	Q96IZ5
RDX	RDX	ENSG00000137710	9944	5962	179410	P35241
RAB10	RAB10	ENSG00000084733	9759	10890	612672	P61026

JAKMIP1	JAKMIP1	ENSG00000152969	26460	152789	611195	Q96N16
STOM	STOM	ENSG00000148175	3383	2040	133090	P27105
RAB14	RAB14	ENSG00000119396	16524	51552	612673	P61106
RAB18	RAB18	ENSG00000099246	14244	22931	602207	Q9NP72
RAB1A	RAB1A	ENSG00000138069	9758	5861	179508	P62820
STC2	STC2	ENSG00000113739	11374	8614	603665	O76061
RALA	RALA	ENSG00000006451	9839	5898	179550	P11233
RAB5C	RAB5C	ENSG00000108774	9785	5878	604037	P51148
RAB7A	RAB7A	ENSG00000075785	9788	7879	602298	P51149
RAB8A	RAB8A	ENSG00000167461	7007	4218	165040	P61006
QSOX2	QSOX2	ENSG00000165661	30249	169714	612860	Q6ZRP7
RAE1	RAE1	ENSG00000101146	9828	8480	603343	P78406
SUN2	SUN2	ENSG00000100242	14210	25777	613569	Q9UH99
TLE1	TLE1	ENSG00000196781	11837	7088	600189	Q04724
TLE3	TLE3	ENSG00000140332	11839	7090	600190	Q04726
TLE5	TLE5	ENSG00000104964	307	166	600188	Q08117
TM2D3	TM2D3	ENSG00000184277	24128	80213	610014	Q9BRN9
TMPRSS2	TMPRSS2	ENSG00000184012	11876	7113	602060	O15393

Table 1 The list of genes responsible for the COVID-19 with the identifiers obtained from GeneCards database.—cont'd

Input term	Symbol	Ensembl	HGNC	NCBI Entrez gene	OMIM	UniProtKB/Swiss-Prot
TMPRSS4	TMPRSS4	ENSG00000137648	11878	56649	606565	Q9NRS4
IL6R	IL6R	ENSG00000160712	6019	3570	147880	P08887
PRKAR2B	PRKAR2B	ENSG00000005249	9392	5577	176912	P31323
PRIM1	PRIM1	ENSG00000198056	9369	5557	176635	P49642
PRIM2	PRIM2	ENSG00000146143	9370	5558	176636	P49643
PPT1	PPT1	ENSG00000131238	9325	5538	600722	P50897
PPIL3	PPIL3	ENSG00000240344	9262	53938	615811	Q9H2H8
TRMT1	TRMT1	ENSG00000104907	25980	55621	611669	Q9NXH9
MYCBP2	MYCBP2	ENSG00000005810	23386	23077	610392	O75592
NARS2	NARS2	ENSG00000137513	26274	79731	612803	Q96I59
CNTRL	CNTRL	ENSG00000119397	1858	11064	605496	Q7Z7A1
NAT14	NAT14	ENSG00000090971	28918	57106	NA	Q8WUY8
NOL10	NOL10	ENSG00000115761	25862	79954	616197	Q9BSC4
CUL2	CUL2	ENSG00000108094	2552	8453	603135	Q13617
MOGS	MOGS	ENSG00000115275	24862	7841	601336	Q13724
PLAT	PLAT	ENSG00000104368	9051	5327	173370	P00750
PLAUR	PLAUR	ENSG00000011422	9053	5329	173391	Q03405

POR	POR	ENSG00000127948	9208	5447	124015	P16435
HYOU1	HYOU1	ENSG00000149428	16931	10525	601746	Q9Y4L1
PMPCA	PMPCA	ENSG00000165688	18667	23203	613036	Q10713
PMPCB	PMPCB	ENSG00000105819	9119	9512	603131	O75439
IL6	IL6	ENSG00000136244	6018	3569	147620	P05231
RBM28	RBM28	ENSG00000106344	21863	55131	612074	Q9NW13
THTPA	THTPA	ENSG00000259431	18987	79178	611612	Q9BU02
TIMM10	TIMM10	ENSG00000134809	11814	26519	602251	P62072
TIMM10B	TIMM10B	ENSG00000132286	4022	26515	607388	Q9Y5J6
TIMM29	TIMM29	ENSG00000142444	25152	90580	617380	Q9BSF4
TIMM8B	TIMM8B	ENSG00000150779	11818	26521	606659	Q9Y5J9
TIMM9	TIMM9	ENSG00000100575	11819	26520	607384	Q9Y5J7
USP54	USP54	ENSG00000166348	23513	159195	NA	Q70EL1
ZC3H7A	ZC3H7A	ENSG00000122299	30959	29066	NA	Q8IWR0
ZDHHC5	ZDHHC5	ENSG00000156599	18472	25921	614586	Q9C0B5
ZC3H18	ZC3H18	ENSG00000158545	25091	124245	NA	Q86VM9
ZNF503	ZNF503	ENSG00000165655	23589	84858	613902	Q96F45
ZNF318	ZNF318	ENSG00000171467	13578	24149	617512	Q5VUA4

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Table 1 The list of genes responsible for the COVID-19 with the identifiers obtained from GeneCards database.—cont'd

Input term	Symbol	Ensembl	HGNC	NCBI Entrez gene	OMIM	UniProtKB/Swiss-Prot
ZYG11B	ZYG11B	ENSG00000162378	25820	79699	618673	Q9C0D3
VPS11	VPS11	ENSG00000160695	14583	55823	608549	Q9H270
VPS39	VPS39	ENSG00000166887	20593	23339	612188	Q96JC1
WASHC4	WASHC4	ENSG00000136051	29174	23325	615748	Q2M389
USP13	USP13	ENSG00000058056	12611	8975	603591	Q92995
VEGFA	VEGFA	ENSG00000112715	12680	7422	192240	P15692
YIF1A	YIF1A	ENSG00000174851	16688	10897	611484	O95070
LMAN2	LMAN2	ENSG00000169223	16986	10960	609551	Q12907

Table 2 The list of plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM.

S.·no	Plants name
1	*Zingiber officinale*
2	*Piper longum*
3	*Syzygium aromaticum*
4	*Tragia involucrata*
5	*Anacyclus pyrethrum*
6	*Andrographis paniculata*
7	*Hygrophila auriculata*
8	*Terminalia chebula*
9	*Justicia adhatoda*
10	*Plectranthus amboinicus*
11	*Saussurea lappa*
12	*Tinospora cordifolia*
13	*Rotheca serrata*
14	*Cypreus rotundus*
15	*Sida acuta* Burm.f.L
16	Adeloda serrata raf
17	*Carica Papaya*
18	*A. paniculata*
19	*Ocimum tenuiflorum*
20	*Vetiveria zizanioides*
21	*Santalum album*
22	*Piper nigrum*
23	*Hedyotis corymbosa*
24	*Plectranthus vettiveroides*
25	*Trichosanthes cucumerina*

Table 3 The list of phytochemical compounds found in the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM with ChEBI ID.

S.·no	Name of the plant	ChEBI ID	Name of the compound
1	*Zingiber officinale*	CHEBI:142262	Gingerenone B
2		CHEBI:64361	Beta–sesquiphellandrene
3		CHEBI:69294	3-(3,4-Dimethoxyphenyl)-4-[(Z)-3,4-dimethoxystyryl]cyclohex-1-ene
4		CHEBI:69295	3-(3,4-Dimethoxyphenyl)-4-[(E)-3,4-dimethoxystyryl]cyclohex-1-ene
5		CHEBI:26137	Pinocarveol
6		CHEBI:66502	Zerumboneoxide
7		CHEBI:68065	Ramonanin A, (rel)-
8		CHEBI:68066	Ramonanin B, (rel)-
9		CHEBI:68067	Ramonanin C, (rel)-
10		CHEBI:68068	Ramonanin D, (rel)-
11		CHEBI:63892	Zerumbone
12		CHEBI:66050	5-Hydroxyzerumbone
13		CHEBI:138043	(2E,6E)–hedycaryol
14		CHEBI:28817	Dodecane
15		CHEBI:146145	7,4′-Dimethylkaempferol
16		CHEBI:10115	Zingiberene
17		CHEBI:5414	Glucoputranjivin(1-)
18		CHEBI:79331	Glucoputranjivin
19		CHEBI:32389	All-cis–octadeca-6,9,12,15-tetraenoic acid
20	*Piper longum*	CHEBI:132658	Pipataline
21		CHEBI:66757	Pipercyclobutanamide A(rel)
22		CHEBI:69686	Pellitorine
23		CHEBI:67582	Gaudichaudianic acid, (−rac)
24		CHEBI:69675	Sarmentosumin A
25		CHEBI:69676	Sarmentosumin B

Table 3 The list of phytochemical compounds found in the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM with ChEBI ID.—cont'd

S.·no	Name of the plant	ChEBI ID	Name of the compound
26		CHEBI:69677	Sarmentosumin C
27		CHEBI:69678	Sarmentosumin D
28		CHEBI:69679	Isochamanetin
29		CHEBI:69680	7-Methoxychamanetin
30		CHEBI:69681	Dichamanetin
31		CHEBI:69682	7-Methoxydichamanetin
32		CHEBI:69683	5″-(2″″-Hydroxybenzyl)uvarinol
33		CHEBI:69687	2,4-Dodecadienamide
34		CHEBI:69689	7-Methoxyisochamanetin
35		CHEBI:70083	(2E,4E)–N–[2-(methylsulfinyl)ethyl]–2,4-decadienamide
36		CHEBI:70084	(2E,4E)–N–[(4-hydroxy-3-methoxyphenyl)ethyl]–2,4-decadienamide
37		CHEBI:70085	3-(4-Hydroxy-3,5-dimethoxyphenyl)propanoylpyrrole
38		CHEBI:70086	3-(3,4,5-Timethoxyphenyl)propanoylpyrrole
39		CHEBI:70087	1-[(2E,4E,6E)-2,4,6-dodecatrienoyl]pyrrolidine
40		CHEBI:70088	1-[(2E,4Z,8E)-9-(3,4-methylenedioxyphenyl)-2,4,8-nonatrienoyl]pyrrolidine
41		CHEBI:70089	1-[(2E,4E,10E)-10-(3,4-methylenedioxyphenyl)-2,4,10-undecatrienoyl]pyrrolidine
42		CHEBI:70090	1-[(4E,10E)-11-(3,4-methylenedioxyphenyl)-4,10-undecadienoyl]pyrrolidine
43		CHEBI:70091	1-[(9E)-10-(3,4-methylenedioxyphenyl)-9-decenoyl]pyrrolidine

Continued

Table 3 The list of phytochemical compounds found in the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM with ChEBI ID.—cont'd

S.·no	Name of the plant	ChEBI ID	Name of the compound
44		CHEBI:70092	1-[(2E,4E)-2,4-decadienoyl]pyrrolidine
45		CHEBI:70093	1-[(2E,4E)-2,4-dodecadienoyl]pyrrolidine
46		CHEBI:70094	1-[(2E)-7-(3,4-methylenedioxyphenyl)-2-heptenoyl]pyrrolidine
47		CHEBI:70095	1-[(2E,4E)-7-(3,4-methylenedioxyphenyl)-2,4-heptadienoyl]pyrrolidine
48		CHEBI:70096	1-[(2E,8E)-9-(3,4-methylenedioxyphenyl)-2,8-nonadienoyl]pyrrolidine
49		CHEBI:70097	1-[(8E)-9-(3,4-methylenedioxyphenyl)-8-nonenoyl]pyrrolidine
50		CHEBI:70098	1-[(2E,4E,8E)-9-(3,4-methylenedioxyphenyl)-2,4,8-nonatrienoyl]pyrrolidine
51		CHEBI:70099	1-[(2E,4E)-11-(3,4-methylenedioxyphenyl)-2,4-undecadienoyl]pyrrolidine
52		CHEBI:70100	1-[(2E,10E)-11-(3,4-methylenedioxyphenyl)-2,10-undecadienoyl]pyrrolidine
53		CHEBI:70101	(2E,4E)-N-isobutyl-2,4-dodecadienamide
54		CHEBI:70102	(2E,4E)-N-isobutyl-7-(3,4-methylenedioxyphenyl)-hepta-2,4-dienamide
55		CHEBI:70103	(8E)-N-isobutyl-9-(3,4-methylenedioxyphenyl)nona-8-enamide
56		CHEBI:70104	(2E,4E,8E)-N-isobutyl-11-(3,4-methylenedioxyphenyl)undeca-2,4,8-trienamide
57		CHEBI:70105	N-trans-sinapoyltyramine

Table 3 The list of phytochemical compounds found in the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM with ChEBI ID.—cont'd

S.·no	Name of the plant	ChEBI ID	Name of the compound
58		CHEBI:70490	Dihydrocubebin, rel–
59		CHEBI:70491	Justiflorinol
60		CHEBI:70485	(−)-Sanguinolignan A
61		CHEBI:70486	(−)-Sanguinolignan B
62		CHEBI:70487	(−)-Sanguinolignan C
63		CHEBI:70488	(−)-Sanguinolignan D
64		CHEBI:70489	(7′S)-parabenzlactone
65		CHEBI:65899	Flavokawain B
66		CHEBI:66709	Methyl 3,4-dihydroxy–5-(3′-methyl–2′-butenyl)benzoate
67		CHEBI:69688	Pipercallosidine
68		CHEBI:132651	Kadsurenin C
69		CHEBI:132652	Kadsurenin K
70		CHEBI:132653	Kadsurenin L
71		CHEBI:69685	Pipercallosine
72		CHEBI:70483	(S)-1′-methylhexyl caffeate
73		CHEBI:132647	Futoenone
74		CHEBI:65684	(−)-Cubebin
75		CHEBI:65685	(−)-3,4-Dimethoxy–3,4-desmethylenedioxycubebin
76		CHEBI:70482	(S)-1′-methylbutyl caffeate
77		CHEBI:70484	(S)-1′-methyloctyl caffeate
78		CHEBI:65937	Futokadsurin B
79		CHEBI:65938	Futokadsurin C
80		CHEBI:28821	Piperine
81		CHEBI:65936	Futokadsurin A
82		CHEBI:132650	Burchellin
83		CHEBI:35697	Trans-cinnamic acid

Continued

Table 3 The list of phytochemical compounds found in the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM with ChEBI ID.—cont'd

S. no	Name of the plant	ChEBI ID	Name of the compound
84		CHEBI:80484	Pinocembrin chalcone
85		CHEBI:132657	Piperlactam S
86		CHEBI:2871	Asebogenin
87		CHEBI:66470	(+)-Sesamin
88		CHEBI:30746	Benzoic acid
89		CHEBI:17818	N-feruloyltyramine
90		CHEBI:132654	Kadsurenin M
91		CHEBI:156227	(−)-Epicubenol
92		CHEBI:70626	Acacetin-8-C-neohesperidoside
93		CHEBI:70148	Monocerin
94		CHEBI:70149	(2S,3aR,9bR)-6,7-dihydroxy-8-methoxy-2-propyl-3,3a-dihydro-2H-furo[3,2-c]isochromen-5(9bH)-one
95		CHEBI:70150	Fusarentin 6,7-dimethyl ether
96		CHEBI:70151	Fusarentin 6-methyl ether
97		CHEBI:70152	(3R,4R)-4,8-dihydroxy-3-((R)-2-hydroxypentyl)-6,7-dimethoxyisochroman-1-one
98		CHEBI:70153	Colletotrialide, (+)-
99		CHEBI:132648	Galgravin
100		CHEBI:8240	Piperonal
101		CHEBI:28157	Pinocembrin
102		CHEBI:80788	1,4-Cineole
103		CHEBI:113455	Sodium benzoate
104		CHEBI:156224	(−)-Cubenol
105		CHEBI:37316	(E,E)-piperic acid
106		CHEBI:6116	Kavapyrone
107		CHEBI:10224	Alpha-cubebene
108		CHEBI:132649	Acuminatin

Table 3 The list of phytochemical compounds found in the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM with ChEBI ID.—cont'd

S.·no	Name of the plant	ChEBI ID	Name of the compound
109	*Syzygium aromaticum*	CHEBI:65486	Betulin di(3-carboxybutanoate)
110		CHEBI:65485	Dihydrobetulinic acid
111		CHEBI:65484	Bevirimat
112		CHEBI:65487	Platanic acid
113		CHEBI:132345	Canophyllal
114		CHEBI:27386	Cinnamic acid
115		CHEBI:69305	Cinnamtannin D-1
116		CHEBI:69307	Cassiatannin A
117		CHEBI:69304	Cinnamtannin B-1
118		CHEBI:69306	Parameritannin A-1
119		CHEBI:133634	Methyl linolenate
120		CHEBI:63892	Zerumbone
121		CHEBI:89729	(Z)-3-phenyl-2-propenal
122		CHEBI:136676	(E)-2-methoxycinnamic acid
123		CHEBI:3087	Betulinic acid
124	*Tragia involucrata*	CHEBI:133981	Heptacosan-1-ol
125	*Anacyclus pyrethrum*	CHEBI:27815	Pyrethrin I
126		CHEBI:27474	Pyrethrin II
127	*Andrographis paniculata*	CHEBI:69808	14-Deoxy-11,12-didehydroandrographolide
128		CHEBI:65408	Andrographolide
129		CHEBI:86612	Dihydroferulic acid
130		CHEBI:132373	Mesembryanthemoidigenic acid
131		CHEBI:142267	Methyl *N*-methylanthranilate
132		CHEBI:132830	Delta-elemene
133		CHEBI:65732	Decussatin
134	*Hygrophila auriculata*	CHEBI:3367	Capensinidin

Table 3 The list of phytochemical compounds found in the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM with ChEBI ID.—cont'd

