chemistry proceedings

MDPI

Proceeding Paper

In Silico Screening Of Natural Phytocompounds Towards Identification Of Potential Lead Compounds From Different Varieties Of Cumin†

Sandeep Waghulde*, Manasi Thakur, Vibha Tele, Pranali Suryarao, Vidhi Tele, Vaishnavi Shirke, Nilesh Gorde, Ajay Kharche, Mohan Kale

[1] Konkan Gyanpeeth Rahul Dharkar College of Pharmacy and Research Institute, Karjat, Dist-Raigad University of Mumbai

† Presented at the 25th International Electronic Conference on Synthetic Organic Chemistry, 15–30 November 2021; Available online: https://ecsoc-25.sciforum.net/.

We probed into the effect of different varieties of cumin for the search of potential leads based on the phytochemical profiles and bioactivities Insilico study were applied to relevant bioactive compounds in search of a lead compound through molinspiration cheminformatics software. Different lead compounds from different varieties of cumin were selected for bioactivity prediction and drug likeness score on the basis of Lipinski's rule. All of the compounds fulfilled Lipinski's rule as their Milog P score was below 5 suggesting these compounds are means these shows good permeability across cell membrane. All the screened compounds had minimum and no violations of Lipinski rule. Different lead compounds from different varieties of cumin showed good bioactivity score for drug targets including nuclear receptor ligand, protease inhibitor and enzyme inhibition and thus expected to have excellent pharmacological activity in vivo. The results of this study justify their topical application as immunomodulators action but some structural modifications in order to make the compound more polar will definitely improve oral bioavailability and thus the usefulness and therapeutic efficacy of different varieties of cumin.All the lead compounds from different varieties of cumin, are predicted to be orally active and is considered as a potential candidate for the further research as its bioactivity score due to high affinity for various drug targets was better than the standard as well as among other tested compounds. Evidence from the present study advocates the need for exploring different lead compounds from different varieties of cumin in an endeavor to discover unique bioactive lead compounds that could target specific ailments. The selected molecules were assessed for Pharmacodynamic parameters like mutagenicity, tumorigenicity, reproductive effect and ocular & skin irritancy and pharmacokinetic properties like solubility, human intestinal absorption and blood brain barrier permeability. Based on the results, each ligand was assigned with respective drug-likeness and drugscore.

Keywords: cumin derivatives, C. cyminum, Nigella sativa, Cuminumnigrum, immunomodulators, Lipinski's rule, Molinspiration, In silico ADME-T studies

Academic Editor: Julio A. Seijas

Published: 15 November 2021

Research Background

Presently, the global public health threat of international concern is the coronavirus disease-2019 (COVID-19), a viral disease of worldwide prevalence caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), at present the disease has no known cure or vaccine. Plants worldwide including Indian traditional plants of ethnopharmacological relevance are a natural source of abundant and diverse phytochemicals with bioactivity against microorganisms including viruses.

Introduction

The fastest method for evaluating the drug-like properties of a compound is to apply "rules."

Rules are a set of guidelines for the structural properties of compounds that have a higher probability of being well absorbed after oral dosing.

Lipinski Rule of Five

There are guidelines given below to help, the most well-known of which is the Lipinski Rule of Five, if

- molecular weight < 500
- logP< 5
- < 5 H-bond donors (sum of NH and OH)
- < 10 H-bond acceptors (sum of N and O)

Otherwise absorption and bioavailability are likely to be poor.

NB: 1. This is for oral drugs only.

2. Although "violation" of one rule may not result in poor absorption, the likelihood of poor absorption increases with the number of rules broken and the extent to which they are exceeded.