S. no	Name of the plant	ChEBI ID	Name of the compound
135	*Terminalia chebula*	CHEBI:66202	Termilignan B
136		CHEBI:69692	(Z)-9-hydroxybenzo[c]oxepin-3(1H)-one
137		CHEBI:69693	Cyclosordariolone, (rac)-
138		CHEBI:69694	(R)-3-Hydroxy-1-[(R)-4-hydroxy-1,3-dihydroisobenzofuran-1-yl]butan-2-one
139		CHEBI:69695	(R)-3-Hydroxy-1-[(S)-4-hydroxy-1,3-dihydroisobenzofuran-1-yl]butan-2-one
140		CHEBI:69696	(E)-2-(Hydroxymethyl)-3-(4-hydroxypent-1-enyl)phenol
141		CHEBI:69697	1-(3,9-Dihydroxy-1,3-dihydrobenzo[c]oxepin-3-yl)ethanone, (rac)-
142		CHEBI:69698	Pestalospirane A
143		CHEBI:69699	Pestalospirane B
144		CHEBI:145828	Methyl 3,4,5-trihydroxybenzoate
145		CHEBI:9908	Ursolic acid
146	*Justicia adhatoda*	CHEBI:2814	Arecoline
147		CHEBI:156072	Propyl benzoate
148	*Plectranthus amboinicus*	CHEBI:66763	Plectranthol A
149		CHEBI:66764	Plectranthol B
150		CHEBI:138963	11,20-Dihydroxysugiol
151		CHEBI:138962	11-Hydroxysugiol
152		CHEBI:86062	Abietatriene
153	*Saussurea lappa*	CHEBI:66024	1beta-hydroxy arbusculin A
154		CHEBI:2540	Alantolactone
155		CHEBI:244418	Dehydrocostus lactone
156		CHEBI:3900	Costunolide

Table 3 The list of phytochemical compounds found in the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM with ChEBI ID.—cont'd

S.·no	Name of the plant	ChEBI ID	Name of the compound
157		CHEBI:132820	Matairesinoside
158		CHEBI:138251	3–Hydroxyhexane-2,5-dione
159		CHEBI:133981	Heptacosan–1-ol
160	*Tinospora cordifolia*	CHEBI:66046	6-Hydroxyluteolin 7-O-laminaribioside
161		CHEBI:89715	Cyclotetradecane
162		CHEBI:142915	Cycloeucalenone
163		CHEBI:141063	Rubimaillin
164		CHEBI:132345	Canophyllal
165		CHEBI:132718	Stepharanine
166		CHEBI:134479	(Z)–icos-13-enoic acid
167		CHEBI:145828	Methyl 3,4,5-trihydroxybenzoate
168	*Rotheca serrata*	CHEBI:156193	Serratol
169		CHEBI:78330	Huperzine A
170		CHEBI:6701	Maytansine
171	*Cypreus rotundus*	CHEBI:66416	Mustakone
172		CHEBI:81377	(+)–Nootkatone
173	*Sida acuta* Burm.f.L	CHEBI:142397	Pectenotoxin–11
174		CHEBI:145981	Dinophysistoxin 2
175		CHEBI:142495	1-Icosanoylglycerol
176		CHEBI:131838	Swertisin
177		CHEBI:156193	Serratol
178		CHEBI:16634	Raffinose
179		CHEBI:90295	PLX–4720
180		CHEBI:78330	Huperzine A
181		CHEBI:6701	Maytansine
182		CHEBI:143119	N–(2-methoxyethyl)-4-{[6-(pyridin-4-yl) quinazolin-2-yl]amino}benzamide

Continued

Table 3 The list of phytochemical compounds found in the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM with ChEBI ID.—cont'd

S. no	Name of the plant	ChEBI ID	Name of the compound
183	*Carica Papaya*	CHEBI:17127	Glucotropeolin
184		CHEBI:58021	Glucotropeolin(1-)
185		CHEBI:142658	Methyl 12-methyltetradecanoate
186		CHEBI:91143	(3*S*,5*R*,6*S*)-beta-cryptoxanthin 5,6-epoxide
187		CHEBI:3433	Carpaine
188		CHEBI:10362	Beta-cryptoxanthin
189		CHEBI:1307	24-Methylenecycloartanol
190		CHEBI:141360	Helvolic acid methyl ester
191		CHEBI:4316	Danielone
192		CHEBI:133683	2-Isobutylthiazole
193	*A. paniculata*	CHEBI:69808	14-Deoxy-11,12-didehydroandrographolide
194		CHEBI:65408	Andrographolide
195		CHEBI:86612	Dihydroferulic acid
196		CHEBI:132373	Mesembryanthemoidigenic acid
197		CHEBI:142267	Methyl *N*-methylanthranilate
198		CHEBI:132830	Delta–elemene
199		CHEBI:65732	Decussatin
200	*Ocimum tenuiflorum*	CHEBI:17580	Linalool
201		CHEBI:7545	Nevadensin
202		CHEBI:63710	7-Epi-sesquithujene
203	*Vetiveria zizanioides*	CHEBI:138051	Selina–4(15),7(11)–diene
204	*Santalum album*	CHEBI:16714	Codeine
205		CHEBI:45373	Sulfanilamide
206		CHEBI:65460	Avicularin

Table 3 The list of phytochemical compounds found in the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM with ChEBI ID.—cont'd

S.·no	Name of the plant	ChEBI ID	Name of the compound
207	*Piper nigrum*	CHEBI:66757	Pipercyclobutanamide A(rel)
208		CHEBI:65684	(−)-cubebin
209		CHEBI:65685	(−)-3,4-dimethoxy-3,4-desmethylenedioxycubebin
210		CHEBI:28821	Piperine
211		CHEBI:69686	Pellitorine
212		CHEBI:67582	Gaudichaudianic acid, (−rac)
213		CHEBI:69675	Sarmentosumin A
214		CHEBI:69676	Sarmentosumin B
215		CHEBI:69677	Sarmentosumin C
216		CHEBI:69678	Sarmentosumin D
217		CHEBI:69679	Isochamanetin
218		CHEBI:69680	7-Methoxychamanetin
219		CHEBI:69681	Dichamanetin
220		CHEBI:69682	7-Methoxydichamanetin
221		CHEBI:69683	5″-(2‴‴-Hydroxybenzyl)uvarinol
222		CHEBI:69687	2,4-Dodecadienamide
223		CHEBI:69689	7-Methoxyisochamanetin
224		CHEBI:70083	(2E,4E)-N-[2-(methylsulfinyl)ethyl]-2,4-decadienamide
225		CHEBI:70084	(2E,4E)-N-[(4-hydroxy-3-methoxyphenyl)ethyl]-2,4-decadienamide
226		CHEBI:70085	3-(4-hydroxy-3,5-dimethoxyphenyl)propanoylpyrrole
227		CHEBI:70086	3-(3,4,5-timethoxyphenyl)propanoylpyrrole
228		CHEBI:70087	1-[(2E,4E,6E)-2,4,6-dodecatrienoyl]pyrrolidine

Continued

Table 3 The list of phytochemical compounds found in the plant involved
in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM with
ChEBI ID.—cont'd

S.·no	Name of the plant	ChEBI ID	Name of the compound
229		CHEBI:70088	1–[(2E,4Z,8E)–9–(3,4–methylenedioxyphenyl)–2,4,8–nonatrienoyl]pyrrolidine
230		CHEBI:70089	1–[(2E,4E,10E)–10–(3,4–methylenedioxyphenyl)–2,4,10–undecatrienoyl]pyrrolidine
231		CHEBI:70090	1–[(4E,10E)–11–(3,4–methylenedioxyphenyl)–4,10–undecadienoyl]pyrrolidine
232		CHEBI:70091	1–[(9E)–10–(3,4–methylenedioxyphenyl)–9–decenoyl]pyrrolidine
233		CHEBI:70092	1–[(2E,4E)–2,4–decadienoyl]pyrrolidine
234		CHEBI:70093	1–[(2E,4E)–2,4–dodecadienoyl]pyrrolidine
235		CHEBI:70094	1–[(2E)–7–(3,4–methylenedioxyphenyl)–2–heptenoyl]pyrrolidine
236		CHEBI:70095	1–[(2E,4E)–7–(3,4–methylenedioxyphenyl)–2,4–heptadienoyl]pyrrolidine
237		CHEBI:70096	1–[(2E,8E)–9–(3,4–methylenedioxyphenyl)–2,8–nonadienoyl]pyrrolidine
238		CHEBI:70097	1–[(8E)–9–(3,4–methylenedioxyphenyl)–8–nonenoyl]pyrrolidine
239		CHEBI:70098	1–[(2E,4E,8E)–9–(3,4–methylenedioxyphenyl)–2,4,8–nonatrienoyl]pyrrolidine
240		CHEBI:70099	1–[(2E,4E)–11–(3,4–methylenedioxyphenyl)–2,4–undecadienoyl]pyrrolidine
241		CHEBI:70100	1–[(2E,10E)–11–(3,4–methylenedioxyphenyl)–2,10–undecadienoyl]pyrrolidine

Table 3 The list of phytochemical compounds found in the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM with ChEBI ID.—cont'd

S.·no	Name of the plant	ChEBI ID	Name of the compound
242		CHEBI:70101	(2E,4E)–N–isobutyl–2,4-dodecadienamide
243		CHEBI:70102	(2E,4E)–N–isobutyl–7–(3,4-methylenedioxyphenyl)–hepta–2,4–dienamide
244		CHEBI:70103	(8E)–N–isobutyl–9–(3,4-methylenedioxyphenyl)nona–8–enamide
245		CHEBI:70104	(2E,4E,8E)–N–isobutyl–11–(3,4-methylenedioxyphenyl)undeca–2,4,8–trienamide
246		CHEBI:70105	N-trans-sinapoyltyramine
247		CHEBI:70490	Dihydrocubebin, rel–
248		CHEBI:70491	Justiflorinol
249		CHEBI:70485	(−)-Sanguinolignan A
250		CHEBI:70486	(−)-Sanguinolignan B
251		CHEBI:70487	(−)-Sanguinolignan C
252		CHEBI:70488	(−)-Sanguinolignan D
253		CHEBI:70489	(7′S)-parabenzlactone
254		CHEBI:65899	Flavokawain B
255		CHEBI:66709	Methyl 3,4-dihydroxy-5-(3′-methyl-2′-butenyl)benzoate
256		CHEBI:69688	Pipercallosidine
257		CHEBI:132651	Kadsurenin C
258		CHEBI:132652	Kadsurenin K
259		CHEBI:132653	Kadsurenin L
260		CHEBI:69685	Pipercallosine
261		CHEBI:70483	(S)-1′-methylhexyl caffeate
262		CHEBI:132647	Futoenone
263		CHEBI:70482	(S)-1′-methylbutyl caffeate

Table 3 The list of phytochemical compounds found in the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM with ChEBI ID.—cont'd

S. no	Name of the plant	ChEBI ID	Name of the compound
264		CHEBI:70484	(S)-1′-methyloctyl caffeate
265		CHEBI:65937	Futokadsurin B
266		CHEBI:65938	Futokadsurin C
267		CHEBI:65936	Futokadsurin A
268		CHEBI:132650	Burchellin
269		CHEBI:8240	Piperonal
270		CHEBI:156224	(−)-Cubenol
271		CHEBI:37316	(E,E)-piperic acid
272		CHEBI:35697	Trans-cinnamic acid
273		CHEBI:80484	Pinocembrin chalcone
274		CHEBI:132657	Piperlactam S
275		CHEBI:2871	Asebogenin
276		CHEBI:51226	Epicocconone
277		CHEBI:66470	(+)-Sesamin
278		CHEBI:132658	Pipataline
279		CHEBI:143911	(−)-Antofine
280		CHEBI:30746	Benzoic acid
281		CHEBI:88764	Ethyl butyrate
282		CHEBI:17818	N–feruloyltyramine
283		CHEBI:132654	Kadsurenin M
284		CHEBI:156227	(−)-Epicubenol
285		CHEBI:70626	Acacetin-8-C-neohesperidoside
286		CHEBI:70148	Monocerin
287		CHEBI:70149	(2S,3aR,9bR)-6,7-dihydroxy-8-methoxy-2-propyl-3,3a-dihydro-2H-furo[3,2-c]isochromen-5(9bH)-one
288		CHEBI:70150	Fusarentin 6,7-dimethyl ether
289		CHEBI:70151	Fusarentin 6-methyl ether

Table 3 The list of phytochemical compounds found in the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM with ChEBI ID.—cont'd

S.·no	Name of the plant	ChEBI ID	Name of the compound
290		CHEBI:70152	(3R,4R)-4,8-dihydroxy-3-((R)-2-hydroxypentyl)-6,7-dimethoxyisochroman-1-one
291		CHEBI:70153	Colletotrialide, (+)-
292		CHEBI:132648	Galgravin
293		CHEBI:133381	9,10-Epoxy-18-hydroxyoctadecanoic acid
294		CHEBI:28157	Pinocembrin
295		CHEBI:80788	1,4-Cineole
296		CHEBI:113455	Sodium benzoate
297		CHEBI:133325	9,10,18-Trihydroxyoctadecanoic acid
298		CHEBI:6116	Kavapyrone
299		CHEBI:10224	Alpha-cubebene
300		CHEBI:132649	Acuminatin
301	*Hedyotis corymbosa*	CHEBI:66123	Jerantinine E
302		CHEBI:66124	Jerantinine F
303		CHEBI:66121	Jerantinine C
304		CHEBI:66120	Jerantinine B
305		CHEBI:66122	Jerantinine D
306		CHEBI:66119	Jerantinine A
307		CHEBI:142075	Tabernaemontanine
308		CHEBI:6682	Mangiferin
309	*Plectranthus vettiveroides*	CHEBI:66763	Plectranthol A
310		CHEBI:66764	Plectranthol B
311		CHEBI:138963	11,20-Dihydroxysugiol
312		CHEBI:138962	11-Hydroxysugiol
313		CHEBI:86062	Abietatriene
314	*Trichosanthes cucumerina*	CHEBI:66838	7-Oxo-10α-cucurbitadienol

Table 4 The Lipinski rule calculation for the phytochemical compounds of the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM.

S.·no	Compounds	MW	#H-bond acceptors	#H-bond donors	iLOGP	Lipinski #violations
1	Gingerenone B	386.44	6	2	3.7	0
2	Beta-sesquiphellandrene	204.35	0	0	3.65	1
3	3-(3,4-Dimethoxyphenyl)-4-[(Z)-3, 4-dimethoxystyryl]cyclohex-1-ene	380.48	4	0	4.43	0
4	3-(3,4-Dimethoxyphenyl)-4-[(E)-3,4-dimethoxystyryl]cyclohex-1-ene	380.48	4	0	4.43	0
5	Pinocarveol	152.23	1	1	2.12	0
6	Zerumboneoxide	234.33	2	0	2.71	0
7	Ramonanin A, (rel)-	680.74	10	4	4.14	1
8	Ramonanin B, (rel)-	680.74	10	4	4.51	1
9	Ramonanin C, (rel)-	680.74	10	4	4.5	1
10	Ramonanin D, (rel)-	680.74	10	4	5.29	1
11	Zerumbone	218.33	1	0	2.72	0
12	5-Hydroxyzerumbone	234.33	2	1	2.14	0
13	(2E,6E)-hedycaryol	222.37	1	1	3.05	0
14	Dodecane	170.33	0	0	3.82	1
15	7,4′-Dimethylkaempferol	314.29	6	2	2.94	0

16	Zingiberene	204.35	0	0	3.63	1
17	Glucoputranjivin(1–)	360.38	10	4	0.86	0
18	Glucoputranjivin	361.39	10	5	0.14	0
19	All-cis-octadeca-6,9,12,15-tetraenoic acid	276.41	2	1	3.29	1
20	Pipataline	288.42	2	0	4.61	1
21	Pipercyclobutanamide A(rel)	570.68	6	0	5.26	1
22	pellitorine	223.35	1	1	3.61	0
23	Gaudichaudianic acid, (−rac)	340.46	3	1	3.85	1
24	Sarmentosumin A	680.74	8	6	3.7	2
25	Sarmentosumin B	680.74	8	6	3.97	2
26	Sarmentosumin C	786.86	9	7	4.13	3
27	Sarmentosumin D	786.86	9	7	4.06	3
28	Isochamanetin	362.38	5	3	2.68	0
29	7-Methoxychamanetin	376.4	5	2	3.2	0
30	Dichamanetin	468.5	6	4	3.01	0
31	7-Methoxydichamanetin	482.52	6	3	3.58	0
32	5″-(2⁗-Hydroxybenzyl)uvarinol	694.77	8	5	4.16	1
33	2,4-Dodecadienamide	195.3	1	1	2.87	0
34	7-Methoxyisochamanetin	376.4	5	2	3.5	0

Table 4 The Lipinski rule calculation for the phytochemical compounds of the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM.—cont'd

S.·no	Compounds	MW	#H-bond acceptors	#H-bond donors	iLOGP	Lipinski #violations
35	(2E,4E)–N–[2-(methylsulfinyl)ethyl]–2,4-decadienamide	257.39	2	1	3.05	0
36	(2E,4E)–N–[(4-hydroxy-3-methoxyphenyl)ethyl]–2,4-decadienamide	317.42	3	2	3.76	0
37	3-(4-Hydroxy-3,5-dimethoxyphenyl)propanoylpyrrole	275.3	4	1	2.63	0
38	3-(3,4,5-Timethoxyphenyl)propanoylpyrrole	289.33	4	0	3.21	0
39	1-[(2E,4E,6E)-2,4,6-dodecatrienoyl]pyrrolidine	247.38	1	0	3.86	0
40	1-[(2E,4Z,8E)-9-(3,4-methylenedioxyphenyl)-2,4,8-nonatrienoyl]pyrrolidine	325.4	3	0	3.88	0
41	1-[(2E,4E,10E)-10-(3,4-methylenedioxyphenyl)-2,4,10-undecatrienoyl]pyrrolidine	353.45	3	0	4.53	0
42	1-[(4E,10E)-11-(3,4-methylenedioxyphenyl)-4,10-undecadienoyl]pyrrolidine	355.47	3	0	4.6	0
43	1-[(9E)-10-(3,4-methylenedioxyphenyl)-9-decenoyl]pyrrolidine	343.46	3	0	4.43	0
44	1-[(2E,4E)-2,4-decadienoyl]pyrrolidine	221.34	1	0	3.45	0
45	1-[(2E,4E)-2,4-dodecadienoyl]pyrrolidine	249.39	1	0	3.95	0
46	1-[(2E)-7-(3,4-methylenedioxyphenyl)-2-heptenoyl]pyrrolidine	301.38	3	0	3.64	0
47	1-[(2E,4E)-7-(3,4-methylenedioxyphenyl)-2,4-heptadienoyl]pyrrolidine	299.36	3	0	3.65	0

48	1-[(2E,8E)-9-(3,4-methylenedioxyphenyl)-2,8-nonadienoyl] pyrrolidine	327.42	3	0	4.04	0
49	1-[(8E)-9-(3,4-methylenedioxyphenyl)-8-nonenoyl]pyrrolidine	329.43	3	0	4.16	0
50	1-[(2E,4E,8E)-9-(3,4-methylenedioxyphenyl)-2,4,8-nonatrienoyl] pyrrolidine	325.4	3	0	3.88	0
51	1-[(2E,4E)-11-(3,4-methylenedioxyphenyl)-2,4-undecadienoyl] pyrrolidine	355.47	3	0	4.51	0
52	1-[(2E,10E)-11-(3,4-methylenedioxyphenyl)-2,10-undecadienoyl] pyrrolidine	355.47	3	0	4.16	0
53	(2E,4E)-N-isobutyl-2,4-dodecadienamide	251.41	1	1	4.06	0
54	(2E,4E)-N-isobutyl-7-(3,4-methylenedioxyphenyl)-hepta-2,4-dienamide	301.38	3	1	3.67	0
55	(8E)-N-isobutyl-9-(3,4-methylenedioxyphenyl)nona-8-enamide	331.45	3	1	4.18	0
56	(2E,4E,8E)-N-isobutyl-11-(3,4-methylenedioxyphenyl)undeca-2,4,8-trienamide	355.47	3	1	4.42	0
57	N-trans-sinapoyltyramine	343.37	5	3	2.71	0
58	Dihydrocubebin, rel-	358.39	6	2	3.19	0
59	Justiflorinol	356.33	7	1	2.76	0
60	(−)-Sanguinolignan A	384.34	8	1	2.82	0
61	(−)-Sanguinolignan B	384.34	8	1	2.79	0
62	(−)-Sanguinolignan C	442.42	9	0	3.36	0

Table 4 The Lipinski rule calculation for the phytochemical compounds of the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM.—cont'd

S.·no	Compounds	MW	#H-bond acceptors	#H-bond donors	iLOGP	Lipinski #violations
63	(−)-Sanguinolignan D	426.37	9	0	2.74	0
64	(7′S)-parabenzlactone	370.35	7	1	3.12	0
65	Flavokawain B	284.31	4	1	2.63	0
66	Methyl 3,4-dihydroxy-5-(3′-methyl-2′-butenyl)benzoate	236.26	4	2	2.62	0
67	Pipercallosidine	303.4	3	1	3.76	0
68	Kadsurenin C	358.43	5	1	3.37	0
69	Kadsurenin K	342.39	5	1	3.02	0
70	Kadsurenin L	400.46	6	0	3.42	0
71	Pipercallosine	329.43	3	1	4.04	0
72	(S)-1′-methylhexyl caffeate	278.34	4	2	3.41	0
73	Futoenone	340.37	5	0	3.15	0
74	(−)-Cubebin	356.37	6	1	3.18	0
75	(−)-3,4-Dimethoxy-3,4-desmethylenedioxycubebin	372.41	6	1	3.06	0
76	(S)-1′-methylbutyl caffeate	250.29	4	2	2.81	0
77	(S)-1′-methyloctyl caffeate	306.4	4	2	3.66	0
78	Futokadsurin B	356.41	5	0	3.89	0
79	Futokadsurin C	356.41	5	0	3.77	0

80	Piperine	285.34	3	0	3.42	0
81	Futokadsurin A	358.43	5	1	3.46	0
82	Burchellin	340.37	5	0	3.26	0
83	Trans-cinnamic acid	148.16	2	1	1.55	0
84	Pinocembrin chalcone	256.25	4	3	1.09	0
85	Piperlactam S	295.29	4	1	2.54	0
86	Asebogenin	288.3	5	3	1.97	0
87	(+)-Sesamin	354.35	6	0	3.46	0
88	Benzoic acid	122.12	2	1	1.11	0
89	N-feruloyltyramine	313.35	4	3	2.58	0
90	Kadsurenin M	328.36	5	0	3.15	0
91	(−)-Epicubenol	222.37	1	1	3.11	0
92	Acacetin-8-C-neohesperidoside	592.55	14	8	1.49	3
93	Monocerin	308.33	6	1	2.99	0
94	(2S,3aR,9bR)-6,7-dihydroxy-8-methoxy-2-propyl-3,3a-dihydro-2H-furo[3,2-c]isochromen-5(9bH)-one	294.3	6	2	2.51	0
95	Fusarentin 6,7-dimethyl ether	310.34	6	2	2.85	0
96	Fusarentin 6-methyl ether	296.32	6	3	2.27	0
97	(3R,4R)-4,8-dihydroxy-3-((R)-2-hydroxypentyl)-6,7-dimethoxyisochroman-1-one	326.34	7	3	2.59	0

Table 4 The Lipinski rule calculation for the phytochemical compounds of the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM.—cont'd

S.·no	Compounds	MW	#H-bond acceptors	#H-bond donors	iLOGP	Lipinski #violations
98	Colletotrialide, (+)-	308.33	6	1	2.49	0
99	Galgravin	372.45	5	0	3.97	0
100	Piperonal	150.13	3	0	1.6	0
101	Pinocembrin	256.25	4	2	2.11	0
102	1,4-Cineole	154.25	1	0	2.68	0
103	Sodium benzoate	144.1	2	0	−11.15	0
104	(−)-Cubenol	222.37	1	1	3.24	0
105	(E,E)-piperic acid	218.21	4	1	2.2	0
106	Kavapyrone	244.24	4	0	2.6	0
107	Alpha-cubebene	204.35	0	0	3.4	1
108	Acuminatin	340.41	4	0	4.05	0
109	Betulin di(3-carboxybutanoate)	670.92	8	2	4.69	2
110	Dihydrobetulinic acid	458.72	3	2	3.91	1
111	Bevirimat	584.83	6	2	4.25	2
112	Platanic acid	458.67	4	2	3.52	1
113	Canophyllal	440.7	2	0	4.07	1
114	Cinnamic acid	148.16	2	1	1.55	0

115	Cinnamtannin D-1	864.76	18	14	2.04	3
116	Cassiatannin A	1153.01	24	19	2.75	3
117	Cinnamtannin B-1	864.76	18	14	2.25	3
118	Parameritannin A-1	1153.01	24	19	2.6	3
119	Methyl linolenate	292.46	2	0	4.94	1
120	Zerumbone	218.33	1	0	2.72	0
121	(Z)-3-phenyl-2-propenal	132.16	1	0	1.65	0
122	(E)-2-methoxcinnamic acid	178.18	3	1	1.76	0
123	Betulinic acid	456.7	3	2	3.81	1
124	Heptacosan-1-ol	396.73	1	1	6.93	1
125	Pyrethrin I	328.45	3	0	4.22	0
126	Pyrethrin II	372.45	5	0	4.2	0
127	14-Deoxy-11,12-didehydroandrographolide	332.43	4	2	3.07	0
128	Andrographolide	350.45	5	3	2.61	0
129	Dihydroferulic acid	196.2	4	2	1.62	0
130	Mesembryanthemoidigenic acid	472.7	4	3	3.56	1
131	Methyl N-methylanthranilate	165.19	2	1	2.02	0
132	Delta-elemene	204.35	0	0	3.43	1
133	Decussatin	302.28	6	1	2.96	0

Table 4 The Lipinski rule calculation for the phytochemical compounds of the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM.—cont'd

S.·no	Compounds	MW	#H-bond acceptors	#H-bond donors	iLOGP	Lipinski #violations
134	Capensinidin	345.32	7	3	−0.95	0
135	Termilignan B	294.34	3	1	2.74	0
136	(Z)-9-hydroxybenzo[c]oxepin-3(1H)-one	176.17	3	1	1.37	0
137	Cyclosordariolone, (rac)-	220.22	4	3	1.44	0
138	(R)-3-Hydroxy-1-[(R)-4-hydroxy-1,3-dihydroisobenzofuran-1-yl]butan-2-one	222.24	4	2	1.7	0
139	(R)-3-Hydroxy-1-[(S)-4-hydroxy-1,3-dihydroisobenzofuran-1-yl]butan-2-one	222.24	4	2	1.51	0
140	(E)-2-(Hydroxymethyl)-3-(4-hydroxypent-1-enyl)phenol	208.25	3	3	1.99	0
141	1-(3,9-Dihydroxy-1,3-dihydrobenzo[c]oxepin-3-yl)ethanone, (rac)-	220.22	4	2	1.53	0
142	Pestalospirane A	408.44	6	2	2.89	0
143	Pestalospirane B	408.44	6	2	3.02	0
144	Methyl 3,4,5-trihydroxybenzoate	184.15	5	3	0.96	0
145	Ursolic acid	456.7	3	2	3.95	1
146	Arecoline	155.19	3	0	2.26	0
147	Propyl benzoate	164.2	2	0	2.46	0
148	Plectranthol A	450.52	6	4	3.49	0

149	Plectranthol B	536.66	7	3	4.59	2
150	11,20-Dihydroxysugiol	332.43	4	3	2.87	0
151	11-Hydroxysugiol	316.43	3	2	3.15	0
152	Abietatriene	270.45	0	0	3.86	1
153	1beta-hydroxy arbusculin A	266.33	4	2	2.23	0
154	Alantolactone	232.32	2	0	2.71	0
155	Dehydrocostus lactone	230.3	2	0	2.67	0
156	Costunolide	232.32	2	0	2.72	0
157	Matairesinoside	520.53	11	5	2.37	2
158	3-Hydroxyhexane-2,5-dione	130.14	3	1	0.6	0
159	Heptacosan-1-ol	396.73	1	1	6.93	1
160	6-Hydroxyluteolin 7-O-laminaribioside	626.52	17	11	1.44	3
161	Cyclotetradecane	196.37	0	0	3.35	1
162	Cycloeucalenone	424.7	1	0	4.98	1
163	Rubimaillin	284.31	4	1	2.87	0
164	Canophyllal	440.7	2	0	4.07	1
165	Stepharanine	324.35	4	2	-0.53	0
166	(Z)-icos-13-enoic acid	310.51	2	1	4.26	1
167	Methyl 3,4,5-trihydroxybenzoate	184.15	5	3	0.96	0

Continued

Table 4 The Lipinski rule calculation for the phytochemical compounds of the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM.—cont'd

S.·no	Compounds	MW	#H-bond acceptors	#H-bond donors	iLOGP	Lipinski #violations
168	Serratol	290.48	1	1	3.82	1
169	Huperzine A	242.32	2	2	2.42	0
170	Maytansine	692.2	10	2	4.27	2
171	Mustakone	218.33	1	0	2.95	0
172	(+)-nootkatone	218.33	1	0	2.83	0
173	Pectenotoxin-11	875.05	15	4	4.09	2
174	Dinophysistoxin 2	805	13	5	6.22	2
175	1-Icosanoylglycerol	386.61	4	2	4.71	0
176	Swertisin	446.4	10	6	2.5	1
177	Serratol	290.48	1	1	3.82	1
178	Raffinose	504.44	16	11	1.12	3
179	PLX-4720	413.83	6	2	2.42	0
180	Huperzine A	242.32	2	2	2.42	0
181	Maytansine	692.2	10	2	4.27	2
182	N-(2-methoxyethyl)-4-{[6-(pyridin-4-yl)quinazolin-2-yl]amino}benzamide	399.45	5	2	2.8	0
183	Glucotropeolin	409.43	10	5	0.57	0

184	Glucotropeolin(1-)	408.42	10	4	1.04	0
185	Methyl 12-methyltetradecanoate	256.42	2	0	4.08	1
186	(3S,5R,6S)-beta-cryptoxanthin 5,6-epoxide	568.87	2	1	7.8	2
187	Carpaine	478.71	6	2	4.4	0
188	Beta-cryptoxanthin	552.87	1	1	7.6	2
189	24-Methylenecycloartanol	440.74	1	1	5.31	1
190	Helvolic acid methyl ester	582.72	8	0	4.5	1
191	Danielone	212.2	5	2	1.63	0
192	2-Isobutylthiazole	141.23	1	0	2.37	0
193	14-Deoxy-11,12-didehydroandrographolide	332.43	4	2	3.07	0
194	Andrographolide	350.45	5	3	2.61	0
195	Dihydroferulic acid	196.2	4	2	1.62	0
196	Mesembryanthemoidigenic acid	472.7	4	3	3.56	1
197	Methyl *N*-methylanthranilate	165.19	2	1	2.02	0
198	Delta-elemene	204.35	0	0	3.43	1
199	Decussatin	302.28	6	1	2.96	0
200	Linalool	154.25	1	1	2.7	0
201	Nevadensin	344.32	7	2	3	0
202	7-Epi-sesquithujene	204.35	0	0	3.37	1

Table 4 The Lipinski rule calculation for the phytochemical compounds of the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM.—cont'd

S.·no	Compounds	MW	#H-bond acceptors	#H-bond donors	iLOGP	Lipinski #violations
203	Selina-4(15),7(11)–diene	204.35	0	0	3.31	1
204	Codeine	299.36	4	1	2.67	0
205	Sulfanilamide	172.2	3	2	0.61	0
206	Avicularin	434.35	11	7	1.86	2
207	Pipercyclobutanamide A(rel)	570.68	6	0	5.26	1
208	(−)-Cubebin	356.37	6	1	3.18	0
209	(−)-3,4-Dimethoxy-3,4-desmethylenedioxycubebin	372.41	6	1	3.06	0
210	Piperine	285.34	3	0	3.42	0
211	Pellitorine	223.35	1	1	3.61	0
212	Gaudichaudianic acid, (−rac)	340.46	3	1	3.85	1
213	Sarmentosumin A	680.74	8	6	3.7	2
214	Sarmentosumin B	680.74	8	6	3.97	2
215	Sarmentosumin C	786.86	9	7	4.13	3
216	Sarmentosumin D	786.86	9	7	4.06	3
217	Isochamanetin	362.38	5	3	2.68	0
218	7-Methoxychamanetin	376.4	5	2	3.2	0
219	Dichamanetin	468.5	6	4	3.01	0

220	7-Methoxydichamanetin	482.52	6	3	3.58	0
221	5″-(2‴′-Hydroxybenzyl)uvarinol	694.77	8	5	4.16	1
222	2,4-Dodecadienamide	195.3	1	1	2.87	0
223	7-Methoxyisochamanetin	376.4	5	2	3.5	0
224	(2E,4E)-N-[2-(methylsulfinyl)ethyl]-2,4-decadienamide	257.39	2	1	3.05	0
225	(2E,4E)-N-[(4-hydroxy-3-methoxyphenyl)ethyl]-2,4-decadienamide	317.42	3	2	3.76	0
226	3-(4-Hydroxy-3,5-dimethoxyphenyl)propanoylpyrrole	275.3	4	1	2.63	0
227	3-(3,4,5-Timethoxyphenyl)propanoylpyrrole	289.33	4	0	3.21	0
228	1-[(2E,4E,6E)-2,4,6-dodecatrienoyl]pyrrolidine	247.38	1	0	3.86	0
229	1-[(2E,4Z,8E)-9-(3,4-methylenedioxyphenyl)-2,4,8-nonatrienoyl]pyrrolidine	325.4	3	0	3.88	0
230	1-[(2E,4E,10E)-10-(3,4-methylenedioxyphenyl)-2,4,10-undecatrienoyl]pyrrolidine	353.45	3	0	4.53	0
231	1-[(4E,10E)-11-(3,4-methylenedioxyphenyl)-4,10-undecadienoyl]pyrrolidine	355.47	3	0	4.6	0
232	1-[(9E)-10-(3,4-methylenedioxyphenyl)-9-decenoyl]pyrrolidine	343.46	3	0	4.43	0
233	1-[(2E,4E)-2,4-decadienoyl]pyrrolidine	221.34	1	0	3.45	0
234	1-[(2E,4E)-2,4-dodecadienoyl]pyrrolidine	249.39	1	0	3.95	0
235	1-[(2E)-7-(3,4-methylenedioxyphenyl)-2-heptenoyl]pyrrolidine	301.38	3	0	3.64	0

Table 4 The Lipinski rule calculation for the phytochemical compounds of the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM.—cont'd

S.·no	Compounds	MW	#H-bond acceptors	#H-bond donors	iLOGP	Lipinski #violations
236	1–[(2E,4E)–7–(3,4–methylenedioxyphenyl)–2,4–heptadienoyl] pyrrolidine	299.36	3	0	3.65	0
237	1–[(2E,8E)–9–(3,4–methylenedioxyphenyl)–2,8–nonadienoyl] pyrrolidine	327.42	3	0	4.04	0
238	1–[(8E)–9–(3,4–methylenedioxyphenyl)–8–nonenoyl]pyrrolidine	329.43	3	0	4.16	0
239	1–[(2E,4E,8E)–9–(3,4–methylenedioxyphenyl)–2,4,8–nonatrienoyl] pyrrolidine	325.4	3	0	3.88	0
240	1–[(2E,4E)–11–(3,4–methylenedioxyphenyl)–2,4–undecadienoyl] pyrrolidine	355.47	3	0	4.51	0
241	1–[(2E,10E)–11–(3,4–methylenedioxyphenyl)–2,10–undecadienoyl] pyrrolidine	355.47	3	0	4.16	0
242	(2E,4E)–N–isobutyl–2,4–dodecadienamide	251.41	1	1	4.06	0
243	(2E,4E)–N–isobutyl–7–(3,4–methylenedioxyphenyl)– hepta–2,4–dienamide	301.38	3	1	3.67	0
244	(8E)–N–isobutyl–9–(3,4–methylenedioxyphenyl)nona–8–enamide	331.45	3	1	4.18	0
245	(2E,4E,8E)–N–isobutyl–11–(3,4–methylenedioxyphenyl)undeca– 2,4,8–trienamide	355.47	3	1	4.42	0
246	N–trans–sinapoyltyramine	343.37	5	3	2.71	0
247	Dihydrocubebin, rel–	358.39	6	2	3.19	0

248	Justiflorinol	356.33	7	1	2.76	0
249	(−)-Sanguinolignan A	384.34	8	1	2.82	0
250	(−)-Sanguinolignan B	384.34	8	1	2.79	0
251	(−)-Sanguinolignan C	442.42	9	0	3.36	0
252	(−)-Sanguinolignan D	426.37	9	0	2.74	0
253	(7′S)-parabenzlactone	370.35	7	1	3.12	0
254	Flavokawain B	284.31	4	1	2.63	0
255	Methyl 3,4-dihydroxy-5-(3′-methyl-2′-butenyl)benzoate	236.26	4	2	2.62	0
256	Pipercallosidine	303.4	3	1	3.76	0
257	Kadsurenin C	358.43	5	1	3.37	0
258	Kadsurenin K	342.39	5	1	3.02	0
259	Kadsurenin L	400.46	6	0	3.42	0
260	Pipercallosine	329.43	3	1	4.04	0
261	(S)-1′-methylhexyl caffeate	278.34	4	2	3.41	0
262	Futoenone	340.37	5	0	3.15	0
263	(S)-1′-methylbutyl caffeate	250.29	4	2	2.81	0
264	(S)-1′-methyloctyl caffeate	306.4	4	2	3.66	0
265	Futokadsurin B	356.41	5	0	3.89	0
266	Futokadsurin C	356.41	5	0	3.77	0