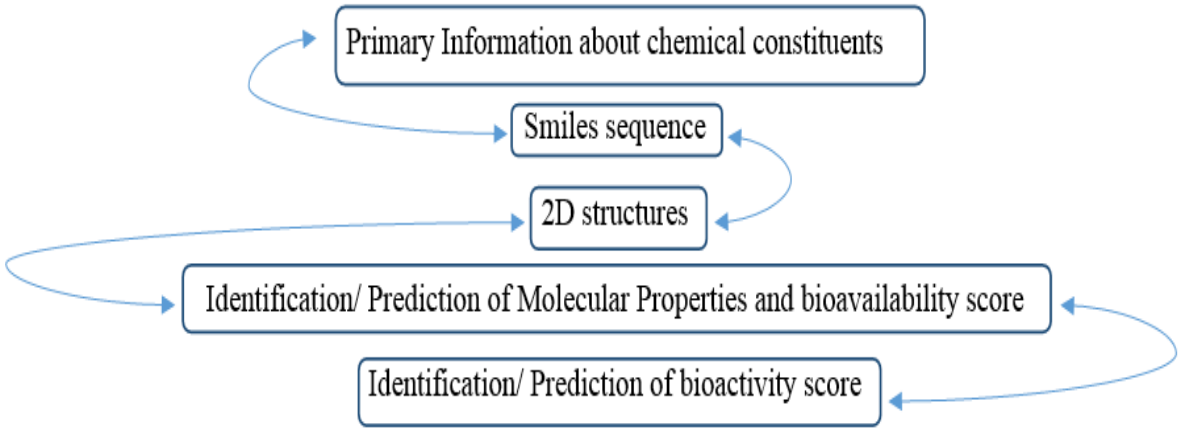


Fig.1. Methodology followed in this study. The above flowchart depicts theschematic representation of methodology followed in this study. The initialsteps involved collecting primary information and deciphering the 2-D structuresof compounds. Subsequently, the major drug targets for each of thecompounds were identified. This was followed by analyzing the function ofeach target.

In this post-genomic era, progressively more research is focused on proteomics. Experimental and computational efforts are devoted tolarge- scale generation and analysis of information derived from 3D structures and dynamics of proteins, with the goal of scientific and commercial break-through in drugdiscovery. This raises the necessity for new and fast computational approaches alternative to wet-labhigh-throughput screens for drug discovery . A necessary prerequisite for successful differentiation between active and non-active ligands in the accurate prediction of their binding affinities to the complexis by use of docking score functions. In this regard, molecular docking has been extensively applied in effective screening of small molecule libraries for lead identification and optimization

Plant Profile

	Cumin **(*C. Cyminum*)**	**Black cumin** **(*Nigella sativa*)**	**Bitter Cumin** **(*C. Nigrum*)**

			
Botanical Name	Cuminum cyminum	Nigella sativa	Cuminum nigrum
Indian Name	Kummel	Black cumin/kalonji	Bitter cumin/kadu jeera
Family	Apiaceae / Cuminum	Ranunculaceae	apiaceae
Synonyms (any two)	1. Cumin 2. Cumin seed	1.nutmeg flower 2.black caraways.	1.bitter cumin 2.shahi jeera
Chemical Constituent	Cuminaledehyde	Tymohydroquinone, p-cymene, carvacrol	Gallic acid,caffeic acid
Use	To treat 1. Chronic diarrhea 2. Dyspepsia	To treat 1.Asthama 2.Bronchitis 3.Rheumatoid arthritis	To treat 1.anthelmetic 2.digestive stimulant 3.diurectic

Chemical Constituent

Sr. No.	**Cumin (*C. Cyminum*)**	**Black cumin (*Nigella sativa*)**	**Bitter Cumin (*C. Nigrum*)**
1.	Cuminaldehyde	Thymohydroquinone	Gallic acid
2.	cymene	P-cymene	Protocatechiuc acid
3.	cuminic alcohol	Carvacrol	Caffeic acid
4.	2-ethoxy-3-isopropylpyrazine	4-terpineol	Ellagic acid
5.	2-methoxy-3-sec butylpyrazine	t-anethole	Ferulic acid
6.	2-methoxy-3-methylpyrazine	Sesquiterpenelongifolene	Quercetin

7.	beta-pinene	Thymol	Kaempferol
8.	safranal	Carvone	--
9.	terpinene	Limonene	--
10.	Cineole	citronellol	--

Materials and methods:

The aim of this study was to analyse and evaluate the possible leads by the various components used in scaffold through molinspiration cheminformatics software. Different lead compounds from different varieties of cumin were selected for bioactivity prediction and drug likeness score on the basis of Lipinski's rule. Traditional analysis methods involve the use of several biochemical tests rather than novel bioinformatics approaches. The methodology followed in this study made use of bioinformatic databases and tools and is depicted using the following flowchart (Fig. 1).

Primary information collected from databases

Chemical and structural information about these components were retrieved from various databases. Primary information was retrieved from PubChem (https://pubchem.ncbi.nlm.nih.gov) and Drugbank databases (https://www.drugbank.ca). PubChem is a significant database that provides information on chemical substances and their corresponding biological functions. The data provided can be primarily classified into three main domains as substances, compound and bioassay. Substance database contains information on chemical aspects of the substance, which are deposited by individual contributors to PubChem [16]. Fig. 2 depicts the homepage of PubChem database.

SMILES sequence and 2D structure

Primary data collected from these databases includes the canonical SMILES sequences of three adjuvant compounds used in preparing the scaffold. The names of each compound were used as query to search for information page of each entry. 2-D structure and sequence were gathered from the database by navigating to the respective titles in home page of each compounds

In silico studies

In-silico ADME-Toxicology prediction:

Organic chemistry portal (http://www.organic-chemistry.org/prog), a web-based application was used for prediction of ADME-T properties. The selected molecules were assessed for Pharmacodynamic parameters like mutagenicity, tumerogenicity, reproductive effect and ocular & skin irritancy and pharmacokinetic properties like solubility, human intestinal absorption and blood brain barrier permeability. Based on the results, each ligand was assigned with respective drug-likeness and drug score. PubChem database primarily provides SMILES sequence in two arrangements. Amongst the two forms, canonical SMILES sequences ofeach of the entries (i.e. chemical constituents)

Results

Primary information

Primary information about the three adjuvant compounds used in preparing this scaffold were retrieved from databases. The data collected from PubChem and Drugbank databases were summarised as in Table 1.

The various information collected includes PubChem CID, other chemical names, molecular formula and molecular weight.

Druglikeness may be defined as a complex balance of various molecular properties and structure features which determine whether particular molecule is similar to the known drugs.

These properties, mainly hydrophobicity, electronic distribution, hydrogen bonding characteristics, molecule size and flexibility and of course presence of various pharmacophoric features influence the behavior of molecule in a living organism, including bioavailability, transport properties, affinity to proteins, reactivity, toxicity, metabolic stability and many others.

Lipinski's rule

Evaluation of drug likeliness

The drug likeness was calculated and discussed on the basis of Lipinski’s rule and its component for all prepared compounds using Molinspiration software.

The physicochemical properties including:

- An octanol-water partition coefficient (Milog P) < 5 that means these shows good permeability across cell membrane,
- polar surface area (TPSA) < 160 Å2 which shown to be a very good descriptor characterizing drug absorption,

- number of violation (n violations) =1 or < 0 it means compound easily bind to receptor
- molecular weight (MW) < 500 required for characterizing drug absorption
- number of rotatable bonds (n rotb) < 10 this measures molecular flexibility
- number hydrogen bond donors (n OHNH) ≤ 5 (The sum of OHs and NHs)
- total molecular polar surface area (TPSA) > 160A^{o}2
- hydrogen bond acceptors (nON) > 7

From the results reveal that these compounds are orally bioactive because they possess groups which act as substrate for transporter.

Potency of compounds according to obtained data

Number of violations

In all the 10 compounds that are more important which have least number or no violations observed.

Molecular weight

All constituents of data pass the Lipinski rule of five for molecular weight.