Table 4 The Lipinski rule calculation for the phytochemical compounds of the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM.—cont'd

S.·no	Compounds	MW	#H-bond acceptors	#H-bond donors	iLOGP	Lipinski #violations
267	Futokadsurin A	358.43	5	1	3.46	0
268	Burchellin	340.37	5	0	3.26	0
269	Piperonal	150.13	3	0	1.6	0
270	(−)-Cubenol	222.37	1	1	3.24	0
271	(E,E)-piperic acid	218.21	4	1	2.2	0
272	Trans-cinnamic acid	148.16	2	1	1.55	0
273	Pinocembrin chalcone	256.25	4	3	1.09	0
274	Piperlactam S	295.29	4	1	2.54	0
275	Asebogenin	288.3	5	3	1.97	0
276	Epicocconone	410.42	7	2	3.17	0
277	(+)-Sesamin	354.35	6	0	3.46	0
278	Pipataline	288.42	2	0	4.61	1
279	(−)-Antofine	363.45	4	0	3.8	0
280	Benzoic acid	122.12	2	1	1.11	0
281	Ethyl butyrate	116.16	2	0	1.9	0
282	N-feruloyltyramine	313.35	4	3	2.58	0
283	Kadsurenin M	328.36	5	0	3.15	0

284	(−)-Epicubenol	222.37	1	1	3.11	0
285	Acacetin-8-C-neohesperidoside	592.55	14	8	1.49	3
286	Monocerin	308.33	6	1	2.99	0
287	(2S,3aR,9bR)-6,7-dihydroxy-8-methoxy-2-propyl-3, 3a-dihydro-2H-furo[3,2-c]isochromen-5(9bH)-one	294.3	6	2	2.51	0
288	Fusarentin 6,7-dimethyl ether	310.34	6	2	2.85	0
289	Fusarentin 6-methyl ether	296.32	6	3	2.27	0
290	(3R,4R)-4,8-dihydroxy-3-((R)-2-hydroxypentyl)- 6,7-dimethoxyisochroman-1-one	326.34	7	3	2.59	0
291	Colletotrialide, (+)-	308.33	6	1	2.49	0
292	Galgravin	372.45	5	0	3.97	0
293	9,10-Epoxy-18-hydroxyoctadecanoic acid	314.46	4	2	3.8	0
294	Pinocembrin	256.25	4	2	2.11	0
295	1,4-Cineole	154.25	1	0	2.68	0
296	Sodium benzoate	144.1	2	0	−11.15	0
297	9,10,18-Trihydroxyoctadecanoic acid	332.48	5	4	3.25	0
298	Kavapyrone	244.24	4	0	2.6	0
299	Alpha-cubebene	204.35	0	0	3.4	1
300	Acuminatin	340.41	4	0	4.05	0
301	Jerantinine E	384.47	5	2	3.52	0

Table 4 The Lipinski rule calculation for the phytochemical compounds of the plant involved in the formulation of Nilavembu kudineer, Kabasura kudineer, and JACOM.—cont'd

S.·no	Compounds	MW	#H-bond acceptors	#H-bond donors	iLOGP	Lipinski #violations
302	Jerantinine F	398.45	6	2	3.4	0
303	Jerantinine C	396.44	5	2	3.13	0
304	Jerantinine B	398.45	6	2	3.29	0
305	Jerantinine D	412.44	6	2	3.07	0
306	Jerantinine A	382.45	5	2	3.49	0
307	Tabernaemontanine	354.44	4	1	2.79	0
308	Mangiferin	422.34	11	8	0.89	2
309	Plectranthol A	450.52	6	4	3.49	0
310	Plectranthol B	536.66	7	3	4.59	2
311	11,20-Dihydroxysugiol	332.43	4	3	2.87	0
312	11–Hydroxysugiol	316.43	3	2	3.15	0
313	Abietatriene	270.45	0	0	3.86	1
314	7–oxo–10α–cucurbitadienol	440.7	2	1	4.65	1

Table 5 The list of phytochemical those satisfies the Lipinski rule of 5 and their structures in SMILES format.

S.·no	Compound	SMILES (chEBI)
1	Gingerenone B	C=1(C(=CC=C(C1)CCC(/C=C/CCC=2C=C(C(=C(C2)OC)O)OC)=O)O)OC
2	Beta-sesquiphellandrene	[H][C@@]1(CCC(=C)C=C1)[C@@H](C)CCC=C(C)C
3	3-(3,4-Dimethoxyphenyl)-4-[(Z)-3, 4-dimethoxystyryl]cyclohex-1-ene	COc1ccc(\C=C/C2CCC=CC2c2ccc(OC)c(OC)c2)cc1OC
4	3-(3,4-Dimethoxyphenyl)-4-[(E)-3, 4-dimethoxystyryl]cyclohex-1-ene	COc1ccc(\C=C\C2CCC=CC2c2ccc(OC)c(OC)c2)cc1OC
5	Pinocarveol	CC1(C)C2CC(O)C(=C)C1C2
6	Zerumboneoxide	[H][C@]12CC(C)(C)\C=C\C(=O)\C(C)=C\CC[C@@]1(C)O2
7	Ramonanin A, (rel)-	COc1cc(ccc1O)[C@H]1O[C@@H](c2ccc(O)c(OC)c2)[C@@]2(CCC3=C(C2)[C@H](O[C@H]3c2ccc(O)c(OC)c2)c2ccc(O)c(OC)c2)C1=C
8	Ramonanin B, (rel)-	COc1cc(ccc1O)[C@@H]1O[C@H](c2ccc(O)c(OC)c2)[C@@]2(CCC3=C(C2)[C@H](O[C@H]3c2ccc(O)c(OC)c2)c2ccc(O)c(OC)c2)C1=C
9	Ramonanin C, (rel)-	COc1cc(ccc1O)[C@H]1O[C@@H](c2ccc(O)c(OC)c2)[C@@]2(CCC3=C(C2)[C@@H](O[C@@H]3c2ccc(O)c(OC)c2)c2ccc(O)c(OC)c2)C1=C
10	Ramonanin D, (rel)-	COc1cc(ccc1O)[C@H]1O[C@@H](c2ccc(O)c(OC)c2)[C@@]2(CCC3=C(C2)[C@H](O[C@@H]3c2ccc(O)c(OC)c2)c2ccc(O)c(OC)c2)C1=C

Table 5 The list of phytochemical those satisfies the Lipinski rule of 5 and their structures in SMILES format.—cont'd

S. no	Compound	SMILES (chEBI)
11	Zerumbone	C\C1=C/CC(C)(C)\C=C\C(=O)\C(C)=C\CC1
12	5-Hydroxyzerumbone	C\C1=C/CC(C)(C)\C=C\C(=O)\C(C)=C\C(O)C1
13	(2E,6E)-hedycaryol	C\C1=C/CC\C(C)=C\C[C@@H](CC1)C(C)(C)O
14	Dodecane	CCCCCCCCCCCC
15	7,4′-Dimethylkaempferol	C12=C(OC(C3=CC=C(OC)C=C3)=C(C1=O)O)C=C(OC)C=C2O
16	Zingiberene	[H][C@@]1(CC=C(C)C=C1)[C@@H](C)CCC=C(C)C
17	Glucoputranjivin(1-)	[C@H]1(O[C@@H]([C@@H](O)[C@@H]([C@H]1O)O)CO)S/C(=N\OS([O-])(=O)=O)/C(C)C
18	Glucoputranjivin	[C@H]1(O[C@@H]([C@@H](O)[C@@H]([C@H]1O)O)CO)S/C(=N\OS(O)(=O)=O)/C(C)C
19	All-cis-octadeca-6,9,12,15-tetraenoic acid	CC\C=C/C\C=C/C\C=C/C\C=C/CCCCC(O)=O
20	Pipataline	O1C=2C=C(\C=C\CCCCCCCCC)C=CC2OC1
21	Pipercyclobutanamide A(rel)	O=C(\C=C/[C@@H]1[C@@H](\C=C\c2ccc3OCOc3c2)[C@@H]([C@H]1c1ccc2OCOc2c1)C(=O)N1CCCCC1)N1CCCCC1
22	Pellitorine	CCCC\C=C\C=C\C(=O)NCC(C)C
23	Gaudichaudianic acid, (−rac)	CC(C)=CCCC1(C)Oc2c(CC=C(C)C)cc(cc2C=C1)C(O)=O
24	Isochamanetin	Oc1ccccc1Cc1c(O)cc2O[C@@H](CC(=O)c2c1O)c1ccccc1

25	7-Methoxychamanetin	COc1cc(*O*)c2C(=O)C[C@H](Oc2c1Cc1ccccc1O)c1ccccc1
26	Dichamanetin	Oc1ccccc1Cc1c(*O*)c(Cc2ccccc2O)c2O[C@@H](CC(=O)c2c1O)c1ccccc1
27	7-Methoxydichamanetin	COc1c(Cc2ccccc2O)c(*O*)c2C(=O)C[C@H](Oc2c1Cc1ccccc1O)c1ccccc1
28	5″-(2⁗-Hydroxybenzyl)uvarinol	COc1c(Cc2cc(Cc3ccccc3O)ccc2O)c(*O*)c2C(=O)C[C@H](Oc2c1Cc1cc(Cc2ccccc2O)ccc1O)c1ccccc1
29	2,4-Dodecadienamide	CCCCCCC\C=C\C=C\C(N)=O
30	7-Methoxyisochamanetin	COc1cc2O[C@@H](CC(=O)c2c(*O*)c1Cc1ccccc1O)c1ccccc1
31	(2E,4E)-N-[2-(methylsulfinyl)ethyl]-2,4-decadienamide	CCCCC\C=C\C=C\C(=O)NCCS(C)=O
32	(2E,4E)-N-[(4-hydroxy-3-methoxyphenyl)ethyl]-2,4-decadienamide	CCCCC\C=C\C=C\C(=O)NCCc1ccc(*O*)c(OC)c1
33	3-(4-Hydroxy-3,5-dimethoxyphenyl)propanoylpyrrole	COc1cc(CCC(=O)n2cccc2)cc(*OC*)c1O
34	3-(3,4,5-Timethoxyphenyl)propanoylpyrrole	COc1cc(CCC(=O)n2cccc2)cc(*OC*)c1OC
35	1-[(2E,4E,6E)-2,4,6-dodecatrienoyl]pyrrolidine	CCCCC\C=C\C=C\C=C\C(=O)N1CCCC1
36	1-[(2E,4Z,8E)-9-(3,4-methylenedioxyphenyl)-2,4,8-nonatrienoyl]pyrrolidine	O=C(\C=C\C=C/CC\C=C\c1ccc2OCOc2c1)N1CCCC1
37	1-[(2E,4E,10E)-10-(3,4-methylenedioxyphenyl)-2,4,10-undecatrienoyl]pyrrolidine	O=C(\C=C\C=C\CCCC\C=C\c1ccc2OCOc2c1)N1CCCC1

Table 5 The list of phytochemical those satisfies the Lipinski rule of 5 and their structures in SMILES format.—cont'd

S..no	Compound	SMILES (chEBI)
38	1-[(4E,10E)-11-(3,4-methylenedioxyphenyl)-4,10-undecadienoyl]pyrrolidine	O=C(CC\C=C\CCCC\C=C\c1ccc2OCOc2c1)N1CCCC1
39	1-[(9E)-10-(3,4-methylenedioxyphenyl)-9-decenoyl]pyrrolidine	O=C(CCCCCCC\C=C\c1ccc2OCOc2c1)N1CCCC1
40	1-[(2E,4E)-2,4-decadienoyl]pyrrolidine	CCCCC\C=C\C=C\C(=O)N1CCCC1
41	1-[(2E,4E)-2,4-dodecadienoyl]pyrrolidine	CCCCCCC\C=C\C=C\C(=O)N1CCCC1
42	1-[(2E)-7-(3,4-methylenedioxyphenyl)-2-heptenoyl]pyrrolidine	O=C(\C=C\CCCCc1ccc2OCOc2c1)N1CCCC1
43	1-[(2E,4E)-7-(3,4-methylenedioxyphenyl)-2,4-heptadienoyl]pyrrolidine	O=C(\C=C\C=C\CCc1ccc2OCOc2c1)N1CCCC1
44	1-[(2E,8E)-9-(3,4-methylenedioxyphenyl)-2,8-nonadienoyl]pyrrolidine	O=C(\C=C\CCCC\C=C\c1ccc2OCOc2c1)N1CCCC1
45	1-[(8E)-9-(3,4-methylenedioxyphenyl)-8-nonenoyl]pyrrolidine	O=C(CCCCCC\C=C\c1ccc2OCOc2c1)N1CCCC1
46	1-[(2E,4E,8E)-9-(3,4-methylenedioxyphenyl)-2,4,8-nonatrienoyl]pyrrolidine	O=C(\C=C\C=C\CC\C=C\c1ccc2OCOc2c1)N1CCCC1
47	1-[(2E,4E)-11-(3,4-methylenedioxyphenyl)-2,4-undecadienoyl]pyrrolidine	O=C(\C=C\C=C\CCCCCCc1ccc2OCOc2c1)N1CCCC1
48	1-[(2E,10E)-11-(3,4-methylenedioxyphenyl)-2,10-undecadienoyl]pyrrolidine	O=C(\C=C\CCCCCC\C=C\c1ccc2OCOc2c1)N1CCCC1

49	(2E,4E)-N-isobutyl-2,4-dodecadienamide	CCCCCCC\C=C\C=C\C(=O)NCC(*C*)C
50	(2E,4E)-N-isobutyl-7-(3,4-methylenedioxyphenyl)-hepta-2,4-dienamide	CC(*C*)CNC(=O)\C=C\C=C\CCc1ccc2OCOc2c1
51	(8E)-N-isobutyl-9-(3,4-methylenedioxyphenyl)nona-8-enamide	CC(*C*)CNC(=O)CCCCCC\C=C\c1ccc2OCOc2c1
52	(2E,4E,8E)-N-isobutyl-11-(3,4-methylenedioxyphenyl)undeca-2,4,8-trienamide	CC(*C*)CNC(=O)\C=C\C=C\CC\C=C\CCc1ccc2OCOc2c1
53	N-trans-sinapoyltyramine	COc1cc(cc(*OC*)c1O)\C=C\C(=O)NCCc1ccc(*O*)cc1
54	Dihydrocubebin, rel-	OC[C@@H](Cc1ccc2OCOc2c1)[C@@H](CO)Cc1ccc2OCOc2c1
55	Justiflorinol	OCC(CC(=O)c1ccc2OCOc2c1)C(=O)c1ccc2OCOc2c1
56	(−)-Sanguinolignan A	O[C@@H]([C@H]1COC(=O)[C@@H]1C(=O)c1ccc2OCOc2c1)c1ccc2OCOc2c1
57	(−)-Sanguinolignan B	O[C@@H]([C@@H]1COC(=O)[C@@H]1C(=O)c1ccc2OCOc2c1)c1ccc2OCOc2c1
58	(−)-Sanguinolignan C	COc1ccc(cc1OC)[C@@H](OC(C)=O)[C@H]1COC(=O)[C@@H]1C(=O)c1ccc2OCOc2c1
59	(−)-Sanguinolignan D	CC(=O)O[C@@H]([C@@H]1[C@H](COC1=O)C(=O)c1ccc2OCOc2c1)c1ccc2OCOc2c1
60	(7′S)-parabenzlactone	O[C@@H]([C@H]1COC(=O)[C@@H]1Cc1ccc2OCOc2c1)c1ccc2OCOc2c1
61	Flavokawain B	COc1cc(*O*)c(C(=O)\C=C\c2ccccc2)c(*OC*)c1

Continued

Table 5 The list of phytochemical those satisfies the Lipinski rule of 5 and their structures in SMILES format.—cont'd

S..no	Compound	SMILES (chEBI)
62	Methyl 3,4–dihydroxy–5–(3′–methyl–2′–butenyl)benzoate	COC(=O)c1cc(O)c(O)c(CC=C(C)C)c1
63	Pipercallosidine	C(/C=C/CCCC=1C=C2C(=CC1)OCO2)(NCC(C)C)=O
64	Kadsurenin C	O([C@@]12[C@@H]([C@H]([C@@]([C@H]1O)(C(=O)C(=C2)CC=C)[H])C3=CC(OC)=C(OC)C=C3)C)C
65	Kadsurenin K	O([C@@]12[C@@H]([C@H]([C@@](C1=O)(C(=O)C(=C2)CC=C)[H])C3=CC(OC)=C(O)C=C3)C)C
66	Kadsurenin L	O([C@@]12[C@@H]([C@H]([C@@]([C@@H]1OC(=O)C)(C(=O)C(=C2)CC=C)[H])C3=CC(OC)=C(OC)C=C3)C)C
67	Pipercallosine	C(/C=C/C=C/CCCC1=CC=C2C(=C1)OCO2)(=O)NCC(C)C
68	(S)–1′–methylhexyl caffeate	CCCCC[C@H](C)OC(=O)\C=C\c1ccc(O)c(O)c1
69	Futoenone	O1[C@@H]2C[C@@]3([C@@H]([C@H](C2)C4=CC=5OCOC5C=C4)C)C1=CC(=O)C(OC)=C3
70	(−)-Cubebin	[H][C@@]1(CO[C@H](O)[C@]1([H])Cc1ccc2OCOc2c1)Cc1ccc2OCOc2c1
71	(−)-3,4-Dimethoxy-3,4-desmethylenedioxycubebin	[H][C@@]1(COC(O)[C@]1([H])Cc1ccc2OCOc2c1)Cc1ccc(OC)c(OC)c1
72	(S)–1′–methylbutyl caffeate	CCC[C@H](C)OC(=O)\C=C\c1ccc(O)c(O)c1
73	(S)–1′–methyloctyl caffeate	CCCCCCC[C@H](C)OC(=O)\C=C\c1ccc(O)c(O)c1

74	Futokadsurin B	COc1ccc(cc1OC)[C@@H]1O[C@@H]([C@H](C)[C@H]1C)c1ccc2OCOc2c1
75	Futokadsurin C	COc1ccc(cc1OC)[C@H]1O[C@H]([C@H](C)[C@@H]1C)c1ccc2OCOc2c1
76	Piperine	O=C(\C=C\C=C\c1ccc2OCOc2c1)N1CCCCC1
77	Futokadsurin A	COc1cc(ccc1O)[C@@H]1O[C@@H]([C@@H](C)[C@@H]1C)c1ccc(OC)c(OC)c1
78	Burchellin	O1[C@@H]([C@H]([C@]2(C1=CC(=O)C(OC)=C2)CC=C)C)C3=CC=4OCOC4C=C3
79	Trans-cinnamic acid	OC(=O)\C=C\c1ccccc1
80	Pinocembrin chalcone	Oc1cc(O)c(C(=O)\C=C\c2ccccc2)c(O)c1
81	Piperlactam S	O(C=1C2=C3C(=CC=4C2=CC=CC4)N(C(C3=CC1O)=O)OC)C
82	Asebogenin	COc1cc(O)c(C(=O)CCc2ccc(O)cc2)c(O)c1
83	(+)-Sesamin	[C@]12([C@@]([C@H](OC1)C3=CC4=C(C=C3)OCO4)(CO[C@@H]2C5=CC6=C(C=C5)OCO6)[H])[H]
84	Benzoic acid	OC(=O)c1ccccc1
85	N-feruloyltyramine	COc1cc(\C=C\C(=O)NCCc2ccc(O)cc2)ccc1O
86	Kadsurenin M	O1[C@@H]([C@H](C2=C1C(OC)=CC(=C2)C(=O)[H])C)C3=CC(OC)=C(OC)C=C3
87	(−)-Epicubenol	[C@]12([C@@H](CC[C@H]([C@]2(CCC(=C1)C)O)C)C(C)C)[H]

Table 5 The list of phytochemical those satisfies the Lipinski rule of 5 and their structures in SMILES format.—cont'd

S. no	Compound	SMILES (chEBI)
88	Monocerin	[H][C@@]12C[C@H](CCC)O[C@]1([H])c1cc(OC)c(OC)c(O)c1C(=O)O2
89	(2S,3aR,9bR)–6,7-dihydroxy-8-methoxy-2-propyl-3,3a-dihydro-2H-furo [3,2-c]isochromen-5(9bH)-one	[H][C@@]12C[C@H](CCC)O[C@]1([H])c1cc(OC)c(O)c(O)c1C(=O)O2
90	Fusarentin 6,7-dimethyl ether	CCC[C@H](O)C[C@@H]1Cc2cc(OC)c(OC)c(O)c2C(=O)O1
91	Fusarentin 6-methyl ether	CCC[C@H](O)C[C@@H]1Cc2cc(OC)c(O)c(O)c2C(=O)O1
92	(3R,4R)–4,8-dihydroxy-3-((R)-2-hydroxypentyl)-6,7-dimethoxyisochroman-1-one	CCC[C@@H](O)C[C@H]1OC(=O)c2c(O)c(OC)c(OC)cc2[C@H]1O
93	Colletotrialide, (+)-	CCCC(=O)CC[C@H]1OC(=O)c2c(O)c(OC)c(OC)cc12
94	Galgravin	C1(=C(C=CC(=C1)[C@@H]2O[C@@H]([C@H]([C@H]2C)C)C3=CC=C(C(=C3)OC)OC)OC)OC
95	Piperonal	[H]C(=O)c1ccc2OCOc2c1
96	Pinocembrin	Oc1cc(O)c2C(=O)C[C@H](Oc2c1)c1ccccc1
97	1,4-Cineole	C1C[C@]2(CC[C@]1(C)O2)C(C)C
98	Sodium benzoate	C(C=1C=CC=CC1)([O-])=O.[Na+]
99	(−)-Cubenol	[C@]12([C@@H](CC[C@H]([C@@]2(CCC(=C1)C)O)C)C(C)C)[H]
100	(E,E)-piperic acid	OC(=O)\C=C\C=C\c1ccc2OCOc2c1

101	Kavapyrone	COc1cc(oc(=O)c1)[C@@H]1O[C@H]1c1ccccc1
102	Alpha-cubebene	C1C[C@H]([C@]2([C@]3([C@@H]1C)CC=C([C@]23[H])C)[H])C(*C*)C
103	Acuminatin	O1[C@H]([C@@H](C2=C1C(OC)=CC(=C2)/C=C/C)C)C3=CC(OC)=C(*OC*)C=C3
104	Dihydrobetulinic acid	[H][C@]12CC[C@]3([H])[C@@]4(C)CC[C@H](O)C(C)(C)[C@]4([H])CC[C@@]3(C)[C@]1(C)CC[C@]1(CC[C@@H](C(*C*)C)[C@]21[H])C(O)=O
105	Platanic acid	[H][C@]12CC[C@]3([H])[C@@]4(C)CC[C@H](O)C(C)(C)[C@]4([H])CC[C@@]3(C)[C@]1(C)CC[C@]1(CC[C@@H](C(C)=O)[C@]21[H])C(O)=O
106	Canophyllal	[C@]12([C@]([C@]3([C@@](CC1)(CCC(C3)(C)C)C(=O)[H])[H])(CC[C@@]4([C@@]2(CC[C@]5([C@]4(CCC([C@@H]5C)=O)[H])C)[H])C)C)C
107	Cinnamic acid	[H]C(=Cc1ccccc1)C(O)=O
108	Methyl linolenate	CC/C=C\C/C=C\C/C=C\CCCCCCC(=O)OC
109	Zerumbone	C\C1=C/CC(C)(C)\C=C\C(=O)\C(C)=C\CC1
110	(Z)-3-phenyl-2-propenal	C1=CC=C(C=C1)/C=C\C=O
111	(E)-2-methoxycinnamic acid	COC=1C=CC=CC1/C=C/C(=O)O
112	Betulinic acid	[H][C@]12CC[C@]3([H])[C@@]4(C)CC[C@H](O)C(C)(C)[C@]4([H])CC[C@@]3(C)[C@]1(C)CC[C@]1(CC[C@@H](C(C)=C)[C@]21[H])C(O)=O

Table 5 The list of phytochemical those satisfies the Lipinski rule of 5 and their structures in SMILES format.—cont'd

S..no	Compound	SMILES (chEBI)
113	Heptacosan-1-ol	C(CCCCCCCCCCCCCCCCO)CCCCCCCCCC
114	Pyrethrin I	CC(C)=C[C@@H]1[C@@H](C(=O)O[C@H]2CC(=O)C(C\C=C/C=C)=C2C)C1(C)C
115	Pyrethrin II	COC(=O)C(\C)=C\[C@@H]1[C@@H](C(=O)O[C@H]2CC(=O)C(C\C=C/C=C)=C2C)C1(C)C
116	14-Deoxy-11,12-didehydroandrographolide	[H][C@]12CCC(=C)[C@@H](\C=C\C3=CCOC3=O)[C@]1(C)CC[C@@H](O)[C@@]2(C)CO
117	Andrographolide	[H][C@]12CCC(=C)[C@@H](C\C=C3/[C@H](O)COC3=O)[C@]1(C)CC[C@@H](O)[C@@]2(C)CO
118	Dihydroferulic acid	C=1(C=C(C(=CC1)O)OC)CCC(=O)O
119	Mesembryanthemoidigenic acid	[C@@]12(C([C@@]3(C[C@@](CO)(C)CC[C@@]3(CC1)C(=O)O)[H])=CC[C@@]4([C@]5(CC[C@@H](C([C@@]5(CC[C@@]24C)[H])(C)C)O)C)[H])C
120	Methyl N-methylanthranilate	CNC1=CC=CC=C1C(OC)=O
121	Delta-elemene	[C@@H]1(C=C(CC[C@@]1(C=C)C)C(C)C)C(C)=C
122	Decussatin	COc1cc(O)c2c(c1)oc1ccc(OC)c(OC)c1c2=O
123	Capensinidin	COc1cc(cc(OC)c1O)-c1[o+]c2cc(O)cc(OC)c2cc1O
124	Termilignan B	Oc1ccc(CC(=C)C(=C)Cc2ccc3OCOc3c2)cc1
125	(Z)-9-hydroxybenzo[c]oxepin-3(1H)-one	Oc1cccc2C=CC(=O)OCc12

126	Cyclosordariolone, (rac)-	CC1(O)C(=O)C=Cc2c(CO)c(O)ccc12
127	(R)-3-Hydroxy-1-[(R)-4-hydroxy-1, 3-dihydroisobenzofuran-1-yl]butan-2-one	C[C@@H](O)C(=O)C[C@H]1OCc2c(O)cccc12
128	(R)-3-Hydroxy-1-[(S)-4-hydroxy-1, 3-dihydroisobenzofuran-1-yl]butan-2-one	C[C@@H](O)C(=O)C[C@@H]1OCc2c(O)cccc12
129	(E)-2-(Hydroxymethyl)-3- (4-hydroxypent-1-enyl)phenol	C[C@@H](O)C\C=C\c1cccc(O)c1CO
130	1-(3,9-Dihydroxy-1, 3-dihydrobenzo[c]oxepin-3-yl)ethanone, (rac)-	CC(=O)C1(O)OCc2c(O)cccc2C=C1
131	Pestalospirane A	C[C@H]1O[C@]2(OCc3c(O)cccc3C=C2)[C@@H](C)O[C@@] 11OCc2c(O)cccc2C=C1
132	Pestalospirane B	C[C@H]1O[C@]2(OCc3c(O)cccc3C=C2)[C@@H](C)O[C@] 11OCc2c(O)cccc2C=C1
133	Methyl 3,4,5-trihydroxybenzoate	OC1=CC(=CC(O)=C1O)C(OC)=O
134	Ursolic acid	C[C@@H]1CC[C@@]2(CC[C@]3(C)C(=CC[C@@H]4[C@@]5(C) CC[C@H](O)C(C)(C)[C@@H]5CC[C@@]34C)[C@@H]2[C@H] 1C)C(O)=O
135	Arecoline	COC(=O)C1=CCCN(C)C1
136	Propyl benzoate	C=1C=CC(=CC1)C(=O)OCCC
137	Plectranthol A	CC(C)c1cc2C=C[C@@]3(C)C(=CCC[C@]3(C)COC (=O)c3ccc(O)c(O)c3)c2c(O)c1O

Table 5 The list of phytochemical those satisfies the Lipinski rule of 5 and their structures in SMILES format.—cont'd

S. no	Compound	SMILES (chEBI)
138	11,20-Dihydroxysugiol	C1=C(C(C)C)C(=C(C2=C1C(C[C@@]3([C@@]2(CCCC3(C)C)CO)[H])=O)O)O
139	11-Hydroxysugiol	C1=C(C(C)C)C(=C(C2=C1C(C[C@@]3([C@@]2(CCCC3(C)C)C)[H])=O)O)O
140	Abietatriene	CC(C)c1ccc2c(CC[C@H]3C(C)(C)CCC[C@]23C)c1
141	1beta-hydroxy arbusculin A	[H][C@@]12CC[C@@]3(C)[C@H](O)CC[C@@](C)(O)[C@]3([H])[C@@]1([H])OC(=O)C2=C
142	Alantolactone	[H][C@@]12C[C@@]3(C)CCC[C@H](C)C3=C[C@]1([H])C(=C)C(=O)O2
143	Dehydrocostus lactone	[H][C@@]12CCC(=C)[C@]1([H])[C@H]1OC(=O)C(=C)[C@@H]1CCC2=C
144	Costunolide	C\C1=C/CC\C(C)=C\[C@H]2OC(=O)C(=C)[C@@H]2CC1
145	3-Hydroxyhexane-2,5-dione	CC(CC(C(C)=O)O)=O
146	Heptacosan-1-ol	C(CCCCCCCCCCCCCCCO)CCCCCCCCCC
147	Cyclotetradecane	C1CCCCCCCCCCCCC1
148	Cycloeucalenone	[C@]123CCC(=O)[C@@H](C)[C@]1([H])CC[C@]4([H])[C@@]2(C3)CC[C@@]5([C@](CC[C@@]45C)([C@@H](CCC(C(C)C)=C)C)[H])C
149	Rubimaillin	C12=CC=CC=C1C3=C(C(=C2O)C(OC)=O)C=CC(O3)(C)C

150	Canophyllal	[C@]12([C@]([C@]3([C@@](CC1)(CCC(C3)(C)C)C(=O)[H])[H])(CC[C@@]4([C@@]2(CC[C@]5([C@]4(CCC([C@@H]5C)=O)[H])C)[H])C)C)C
151	Stepharanine	O(C=1C2=C[N+]=3CCC=4C(C3C=C2C=CC1O)=CC(O)=C(*OC*)C4)C
152	(Z)-icos-13-enoic acid	CCCCCC/C=C\CCCCCCCCCCCC(O)=O
153	Methyl 3,4,5-trihydroxybenzoate	OC1=CC(=CC(O)=C1O)C(OC)=O
154	Serratol	C1C(=CCCC(=CCCC(=CC[C@@](C1)(C(*C*)C)O)C)C)C
155	Huperzine A	C\C=C1/[C@@H]2Cc3[nH]c(=O)ccc3[C@@]1(N)CC(C)=C2
156	Mustakone	CC(C)[C@@H]1CCC2(C)C3C1C2C(C)=CC3=O
157	(+)-Nootkatone	[C@@]12(C(CC[C@H](C1)C(C)=C)=CC(C[C@H]2C)=O)C
158	1-Icosanoylglycerol	C(CCCCCCCCCCC(OCC(*CO*)O)=O)CCCCCCC
159	Swertisin	O1[C@@H](C2=C(*O*)C3=C(OC(=CC3=O)C4=CC=C(*O*)C=C4)C=C2OC)[C@H](O)[C@@H](O)[C@H](O)[C@H]1CO
160	Serratol	C1C(=CCCC(=CCCC(=CC[C@@](C1)(C(*C*)C)O)C)C)C
161	PLX-4720	C(*CC*)S(NC1=CC=C(C(=C1F)C(C=2C3=C(N=CC(=C3)Cl)NC2)=O)F)(=O)=O
162	Huperzine A	C\C=C1/[C@@H]2Cc3[nH]c(=O)ccc3[C@@]1(N)CC(C)=C2
163	N-(2-methoxyethyl)-4-{[6-(pyridin-4-yl)quinazolin-2-yl]amino}benzamide	O=C(C1=CC=C(NC2=NC3=CC=C(C4=CC=NC=C4)C=C3C=N2)C=C1)NCCOC

Continued

Table 5 The list of phytochemical those satisfies the Lipinski rule of 5 and their structures in SMILES format.—cont'd

S.·no	Compound	SMILES (chEBI)
164	Glucotropeolin	[C@H]1(O[C@@H]([C@@H](O)[C@@H]([C@H]1O)O)CO)S/C(=N\OS(O)(=O)=O)/CC=2C=CC=CC2
165	Glucotropeolin(1–)	[C@H]1(O[C@@H]([C@@H](O)[C@@H]([C@H]1O)O)CO)S/C(=N\OS([O-])(=O)=O)/CC=2C=CC=CC2
166	Methyl 12-methyltetradecanoate	O(C(=O)CCCCCCCCCCC(CC)C)C
167	Carpaine	C[C@@H]1N[C@H]2CC[C@@H]1OC(=O)CCCCCCC[C@@H]1CC[C@H](OC(=O)CCCCCCC2)[C@H](C)N1
168	24-Methylenecycloartanol	[C@]123[C@@]4([C@](C([C@@H](O)CC4)(C)C)(CC[C@]1([C@]5([C@]([C@@]([C@@H](CCC(C(C)C)=C)C)(CC5)[H])(C)CC2)C)[H])[H])C3
169	Helvolic acid methyl ester	C=1[C@@]2([C@@]3(CC[C@@]/4([C@@]([C@]3(C([C@H]([C@]2([C@@H](C(C1)=O)C)[H])OC(=O)C)=O)C)(C[C@@H](\C4=C(\CCC=C(C)C)/C(=O)OC)OC(=O)C)C)[H])[H])C
170	Danielone	COc1cc(cc(OC)c1O)C(=O)CO
171	2-Isobutylthiazole	N1=C(SC=C1)CC(C)C
172	14-Deoxy-11,12-didehydroandrographolide	[H][C@]12CCC(=C)[C@@H](\C=C\C3=CCOC3=O)[C@]1(C)CC[C@@H](O)[C@@]2(C)CO
173	Andrographolide	[H][C@]12CCC(=C)[C@@H](C\C=C3/[C@H](O)COC3=O)[C@]1(C)CC[C@@H](O)[C@@]2(C)CO
174	Dihydroferulic acid	C=1(C=C(C(=CC1)O)OC)CCC(=O)O

175	Mesembryanthemoidigenic acid	[C@@]12(C([C@@]3(C[C@@](CO)(C)CC[C@@]3(CC1)C(=O)O)[H])=CC[C@@]4([C@]5(CC[C@@H](C([C@@]5(CC[C@@]24C)[H])(C)C)O)C)[H])C
176	Methyl *N*-methylanthranilate	CNC1=CC=CC=C1C(OC)=O
177	Delta-elemene	[C@@H]1(C=C(CC[C@@]1(C=C)C)C(*C*)C)C(C)=C
178	Decussatin	COc1cc(*O*)c2c(c1)oc1ccc(*OC*)c(*OC*)c1c2=O
179	Linalool	CC(C)=CCCC(C)(*O*)C=C
180	Nevadensin	COc1ccc(cc1)-c1cc(=O)c2c(*O*)c(OC)c(*O*)c(OC)c2o1
181	7-Epi-sesquithujene	C[C@H](CCC=C(*C*)C)[C@@]12CC=C(C)[C@@H]1C2
182	Selina-4(15),7(11)-diene	C1CCC([C@]2([C@]1(CCC(C2)=C(*C*)C)C)[H])=C
183	Codeine	[H][C@]12C=C[C@H](O)[C@@H]3Oc4c(*OC*)ccc5C[C@H]1N(*C*)CC[C@@]23c45
184	Sulfanilamide	Nc1ccc(cc1)S(N)(=O)=O
185	Pipercyclobutanamide A(rel)	O=C(\C=C/[C@@H]1[C@@H](\C=C\c2ccc3OCOc3c2)[C@@H]([C@H]1c1ccc2OCOc2c1)C(=O)N1CCCCC1)N1CCCCC1
186	(−)-cubebin	[H][C@@]1(CO[C@H](O)[C@]1([H])Cc1ccc2OCOc2c1)Cc1ccc2OCOc2c1
187	(−)-3,4-dimethoxy-3,4-desmethylenedioxycubebin	[H][C@@]1(COC(O)[C@]1([H])Cc1ccc2OCOc2c1)Cc1ccc(*OC*)c(OC)c1
188	Piperine	O=C(\C=C\C=C\c1ccc2OCOc2c1)N1CCCCC1