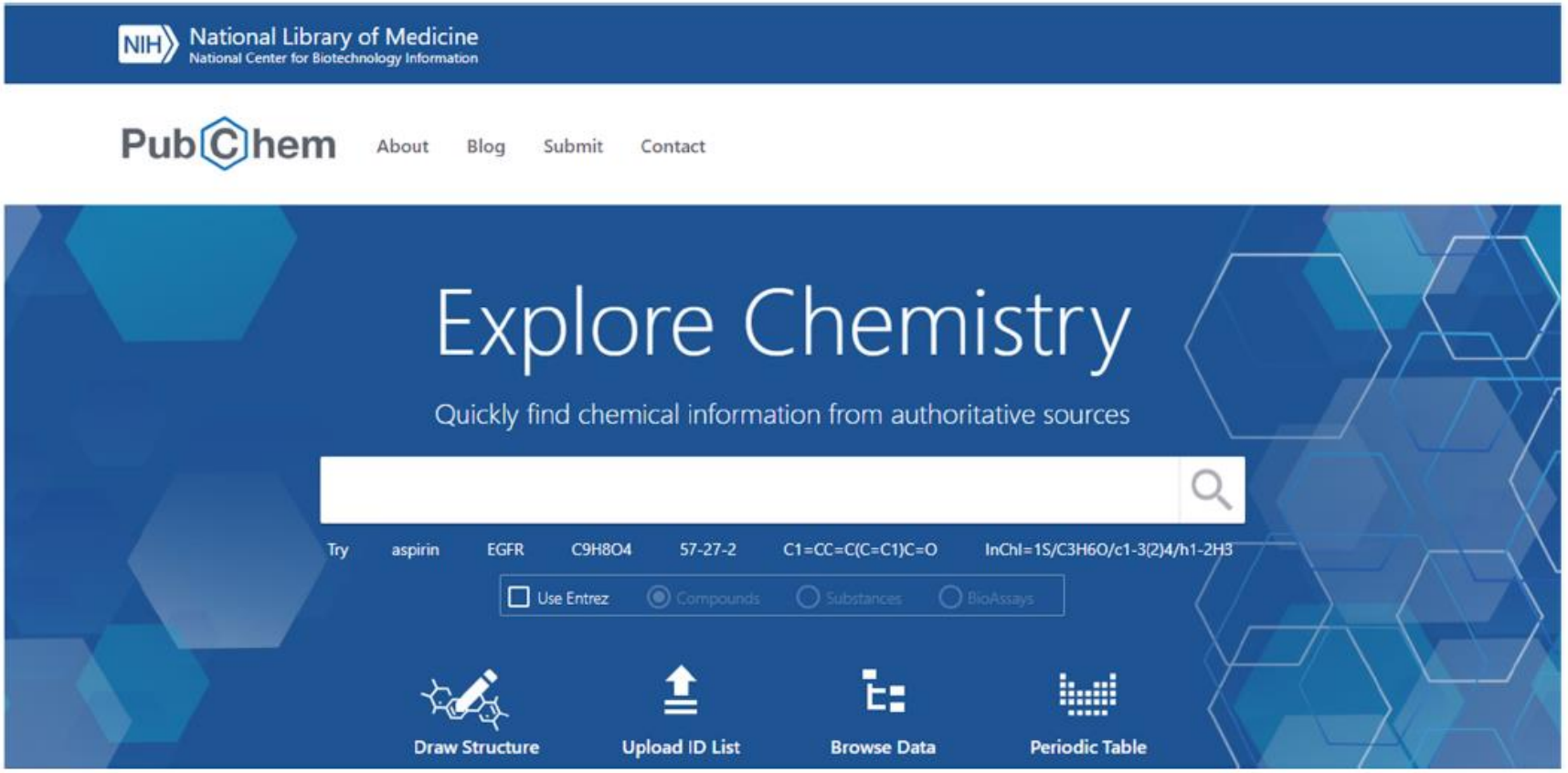


Fig. 2 Homepage of PubChem database. The screenshot depicts the homepage of PubChem database with various search options (as retrieved from https://pubchem.ncbi.nlm.nih.gov/). The box portrays the query box for searches. The tabs above the query box specifies the three main domains of information provided by the database