Table 5 The list of phytochemical those satisfies the Lipinski rule of 5 and their structures in SMILES format.—cont'd

S.·no	Compound	SMILES (chEBI)
189	Pellitorine	CCCCC\C=C\C=C\C(=O)NCC(*C*)C
190	Gaudichaudianic acid, (−rac)	CC(C)=CCCC1(C)Oc2c(CC=C(*C*)C)cc(cc2C=C1)C(O)=O
191	Isochamanetin	Oc1ccccc1Cc1c(*O*)cc2O[C@@H](CC(=O)c2c1O)c1ccccc1
192	7-Methoxychamanetin	COc1cc(*O*)c2C(=O)C[C@H](Oc2c1Cc1ccccc1O)c1ccccc1
193	Dichamanetin	Oc1ccccc1Cc1c(*O*)c(Cc2ccccc2O)c2O[C@@H](CC(=O)c2c1O)c1ccccc1
194	7-Methoxydichamanetin	COc1c(Cc2ccccc2O)c(*O*)c2C(=O)C[C@H](Oc2c1Cc1ccccc1O)c1ccccc1
195	5″-(2⁗-Hydroxybenzyl)uvarinol	COc1c(Cc2cc(Cc3ccccc3O)ccc2O)c(*O*)c2C(=O)C[C@H](Oc2c1Cc1cc(Cc2ccccc2O)ccc1O)c1ccccc1
196	2,4-Dodecadienamide	CCCCCCC\C=C\C=C\C(N)=O
197	7-Methoxyisochamanetin	COc1cc2O[C@@H](CC(=O)c2c(*O*)c1Cc1ccccc1O)c1ccccc1
198	(2E,4E)–N-[2-(methylsulfinyl)ethyl]-2, 4-decadienamide	CCCCC\C=C\C=C\C(=O)NCCS(C)=O
199	(2E,4E)–N-[(4-hydroxy-3-methoxyphenyl)ethyl]-2,4-decadienamide	CCCCC\C=C\C=C\C(=O)NCCc1ccc(*O*)c(OC)c1
200	3-(4-Hydroxy-3, 5-dimethoxyphenyl)propanoylpyrrole	COc1cc(CCC(=O)n2cccc2)cc(*OC*)c1O
201	3-(3,4,5-Timethoxyphenyl)propanoylpyrrole	COc1cc(CCC(=O)n2cccc2)cc(*OC*)c1OC

202	1-[(2E,4E,6E)-2,4,6-dodecatrienoyl]pyrrolidine	CCCCC\C=C\C=C\C=C\C(=O)N1CCCC1
203	1-[(2E,4Z,8E)-9-(3,4-methylenedioxyphenyl)-2,4,8-nonatrienoyl]pyrrolidine	O=C(\C=C\C=C/CC\C=C\c1ccc2OCOc2c1)N1CCCC1
204	1-[(2E,4E,10E)-10-(3,4-methylenedioxyphenyl)-2,4,10-undecatrienoyl]pyrrolidine	O=C(\C=C\C=C\CCCC\C=C\c1ccc2OCOc2c1)N1CCCC1
205	1-[(4E,10E)-11-(3,4-methylenedioxyphenyl)-4,10-undecadienoyl]pyrrolidine	O=C(CC\C=C\CCCC\C=C\c1ccc2OCOc2c1)N1CCCC1
206	1-[(9E)-10-(3,4-methylenedioxyphenyl)-9-decenoyl]pyrrolidine	O=C(CCCCCCC\C=C\c1ccc2OCOc2c1)N1CCCC1
207	1-[(2E,4E)-2,4-decadienoyl]pyrrolidine	CCCCC\C=C\C=C\C(=O)N1CCCC1
208	1-[(2E,4E)-2,4-dodecadienoyl]pyrrolidine	CCCCCCC\C=C\C=C\C(=O)N1CCCC1
209	1-[(2E)-7-(3,4-methylenedioxyphenyl)-2-heptenoyl]pyrrolidine	O=C(\C=C\CCCCc1ccc2OCOc2c1)N1CCCC1
210	1-[(2E,4E)-7-(3,4-methylenedioxyphenyl)-2,4-heptadienoyl]pyrrolidine	O=C(\C=C\C=C\CCc1ccc2OCOc2c1)N1CCCC1
211	1-[(2E,8E)-9-(3,4-methylenedioxyphenyl)-2,8-nonadienoyl]pyrrolidine	O=C(\C=C\CCCC\C=C\c1ccc2OCOc2c1)N1CCCC1
212	1-[(8E)-9-(3,4-methylenedioxyphenyl)-8-nonenoyl]pyrrolidine	O=C(CCCCCC\C=C\c1ccc2OCOc2c1)N1CCCC1
213	1-[(2E,4E,8E)-9-(3,4-methylenedioxyphenyl)-2,4,8-nonatrienoyl]pyrrolidine	O=C(\C=C\C=C\CC\C=C\c1ccc2OCOc2c1)N1CCCC1

Table 5 The list of phytochemical those satisfies the Lipinski rule of 5 and their structures in SMILES format.—cont'd

S.·no	Compound	SMILES (chEBI)
214	1-[(2E,4E)-11-(3,4-methylenedioxyphenyl)-2, 4-undecadienoyl]pyrrolidine	O=C(\C=C\C=C\CCCCCCc1ccc2OCOc2c1)N1CCCC1
215	1-[(2E,10E)-11-(3,4-methylenedioxyphenyl)-2, 10-undecadienoyl]pyrrolidine	O=C(\C=C\CCCCCC\C=C\c1ccc2OCOc2c1)N1CCCC1
216	(2E,4E)-N-isobutyl-2,4-dodecadienamide	CCCCCCC\C=C\C=C\C(=O)NCC(C)C
217	(2E,4E)-N-isobutyl-7-(3,4-methylenedioxyphenyl)- hepta-2,4-dienamide	CC(C)CNC(=O)\C=C\C=C\CCc1ccc2OCOc2c1
218	(8E)-N-isobutyl-9- (3,4-methylenedioxyphenyl)nona-8-enamide	CC(C)CNC(=O)CCCCCC\C=C\c1ccc2OCOc2c1
219	(2E,4E,8E)-N-isobutyl-11- (3,4-methylenedioxyphenyl)undeca-2,4,8-trienamide	CC(C)CNC(=O)\C=C\C=C\CC\C=C\CCc1ccc2OCOc2c1
220	N-trans-sinapoyltyramine	COc1cc(cc(OC)c1O)\C=C\C(=O)NCCc1ccc(O)cc1
221	Dihydrocubebin, rel–	OC[C@@H](Cc1ccc2OCOc2c1)[C@@H](CO)Cc1ccc2OCOc2c1
222	Justiflorinol	OCC(CC(=O)c1ccc2OCOc2c1)C(=O)c1ccc2OCOc2c1
223	(−)-Sanguinolignan A	O[C@@H]([C@H]1COC(=O)[C@@H]1C(=O)c1ccc2OCOc2c1) c1ccc2OCOc2c1
224	(−)-Sanguinolignan B	O[C@@H]([C@@H]1COC(=O)[C@@H]1C(=O)c1ccc2OCOc2c1) c1ccc2OCOc2c1
225	(−)-Sanguinolignan C	COc1ccc(cc1OC)[C@@H](OC(C)=O)[C@H]1COC(=O)[C@@H] 1C(=O)c1ccc2OCOc2c1

226	(−)-Sanguinolignan D	CC(=O)O[C@@H]([C@@H]1[C@H](COC1=O)C(=O)c1ccc2OCOc2c1)c1ccc2OCOc2c1
227	(7'S)-Parabenzlactone	O[C@@H]([C@H]1COC(=O)[C@@H]1Cc1ccc2OCOc2c1)c1ccc2OCOc2c1
228	Flavokawain B	COc1cc(O)c(C(=O)\C=C\c2ccccc2)c(OC)c1
229	Methyl 3,4-dihydroxy-5-(3′-methyl-2′-butenyl)benzoate	COC(=O)c1cc(O)c(O)c(CC=C(C)C)c1
230	Pipercallosidine	C(/C=C/CCCC=1C=C2C(=CC1)OCO2)(NCC(C)C)=O
231	Kadsurenin C	O([C@@]12[C@@H]([C@H]([C@@]([C@H]1O)(C(=O)C(=C2)CC=C)[H])C3=CC(OC)=C(OC)C=C3)C)C
232	Kadsurenin K	O([C@@]12[C@@H]([C@H]([C@@](C1=O)(C(=O)C(=C2)CC=C)[H])C3=CC(OC)=C(O)C=C3)C)C
233	Kadsurenin L	O([C@@]12[C@@H]([C@H]([C@@]([C@@H]1OC(=O)C)(C(=O)C(=C2)CC=C)[H])C3=CC(OC)=C(OC)C=C3)C)C
234	Pipercallosine	C(/C=C/C=C/CCCC1=CC=C2C(=C1)OCO2)(=O)NCC(C)C
235	(S)-1′-methylhexyl caffeate	CCCCC[C@H](C)OC(=O)\C=C\c1ccc(O)c(O)c1
236	Futoenone	O1[C@@H]2C[C@@]3([C@@H]([C@H](C2)C4=CC=5OCOC5C=C4)C)C1=CC(=O)C(OC)=C3
237	(S)-1′-methylbutyl caffeate	CCC[C@H](C)OC(=O)\C=C\c1ccc(O)c(O)c1
238	(S)-1′-methyloctyl caffeate	CCCCCCC[C@H](C)OC(=O)\C=C\c1ccc(O)c(O)c1

Table 5 The list of phytochemical those satisfies the Lipinski rule of 5 and their structures in SMILES format.—cont'd

S.·no	Compound	SMILES (chEBI)
239	Futokadsurin B	COc1ccc(cc1OC)[C@@H]1O[C@@H]([C@H](C)[C@H]1C)c1ccc2OCOc2c1
240	Futokadsurin C	COc1ccc(cc1OC)[C@H]1O[C@H]([C@H](C)[C@@H]1C)c1ccc2OCOc2c1
241	Futokadsurin A	COc1cc(ccc1O)[C@@H]1O[C@@H]([C@@H](C)[C@@H]1C)c1ccc(OC)c(OC)c1
242	Burchellin	O1[C@@H]([C@H]([C@]2(C1=CC(=O)C(OC)=C2)CC=C)C)C3=CC=4OCOC4C=C3
243	Piperonal	[H]C(=O)c1ccc2OCOc2c1
244	(−)-Cubenol	[C@]12([C@@H](CC[C@H]([C@@]2(CCC(=C1)C)O)C)C(C)C)[H]
245	(E,E)-piperic acid	OC(=O)\C=C\C=C\c1ccc2OCOc2c1
246	Trans-cinnamic acid	OC(=O)\C=C\c1ccccc1
247	Pinocembrin chalcone	Oc1cc(O)c(C(=O)\C=C\c2ccccc2)c(O)c1
248	Piperlactam S	O(C=1C2=C3C(=CC=4C2=CC=CC4)N(C(C3=CC1O)=O)OC)C
249	Asebogenin	COc1cc(O)c(C(=O)CCc2ccc(O)cc2)c(O)c1
250	Epicocconone	C\C=C\C=C\C=C\C(=O)\C=C(O)\C1=C2C=C3C[C@@H](CO)OC=C3C(=O)[C@@]2(C)OC1=O
251	(+)-Sesamin	[C@]12([C@@]([C@H](OC1)C3=CC4=C(C=C3)OCO4)(CO[C@@H]2C5=CC6=C(C=C5)OCO6)[H])[H]

252	Pipataline	O1C=2C=C(\C=C\CCCCCCCCCC)C=CC2OC1
253	(−)-Antofine	C=1C2=C(C=C(C1OC)OC)C=3C=C(C=CC3C4=C2C[C@]5(CCCN5C4)[H])OC
254	Benzoic acid	OC(=O)c1ccccc1
255	Ethyl butyrate	CCCC(=O)OCC
256	N-feruloyltyramine	COc1cc(\C=C\C(=O)NCCc2ccc(O)cc2)ccc1O
257	Kadsurenin M	O1[C@@H]([C@H](C2=C1C(OC)=CC(=C2)C(=O)[H])C)C3=CC(OC)=C(OC)C=C3
258	(−)-Epicubenol	[C@]12([C@@H](CC[C@H]([C@]2(CCC(=C1)C)O)C)C(C)C)[H]
259	Monocerin	[H][C@@]12C[C@H](CCC)O[C@]1([H])c1cc(OC)c(OC)c(O)c1C(=O)O2
260	(2S,3aR,9bR)-6,7-dihydroxy-8-methoxy-2-propyl-3,3a-dihydro-2H-furo[3,2-c]isochromen-5(9bH)-one	[H][C@@]12C[C@H](CCC)O[C@]1([H])c1cc(OC)c(O)c(O)c1C(=O)O2
261	Fusarentin 6,7-dimethyl ether	CCC[C@H](O)C[C@@H]1Cc2cc(OC)c(OC)c(O)c2C(=O)O1
262	Fusarentin 6-methyl ether	CCC[C@H](O)C[C@@H]1Cc2cc(OC)c(O)c(O)c2C(=O)O1
263	(3R,4R)-4,8-dihydroxy-3-((R)-2-hydroxypentyl)-6,7-dimethoxyisochroman-1-one	CCC[C@@H](O)C[C@H]1OC(=O)c2c(O)c(OC)c(OC)cc2[C@H]1O
264	Colletotrialide, (+)-	CCCC(=O)CC[C@H]1OC(=O)c2c(O)c(OC)c(OC)cc12
265	Galgravin	C1(=C(C=CC(=C1)[C@@H]2O[C@@H]([C@H]([C@H]2C)C)C3=CC=C(C(=C3)OC)OC)OC)OC

S.·no	Compound	SMILES (chEBI)
266	9,10-Epoxy-18-hydroxyoctadecanoic acid	C1(CCCCCCCC(=O)O)C(CCCCCCCCO)O1
267	Pinocembrin	Oc1cc(O)c2C(=O)C[C@H](Oc2c1)c1ccccc1
268	1,4-Cineole	C1C[C@]2(CC[C@]1(C)O2)C(*C*)C
269	Sodium benzoate	C(C=1C=CC=CC1)([O-])=O.[Na+]
270	9,10,18-Trihydroxyoctadecanoic acid	C(C(C(CCCCCCCCO)O)O)CCCCCCC(=O)O
271	Kavapyrone	COc1cc(oc(=O)c1)[C@@H]1O[C@H]1c1ccccc1
272	Alpha-cubebene	C1C[C@H]([C@]2([C@]3([C@@H]1C)CC=C([C@]23[H])C)[H])C(*C*)C
273	Acuminatin	O1[C@H]([C@@H](C2=C1C(OC)=CC(=C2)/C=C/C)C)C3=CC(OC)=C(*OC*)C=C3
274	Jerantinine E	[H][C@]12N3CCC[C@@]1(CC)CC(C(=O)OC)=C1Nc4cc(*OC*)c(O)cc4[C@]21CC3
275	Jerantinine F	[H][C@]12CCN3CC[C@@]45C(Nc6cc(*OC*)c(O)cc46)=C(C[C@@]1(CCO2)[C@]35[H])C(=O)OC
276	Jerantinine C	[H][C@@]12N3CC[C@]11C(Nc4cc(*OC*)c(O)cc14)=C(C[C@]2(CC)C=CC3=O)C(=O)OC
277	Jerantinine B	[H][C@]12CN3CC[C@@]45C(Nc6cc(*OC*)c(O)cc46)=C(C[C@](CC)([C@@]1([H])O2)[C@]35[H])C(=O)OC
278	Jerantinine D	[H][C@@]12O[C@]1([H])[C@@]1(CC)CC(C(=O)OC)=C3Nc4cc(*OC*)c(O)cc4[C@@]33CCN(C2=O)[C@@]13[H]

279	Jerantinine A	[H][C@@]12N3CC[C@]11C(Nc4cc(*OC*)c(O)cc14)=C(C[C@]2(CC)C=CC3)C(=O)OC
280	Tabernaemontanine	CC[C@@H]1CN(C)[C@]2(CC=3C4=CC=CC=C4NC3C(C[C@@]1([C@@]2(C(=O)OC)[H])[H])=O)[H]
281	Plectranthol A	CC(*C*)c1cc2C=C[C@@]3(C)C(=CCC[C@]3(C)COC(=O)c3ccc(O)c(O)c3)c2c(O)c1O
282	11,20-Dihydroxysugiol	C1=C(C(*C*)C)C(=C(C2=C1C(C[C@@]3([C@@]2(CCCC3(C)C)CO)[H])=O)O)O
283	11-Hydroxysugiol	C1=C(C(*C*)C)C(=C(C2=C1C(C[C@@]3([C@@]2(CCCC3(C)C)C)[H])=O)O)O
284	Abietatriene	CC(*C*)c1ccc2c(CC[C@H]3C(C)(C)CCC[C@]23C)c1
285	7-Oxo-10α-cucurbitadienol	[H][C@@]1(CC[C@@]2(C)[C@]3([H])C(=O)C=C4[C@@]([H])(CC[C@H](O)C4(C)C)[C@]3(C)CC[C@]12C)[C@H](C)CCC=C(*C*)C

3.5 Common target identification

The list of common targets between the COVID-19 infection (339 proteins) and phytochemical targets (24843) were analyzed using the Venn diagram (Fig. 1). The Venn diagram was plotted using a web server embedded in Bioinformatics & Evolutionary Genomics. From the analysis, 13 targets, namely, ACE, IMPDH2, EGFR, DPP4, RIPK1, HDAC2, CTSL, POLA1, CTSB, PABPC1, VEGFA, SIGMAR1, and IL6, were identified as potent protein targets.