Table 1: Primary information for chemical constituents of Cumin (C. Cyminum):

Sr. No.	Compounds	PubChem CID	Drugbank accessionNumber	Chemical names	Molecular formula	Molecular weight
1.	Cuminaldehyde	326	JP008712	4-isopropylbenzaldehyde	$C_{10}H_{12}O$	148.20g/mol
2.	Cymene	7463	JP001543	1-methyl-4-propan-2-ylbenzene	$C_{10}H_{14}$	134.22g/mol
3.	Cuminic alcohol	325	JP005647	4-isopropylbenzyl alcohol	$C_{10}H_{14}O$	150.22g/mol
4.	2-Ethoxy-3-Isopropylpyrazine	175170	----	----	$C_9H_{14}N_2O$	166.22g/mol
5.	2-Methoxy-3-Sec Butylpyrazine	520098	----	----	$C_9H_{14}N_2O$	166.22g/mol
6.	2-Methoxy-3-Methylpyrazine	17898	----	----	$C_6H_8N_2O$	124.14g/mol
7.	Beta-Pinene	14896	JP000246	6,6-dimehyl-2-methyllidenebicylo[‘3.1.1]heptanepon-2(10)-ene	$C_{10}H_{16}$	136.23g/mol
8.	Safranal	61041		1-isopropyl-4-methyl-1,3-cyclohexadiene	$C_{10}H_{14}O$	150.229/mol

9.	Terpinene	7461	JP007120	1-methyl-4-propan-2-ylcyclohexa-1,4-diene	$C_{10}H_{16}$	136.23g/mol
10.	Cineole	2758	JP006594	1,3,3-trimethyl-2-oxabicyclo[2.2.2]octane	$C_{10}H_{18}O$	154.25g/mol

Table 2: Primary information for chemical constituents of Black cumin(Nigella sativa):

Sr. No.	Compounds	PubChem CID	Drugbankaccession Number	Chemical names	Molecular formula	Molecular weight
1.	Thymohydroquinone	95779	DB16447	2-methyl-5-propan-2-ylbenzene-1,4-diol	$C_{10}H_{12}O_2$	164.20g/mol
2.	P-cymene	7463	----	1-methyl-4-(propan-2-yi)benzon	$C_{10}H_{14}$	134.22g/$_{mol}$
3.	Carvacrol	10364	DB16404	2-methyl-5-propan-2-ylphenol	$C_{10}H_{14}O$	150.22g/mol
4.	4-terpineol	11230	DB12816	Terpienen-4-ol-(4-methyl-1-	$C_{10}H_{18}O$	154.25g/mol

				(propan-2-yl)cycohex-3-en-1-ol)		
5.	T-Anethole	637563	DB15916	5-(4-methoxyphenyl) dithiole-3-thione	$C_{10}H_{12}O$	148.20g/mol
6.	Sesquiterpenelongifolene	289151	----	3,3,7-trimethyl-8-methyllidenetricyco[5.4.0.02,9]undecane	$C_{15}H_{24}$	204.35g/mol
7.	Thymol	6989	DB62513	5-methyl-2-propan-2-yl-phenol	$C_{10}H_{14}O$	150.22g/mol
8.	Carvone	16724	----	2-methyl-5-(prop-1-en-2-yl)cycohex-2-Enone	$C_{12}H_{14}O$	150.22g/mol
9.	Limonene	22311	DB02924		$C_{10}H_{16}$	136.23g/mol
10.	Citronellol	7794	DB16601	3,7-dimethyloct-6-en-1-ol	$C_{10}H_{20}O$	156.26g/mol

Table 3: Primary information for chemical constituents of Bitter Cumin(C. Nigrum):

Sr. No.	Compounds	PubChem CID	DrugbankaccessionNumber	Chemical names	Molecular formula	Molecular weight
1.	Gallic acid	370	OUF00237	3,4,5-trihydroxybenzoicacid	$C_7H_6O_5$	170.12g/mol
2.	Protocatechiuc acid	195945	DB03946	3-hydroxy-4-sulfoxybenzoic acid	$C_7H_6O_7S$	234.19/mol
3.	Caffeic acid	689045	OUF00132	(E)-3-(3,4-dihydroxyphenyl)prop-2-enoic acid	$C_9H_8O_4$	180.16g/mol
4.	Ellagic acid	5281855	DB08846	6,7,13,14-tetrahydroxy-2,9-	$C_{14}H_6O_8$	302.19g/mol

				dioxatetracyclo[6.6.2.04,16.011,15]hexadeca-1(15),4,6,8,(16),11,13-hexaene-3,10-dione		
5.	Ferulic acid	445858	DB07767	(E)-3-(4-hydroxy-3-methoxyphenyl) prop-2-enolic acid	$C_{10}H_{10}O_4$	194.18g/mol
6.	Quercetin	5280343	DB04216	2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxychromen-4-one	$C_{15}H_{10}O_7$	302.23g/mol
7.	Kaempferol	5280863	DB04216	3,5,7-trihydroxy-2-(4-hydroxyphenyl) chromen-4-one		286.24g/mol

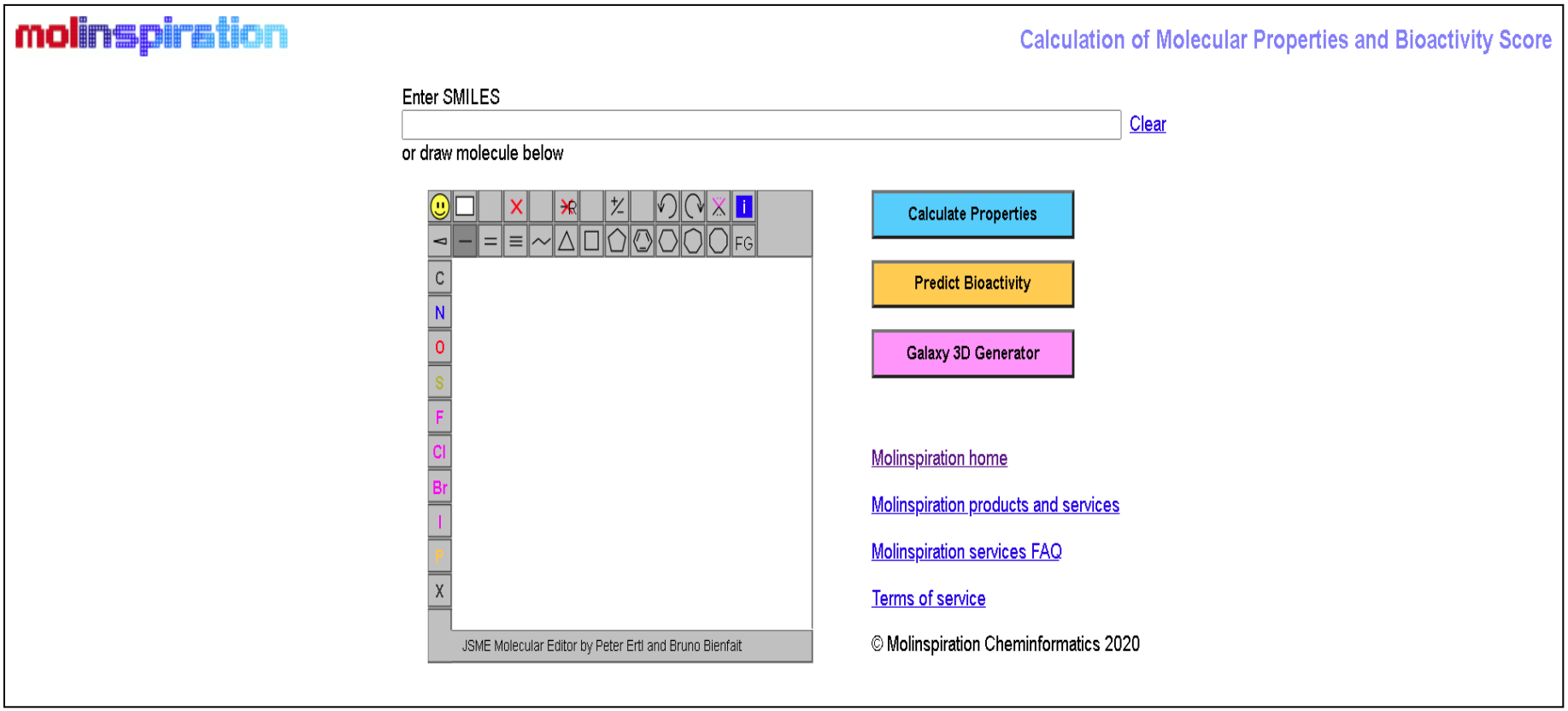
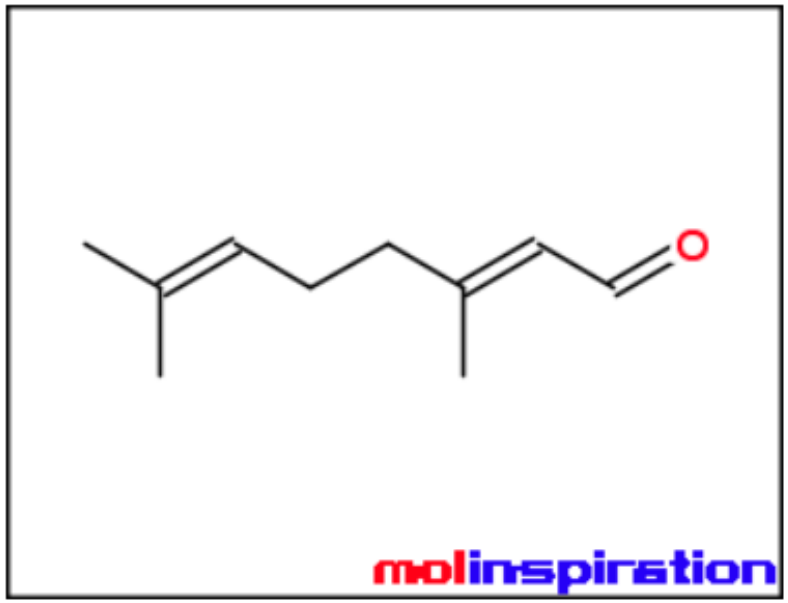