3.6 Enrichment analysis

BP, CC, biological pathways, and MF were identified using the FunRich tool. Energy pathways, immune response, nucleoside, nucleic acid metabolism, nucleotide, and regulation of nucleobase were identified as the top biological process for the common receptor (Fig. 2A). Nucleus, plasma membrane, cytoplasm, exosome, lysosome, and extracellular were identified as the top cellular component for typical receptors (Fig. 2B). PAR1-mediated thrombin signaling events, IFN-gamma pathway, Nectin adhesion pathway, IL3-mediated pathway events, signaling events mediated by hepatocyte growth factor receptor (c-Met), and PDGF receptor signaling network were identified as the biological pathway for the typical receptors (Fig. 2C). Cytokine activity, transmembrane receptor protein tyrosine kinase activity, peptidase activity, transmembrane receptor activity, DNA-directed DNA polymerase activity, and cysteine-type peptidase activity (Fig. 2D). The complete results obtained from the FunRich analysis are tabulated in Supplementary Table 3 in the online version at https://doi.org/10.1016/bs.apcsb.2021.11.007.
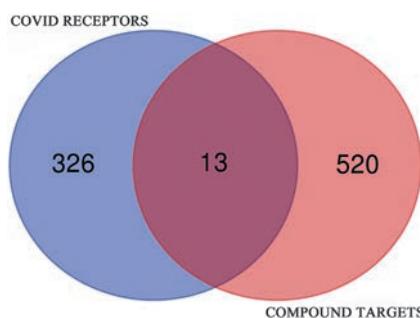
Fig. 1 Venn diagram showing the number of COVID-19 receptors, Compound targets and the common genes between the COVID-19 receptors and compound targets.
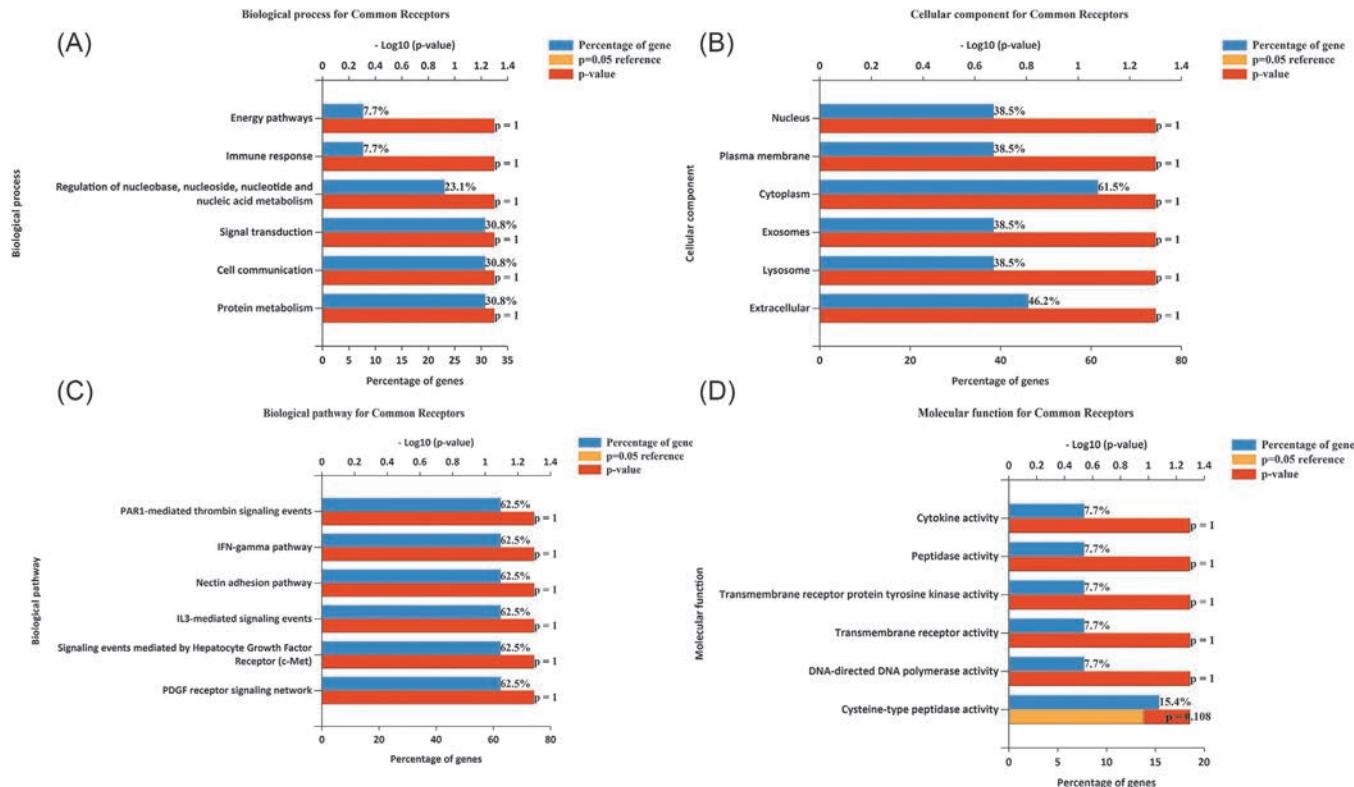
Fig. 2 Enrichment analysis using FunRich shows the most significant biological process, cellular component, biological pathway, and molecular function of the identified targets as the input. (A) Biological process for common receptors, (B) Cellular component for common receptors, (C) Biological pathway for common receptors, and (D) Molecular function for common receptors.

3.7 Pathway analysis

Pathway analysis was performed using the Reactome version 76 on 05/06/2021. All the 13 identifiers in the sample were found in Reactome, where 256 pathways were hit by at least one of them. The 25 most relevant significant pathways sorted by *P-value* are tabulated in Table 6. TFAP2 (AP-2) family regulates the transcription of growth factors and their receptors. Potential therapeutics for SARS and SARS-CoV (SARS-CoV-1 & SARS-CoV-2) Infections were identified as the top 3 significant pathways with 4/21, 5/84, and 6/203 entities found, respectively (Fig. 3A and B).

3.8 Gene–gene interaction analysis

The gene–gene interaction analysis helped to prioritize the study of genes in the pathway that helped to understand the underlying mechanism of COVID. The gene–gene interaction analysis was performed using the STRING online server. The number of nodes and edges were found to be 13 and 17, respectively. The average degree of nodes and clustering coefficient of local was found to be 2.62 and 0.566. The anticipated amount of edges was 9 with a PPI enrichment *P-value* of 0.0115. Except for IMPDH2, PABPC1, SIGMAR1, and POLA1, all the other genes interacted with at least one gene (Fig. 4).

3.9 Virtual screening and molecular interaction analysis

The identified targets such as VEGFA, CTSL, CTSB, EGFR, and IL6 have been identified as the target by more than one phytochemical compound (Table 7). Virtual screenings were performed to identify the most suitable phytochemical compound. The compound with the highest binding affinity was taken for the molecular interaction analysis using AutoDock (Supplementary Table 3 in the online version at https://doi.org/10.1016/bs.apcsb.2021.11.007). We observed that betulinic acid was found to interact best with the ACE protein with the binding energy −9.32 kcal/mol from the molecular docking results. The 5″-(2″″-Hydroxybenzyl) uvarinol was found to interact best with Cathepsin L, Cathepsin B, Cathepsin K with the binding energy −6.71 kcal/mol and −6.06 kcal/mol, respectively. The (-)–antofine, S)-1′-methyloctyl caffeate, (Z)-3-phenyl–2-propenal, 7-oxo–10α-cucurbitadienol, PLX-4720, and 5″-(2″″-Hydroxybenzyl) uvarinol were found to interact best to the DPP4, EGFR, HDAC2, IL6, RIPK1, and VEGFA with binding energies −8.25 kcal/mol, −4.76 kcal/mol, −4.39 kcal/mol, −6.9 kcal/mol, −5.91 kcal/mol, and −5.66 kcal/mol respectively. The interactions between the compounds and the proteins are shown in Fig. 5.

Table 6 The list of 25 most relevant pathways sorted by *P* value.

S.·no	Pathway name	Entities found	Ratio	*P* value	FDR[a]	Reactions found	Ratio
1	TFAP2 (AP–2) family regulates transcription of growth factors and their receptors	4/21	0.001	2.57E–08	6.88E–06	4/18	0.001
2	Potential therapeutics for SARS	5/84	0.006	0.000000122	0.0000163	6/32	0.002
3	SARS-CoV infections	6/203	0.014	0.000000338	0.0000301	9/254	0.019
4	Transcriptional regulation by the AP-2 (TFAP2) family of transcription factors	4/52	0.004	9.37e–07	6.28e–05	4/44	0.003
5	Trafficking and processing of endosomal TLR	3/16	0.001	1.75e–06	9.29e–05	2/7	5.21e–04
6	Infectious disease	9/1343	0.092	0.0000516	0.002	16/750	0.056
7	VEGF ligand–receptor interactions	2/8	0.000551	0.0000633	0.002	3/4	0.000298
8	VEGF binds to VEGFR leading to receptor dimerization	2/8	5.51e–04	6.33e–05	0.002	2/3	2.23e–04
9	RUNX1 regulates transcription of genes involved in differentiation of keratinocytes	2/11	7.57e–04	1.19e–04	0.003	1/8	5.96e–04
10	Assembly of collagen fibrils and other multimeric structures	3/67	0.005	1.23e–04	0.003	1/26	0.002
11	Toll-like receptor cascades	4/188	0.013	0.000141	0.003	14/185	0.014
12	Disease	11/2360	0.163	0.000148	0.003	99/1591	0.119

Continued

Table 6 The list of 25 most relevant pathways sorted by *P* value.—cont'd

S.·no	Pathway name	Entities found	Ratio	P value	FDR[a]	Reactions found	Ratio
13	Generic transcription pathway	9/1555	0.107	0.000163	0.003	17/824	0.061
14	Interleukin–4 and interleukin–13 signaling	4/211	0.015	2.19e–04	0.004	2/47	0.004
15	Regulation of gene expression by hypoxia–inducible factor	2/15	0.001	2.21e–04	0.004	1/7	5.21e–04
16	RNA polymerase II transcription	9/1694	0.117	0.000314	0.004	17/885	0.066
17	ERBB2 activates PTK6 signaling	2/18	0.001	0.000318	0.004	2/2	0.000149
18	ERBB2 regulates cell motility	2/19	0.001	0.000354	0.005	2/2	0.000149
19	Collagen formation	3/104	0.007	0.000444	0.006	1/77	0.006
20	PI3K events in ERBB2 signaling	2/22	0.002	0.000473	0.006	5/7	0.000521
21	Gene expression (transcription)	9/1855	0.128	0.000622	0.007	23/1000	0.074
22	Signaling by VEGF	3/137	0.009	0.000983	0.011	49/86	0.006
23	Signaling by ERBB2 KD Mutants	2/35	0.002	0.001	0.011	15/17	0.001
24	MHC class II antigen presentation	3/148	0.01	0.001	0.011	3/26	0.002
25	Degradation of the extracellular matrix	3/148	0.01	0.001	0.011	6/105	0.008

[a]False discovery rate.

Transcriptional regulation by the AP-2 (TFAP2) family of transcription factors
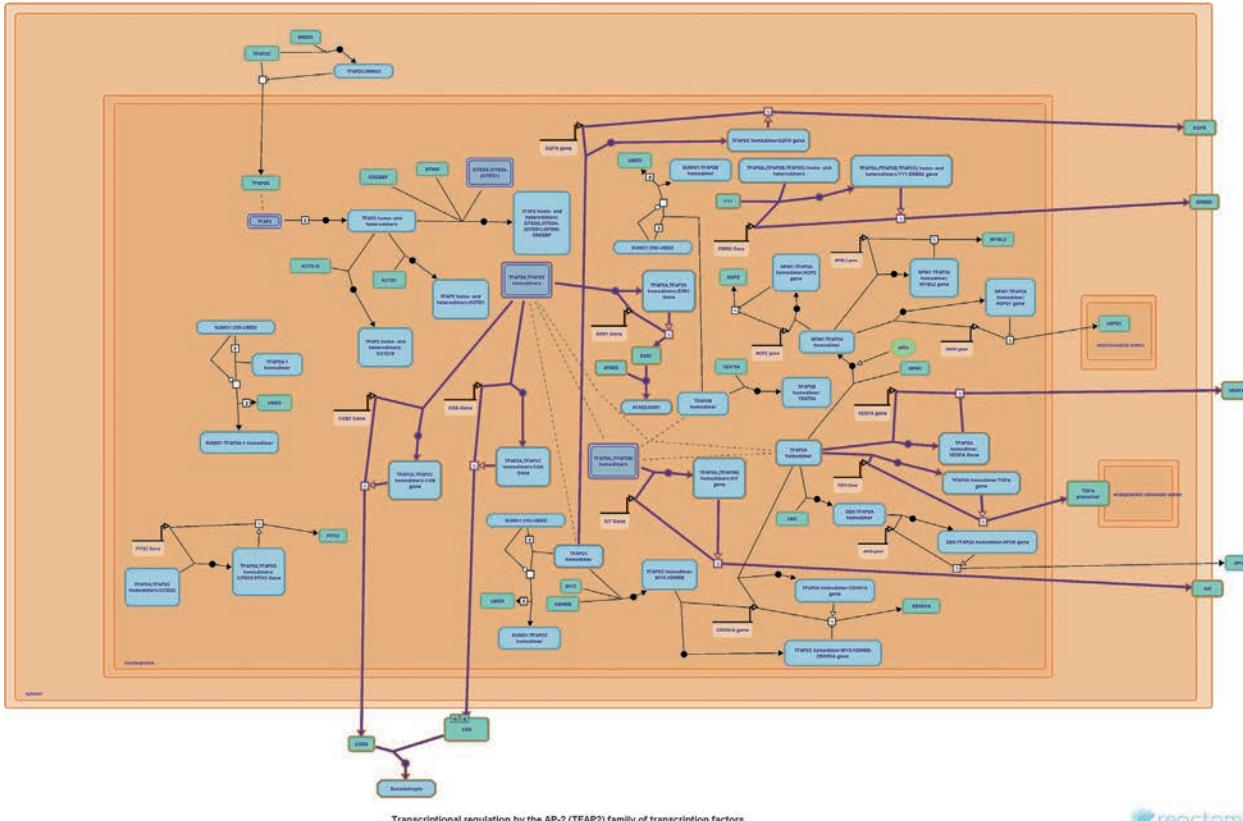
Fig. 3 (A) Pathway shows the transcriptional regulation by the AP-2 (TFAP2) transcription factor family. (B) Pathway showing the potential therapeutics for SARS.

(Continued)
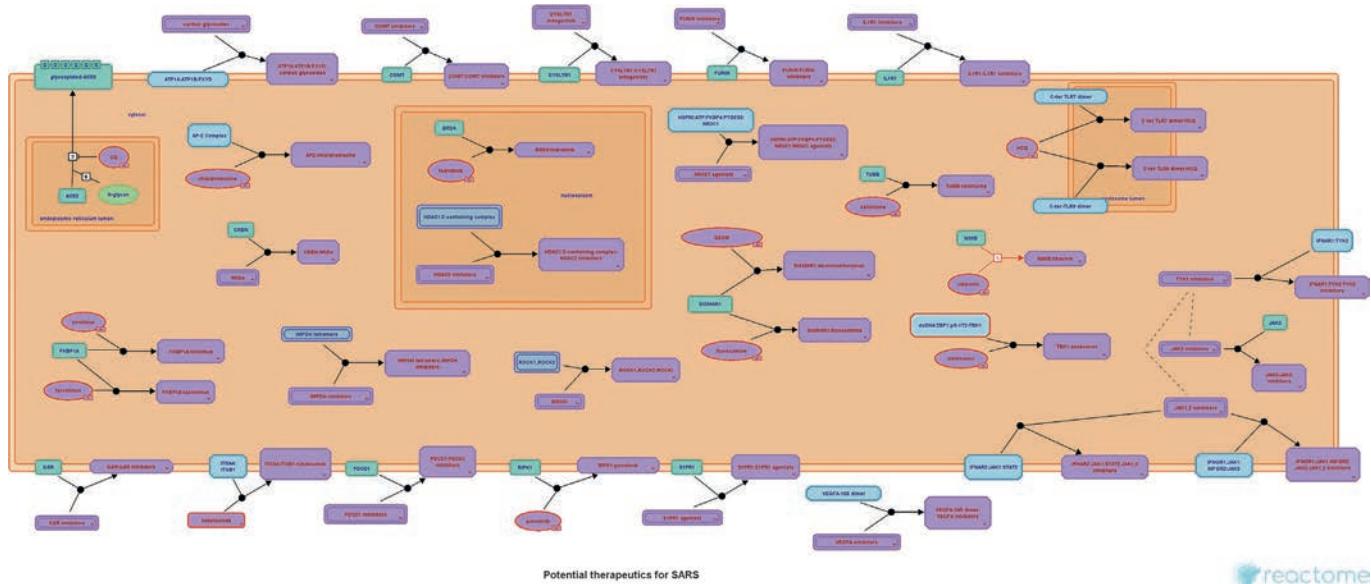
Fig. 3—Cont'd
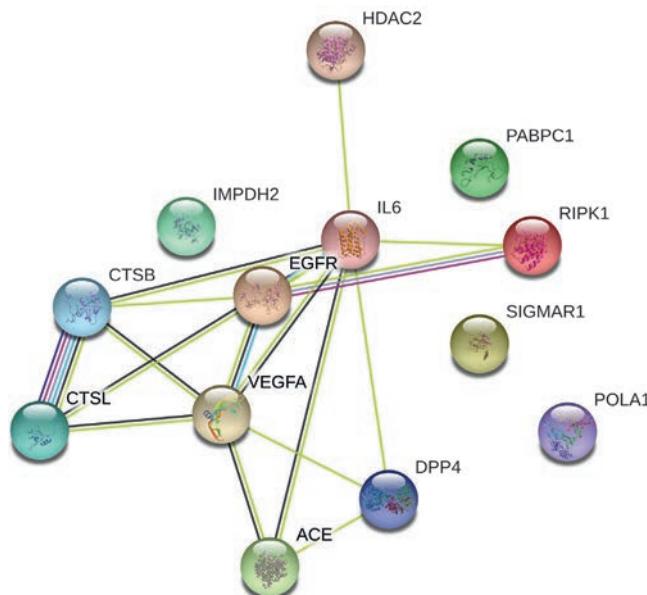
Fig. 4 The gene-gene interaction between the identified targets common to the COVID-19 receptors and compound targets.

Table 7 The list of selected receptors of the COVID-19 and the identified interacting phytochemical compounds.

S. no	Name of the receptor	Name of the compound
1	Angiotensin–converting enzyme	Betulinic acid
2	Dipeptidyl peptidase IV	(−)-Antofine
3	Vascular endothelial growth factor A	Isochamanetin
		7–Methoxychamanetin
		Dichamanetin
		7–Methoxydichamanetin
		5″-(2″″-Hydroxybenzyl)uvarinol
		7–Methoxyisochamanetin
		Pinocembrin
		1,4–Cineole
4	Cathepsin L	Isochamanetin
		7–Methoxychamanetin
		Dichamanetin
		7–Methoxydichamanetin

Table 7 The list of selected receptors of the COVID-19 and the identified interacting phytochemical compounds.—cont'd

S.·no	Name of the receptor	Name of the compound
		5″–(2‴″–Hydroxybenzyl)uvarinol
		7–Methoxyisochamanetin
		Pinocembrin chalcone
		Pinocembrin
		1,4–Cineole
		Carpaine
5	Cathepsin (B and K)	Isochamanetin
		7–Methoxychamanetin
		Dichamanetin
		7–Methoxydichamanetin
		5″–(2‴″–Hydroxybenzyl)uvarinol
		7–Methoxyisochamanetin
		Asebogenin
		Pinocembrin
		1,4–Cineole
		Carpaine
6	Epidermal growth factor receptor erbB1	7,4′–dimethylkaempferol
		Pipataline
		N–trans–sinapoyltyramine
		Flavokawain B
		(S)–1′–methylhexyl caffeate
		(S)–1′–methylbutyl caffeate
		(S)–1′–methyloctyl caffeate
		Trans–cinnamic acid
		Pinocembrin chalcone
		N–feruloyltyramine
		Cinnamic acid
		Dihydroferulic acid
		Capensinidin
		Nevadensin

Table 7 The list of selected receptors of the COVID-19 and the identified interacting phytochemical compounds.—cont'd

S.·no	Name of the receptor	Name of the compound
7	Interleukin–6	All–cis–octadeca–6,9,12,15–tetraenoic acid
		7–Oxo–10α–cucurbitadienol
8	Receptor–interacting serine/ threonine–protein kinase 1	PLX–4720
9	Histone deacetylase 2	(Z)–3–phenyl–2–propenal
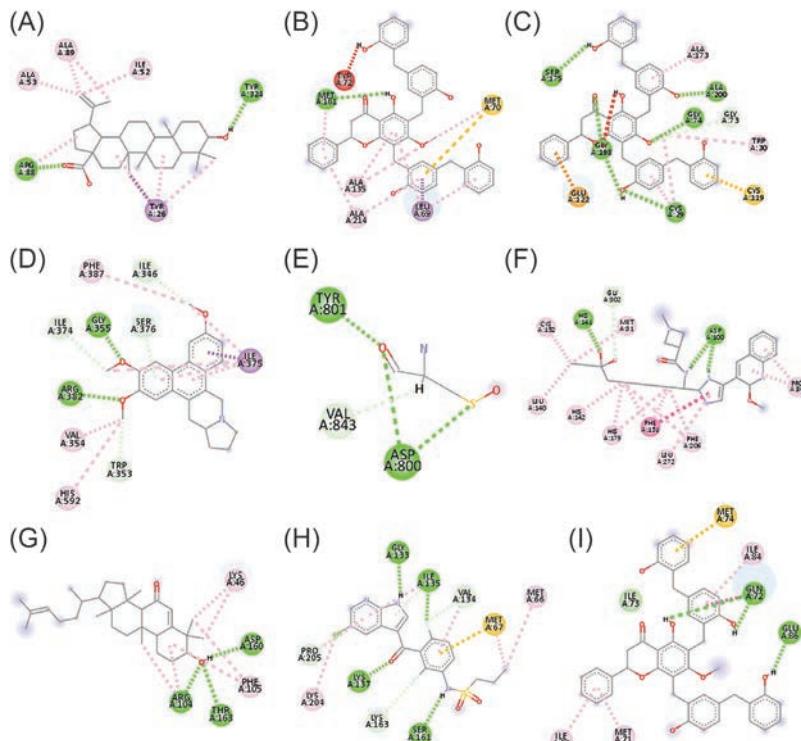
Fig. 5 Visualization of the best interacting phytochemical with the identified targets. (A) ACE receptor with betulinic acid, (B) Cathepsin L receptor with 5″-(2″″-Hydroxybenzyl)uvarinol, (C) Cathepsin B & K receptor with 5″-(2″″-Hydroxybenzyl)uvarinol, (D) DPPR receptor with (−)-antofine, (E) EGFR receptor with S)-1′-methyloctyl caffeate, (F) HDAC2 with (Z)-3-phenyl-2-propenal, (G) IL6 with 7-oxo-10α-cucurbitadienol, (H) RIPK1 with PLX-4720, and (I) VEGFA with 5″-(2″″-Hydroxybenzyl)uvarinol.
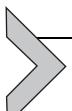
4. Discussion

SARS–CoV-2 belongs to a genetic group of viruses that cause respiratory sickness and was declared a worldwide pandemic on March 11th, 2020 (Cucinotta & Vanelli, 2020). As of September 6th, 2021, the reported cases are more than 220,563,227, and at least 4,565,483 people have died (WHO, 2021b). The number of cases across the globe is gradually increasing and decreasing in terms of the COVID-19 infection wave. The countries in America, Europe, and the South Asian region are highly infected with the second wave of COVID-19 infection. Few countries have started to face the third wave of COVID-19 (Taboada et al., 2021).

On the other hand, drug discovery is still far behind, and only drug repurposing serves as the day's choice (Lamontagne et al., 2020; Wu et al., 2020). Unfortunately, several repurposed drugs that showed promising results in the early studies were failed to treat COVID-19; this also includes hydroxychloroquine (Boulware et al., 2020; Geleris et al., 2020). With this less efficiency of repurposed drugs, the search for the vaccine was on a serious note, and several vaccines were developed across the globe, but none were 100% active. Further, there is always a chance of vaccine failure with the mutations and their evolution in the SARS–CoV-2 (Williams & Burgers, 2021). Developing an immune response against COVID-19 can only be a ray of hope in this scenario.

Traditional medicines have been immune boosters since the ancient days (Ravishankar & Shukla, 2007). Siddha herbal formulations with medicinal value effectively against various causative agents, including influenza, dengue fever, chikungunya, tuberculosis, and others (Jain et al., 2020; Jain, Narayanan, Chaturvedi, Pai, & Sunil, 2018; Jain, Pai, & Sunil, 2018). Currently, the ministry of AYUSH has also approved the use of Kabasura kudineer and Nilavembu kudineer against COVID-19 (Alagu Lakshmi, Shafreen, Priya, & Shunmugiah, 2020; Natarajan et al., 2020). This study is intended to understand the immune-boosting mechanism by the JACOM, Kabasura kudineer, and Nilavembu kudineer against COVID-19. A total of 339 human genes were found to be involved in COVID-19. This list was obtained from the GeneCards database (Table 1). Twenty-five plants were found in the Kabasura kudineer, Nilavembu kudineer, and JACOM formulations (Table 2). A list of 314 phytochemicals was obtained from these 25 plants from the ChEBI database (Table 3). The drug-likeness properties of the 314 phytochemical compounds were evaluated using the online

SwissADME server (Table 4). From the analysis, we observed 285 compounds to satisfy the Lipinski rule of 5, and these could be considered drug–like compounds (Table 5). The possible targets for these drug–like compounds were predicted using the online SwissTargetPrediction server. An overall of 24,839 targets was predicted for these 285 compounds (Supplementary Table 1 in the online version at https://doi.org/10.1016/bs.apcsb.2021.11.007). The targets were ranked based on the probability score. Out of 24,839 targets, 5129 genes (with repeats) were the promising target with a probability score of more than 0 (Supplementary Table 2 in the online version at https://doi.org/10.1016/bs.apcsb.2021.11.007). A Venn diagram was plotted to find the common targets between the genes involved in the COVID-19 and the compounds target (Tables 1 and 5). From the Venn diagram, 13 targets (ACE, IMPDH2, EGFR, DPP4, RIPK1, HDAC2, CTSL, POLA1, CTSB, PABPC1, VEGFA, SIGMAR1, and IL6) were found to be common between the causative and treatment for COVID-19. Three hundred and twenty-six and 520 genes were COVID-19 receptors and targets for compounds, respectively (Fig. 1). The enrichment analysis was performed to understand the role of identified targets in their BP, CC, biological pathways, and MF. Energy pathways, nucleoside, immune response, nucleotide, regulation of nucleobase, and nucleic acid metabolism were identified as the top biological process for the common receptor (Fig. 2A). Nucleus, plasma membrane, cytoplasm, exosome, lysosome, and extracellular were identified as the top cellular component for common receptors (Fig. 2B). PAR1-mediated thrombin signaling events, Nectin adhesion pathway, IL3-mediated signaling events, IFN–gamma pathway, cellular pathways engaged by hepatocyte growth factor receptor (c-Met), and PDGF receptor signaling network were identified as the biological pathway for the common receptors (Fig. 2C). Cytokine activity, peptidase activity, transmembrane receptor protein tyrosine kinase activity, transmembrane receptor activity, DNA-directed DNA polymerase activity, and cysteine-type peptidase activity (Fig. 2D). Further, the pathways involved in these gene targets were predicted using the Reactome database (Jassal et al., 2020). The pathways such as the TFAP2 (AP-2) family that controls the expression of growth factors and their receptors, Potential therapeutics for SARS, and SARS-CoV Infections were identified as the top 3 pathways out of significant 25 pathways (Table 6). The clear pathway of the TFAP2 (AP-2) family regulates the transcription of growth factors, and their receptors are shown in Fig. 3A. There are five transcription factors in the AP-2 (TFAP2) family in mammals: TFAP2A, TFAP2B, TFAP2C, TFAP2D, and TFAP2E (AP-2 epsilon). The AP-2 transcription factors have

a helix–span–helix motif at the C-terminus, a core basic region, and a transactivation domain at the N-terminus, and are evolutionarily conserved in metazoans (Eckert, Buhl, Weber, Jäger, & Schorle, 2005). EGFR and VEGFA identified genes were found to be involved in this pathway. The identified second most significant pathway was potential therapeutics for SARS. The detailed pathway is shown in Fig. 3B. Based on their efficacy in treating infectious disease with other RNA viruses or in reducing cytokine storms and other illnesses caused by viruses are identical to SARS-CoV-1 and SARS-CoV-2. A significant number of intriguing therapeutic candidates have been found to be also similar. HDAC2, SIGMAR1, IMPDH2, VEGFA, and RIPK1 identified genes were found to be involved in this pathway. SARS-CoV-2 infection pathway is not well annotated. However, the viral infection pathways are curated based on the SARS-CoV-1 and SARS-CoV-2 infection processes and drug responses. Many of the steps in SARS-CoV-1 infections are well studied experimentally correlated with the steps involved in SARS-CoV-2 infection. In comparison with the other two significant pathways, a maximum of 6 targets (CTSL, RIPK1, HDAC2, SIGMAR1, IMPDH2, and VEGFA) are found to be in this pathway (Supplementary Data 1 and 2 in the online version at https://doi.org/10.1016/bs.apcsb.2021.11.007).

The common genes were subjected to the gene–gene interaction study using the online STRING database to identify the connected genes (Szklarczyk et al., 2019). Out of the identified targets, HDAC2, IL6, EGFR, DPP4, ACE, VEGFA, CTSL, CTSB, and RIPK1 were interlinked with another target (Fig. 4). These targets were already promising targets for COVID-19 treatment in several previous studies. Therefore, activating or suppressing one of these genes could impact the other and improve efficacy.

The Histone deacetylase 2 (HDAC2) plays a crucial role in monocytes' regular immune response function. These monocytes were found to maintain the immune system's regular role when combined with the macrophages. The HDAC2 drugs such as Theophylline, Macrolides, Nortriptyline, and many others have been shown to prevent the pathological response of the inflammatory monocytes and thereby regulate the normal lung function (HDAC2 Regulates Response of Inflammatory Monocytes: A COVID-19 Target, 2020). A study by Liu et al. in 2020 has also proposed that the inhibition of HDAC could be a promising target for the COVID-19 infection (Liu et al., 2020).

T-lymphocytes, adipose tissues, and macrophages all produce interleukin-6 (IL-6), a pro-inflammatory cytokine protein. It plays a significant role in atherogenesis and is linked to cardiovascular clinical outcomes (Gabay, 2006). The COVID-19 patients with more severe illnesses had

higher inflammatory cytokines linked to pulmonary inflammation, lung destruction, and multiple organ failure. SARS–CoV-2 patients exhibit low concentrations of the modulator of cytokine signaling–3, which again is involved in the stimulation of the IL–6 negative feedback loop. Increased IL 6 has also been discovered to be an indicator of the change from a mild to a severe illness, limiting the severity if caught early (Vatansever & Becer, 2020).

The progression of SARS–CoV induces fibrosis, as well as a review of evidence indicating pulmonary fibrosis is generated by an overactive host response to lung damage driven through epidermal growth factor receptor (EGFR) signaling (Venkataraman & Frieman, 2017). Adeno-associated virus 2 (AAV2) second-strand DNA synthesis and transgene expression are inhibited by FK506-binding protein (FKBP52), which is phosphorylated at tyrosine residues by EGFR–PTK (Yano et al., 2003). Because EGFR is abundantly expressed in various solid tumors and its expression is linked to tumor progression, leading to chemotherapy resistance and poor prognosis. It is a promising strategy for the rational development of new anticancer drugs.

DPP4 is widely known to involve in type 2 diabetic conditions. DPP4 activity affects glucose homeostasis and inflammation in numerous ways. The change in expression levels of DPP4 in the early MERS infections was also studied several years ago (Chan et al., 2015). Currently, the SARS-CoV-2 being the same family of MERS infection, the role of DPP4 in SARS-CoV-2 conditions is also widely studied and found to be a promising target for COVID-19 treatment (Scheen, 2021; Solerte, Di Sabatino, Galli, & Fiorina, 2020).

ACE2 acts as a functional receptor on the cell's surface through which the SARS-CoV-2 can enter the human cell. This ACE2 is expressed highly in the heart, kidney, and lungs. The ACE/ACE2 balance disruption with RAAS (renin-angiotensin-aldosterone system) activation can lead to severe COVID-19, especially in diabetes, cardiovascular diseases, and hypertension (Beyerstedt, Casaro, & Rangel, 2021).

In ICU and non–ICU COVID-19 patients, VEGF concentrations were more significant than in healthy controls. Angiogenesis, neurogenesis, and neuroprotection are all aided by VEGFs, leading to vascular leakiness and permeability. ACE2 inhibits VEGF-A, which reduces vascular permeability in patients with acute lung damage. In the account of SARS-downregulation CoV-2's of ACE2, the VEGF-A antagonistic effect of ACE2 is expected to be canceled, resulting in overexpression of VEGF and increased vascular permeability and exacerbation of endothelial injury (Yazihan et al., 2021).

The *CTSL1* gene codes for a lysosomal cysteine protease involved in intracellular protein degradation. It impacts collagen and elastin, along with alpha-1 protease inhibitor, a key regulator of neutrophil elastase function. CatL is essential in degrading the extracellular matrix, a crucial mechanism for SARS-CoV-2 to enter host cells and is upregulated during chronic inflammation. CatL is also likely involved in the processing of SARS-CoV-2 spike protein. CatL could have been regarded as a valuable therapeutic target because its suppression damages SARS-CoV-2 infection and maybe egress from cells through late stages of infection (Gomes et al., 2020; Pišlar et al., 2020).

Because several patients had greater serum RIPK3 (a family of RIPK1) levels, it is possible that RIPK-3-mediated signaling may lead to necroptosis; it is implicated in the development of COVID-19 pneumonia-related acute lung injury. In ARDS patients, RIPK-3 levels were considerably more significant than in non-ARDS patients. In immunohistochemistry, all epithelial cell samples from COVID-19 individuals were confirmed for active phosphorylated RIPK1. Thus, ICD mediated by RIPK1 may have a part in the progression of SARS-CoV-2 infection and can be a new therapeutic target (Nakamura et al., 2020).

Several compounds targeting these genes can interact with more than one gene. Virtual screenings were performed to identify the best interaction of the compounds with these targets. From the virtual screening analysis, betulinic acid was found to interact with ACE, 5″-(2‴′-Hydroxybenzyl)uvarinol was found to interact with Cathepsin L, Cathepsin B, and Cathepsin K, -(-)-antofine was found to interact with DPP4, (S)-1′-methyloctyl caffeate was found to interact with EGFR, (Z)-3-phenyl-2-propenal was found to interact with HDAC2, 7-oxo-10α-cucurbitadienol was found to interact with IL6, PLX-4720 was found to interact with RIPK1, and 5″-(2‴′-Hydroxybenzyl)uvarinol was found to interact with VEGFA (Supplementary Table 3 in the online version at https://doi.org/10.1016/bs.apcsb.2021.11.007). The molecular dockings were performed using the AutoDock, and the interactions were studied using the Discovery Studio (Fig. 5). Thus collectively, these compounds targeting the identified targets could improve the immune system, fighting against the COVID-19 infection.
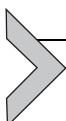
5. Conclusion

The COVID-19 infection is widely increasing across the globe. The drugs to treat COVID-19 are still in the clinical trials, which might take years for approval. Drugs such as Hydroxychloroquine, Remdesivir, Favipiravir, Lopinavir/ritonavir are widely repurposed to treat the COVID-19 during the earlier outbreak. On the other hand, various vaccine manufacturers such

as COVID-19 Vaccine AstraZeneca, COVID-19 Vaccine Janssen, Sputnik, and Covaxin are in the race to develop vaccines, yet none seems to be 100% efficient. In addition, with the evolution of SARS–CoV-2 mutations, the efficiency of the vaccines is becoming a interrogation point every day.

Similarly, these mutations might lead to drug inefficacy and drug-resistant. The promising approach to be safe from COVID-19 is to develop the immune system. The traditional medicines are immune boosters, serving as a promising remedy for various diseases since ancient days. This study used the network pharmacology approach and analyzed the phytochemical compounds in Nilavembu kudineer, Kabasura kudineer, and JACOM and their interacting human protein targets, activating or suppressing the target. These identified compounds can be tested *in vivo* and *in vitro* to compare the toxicity and efficiency of the currently available formulations.

Conflict of interest

The authors have declared that no conflicts of interest exist.

Author contributions

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