Fig. 3 Molinspiration online portal for Calculation of Molecular Properties and Bioactivity Score

molinspiration

originalSMILES CC(=CCCC(=CC=O)C)C
miSMILES: CC(=CCCC(=CC=O)C)C
3,7-Dimethyl-2,6-octadienal



Molinspiration property engine v2018.10

miLogP	3.65
TPSA	17.07
natoms	11
MW	152.24
nON	1
nOHNH	0
nviolations	0
nrotb	4
volume	169.74

Get data as text (for copy / paste).

Fig. 4 Molinspiration online portal shows Molecular Properties and Bioactivity Score of Citral

Table 4: Drug likeness score for compounds Cumin (C. Cyminum):

Sr. No.	Compounds	milog P	TPSA	n atoms	MW	n ON	N OHNH	n violations	n rotb	Volume
1.	Cuminaldehyde	3.24	17.07	11	148.21	1	0	0	2	152.98
2.	Cymene	3.90	0.00	10	134.22	0	0	0	1	150.55
3.	Cuminic alcohol	2.79	20.23	11	150.22	1	1	0	2	158.81
4.	2-Ethoxy-3-Isopropylpyrazine	2.79	20.23	11	150.22	1	1	0	2	158.81
5.	2-Methoxy-3-Sec Butylpyrazine	2.03	35.02	12	166.22	3	0	0	3	168.03
6.	2-Methoxy-3-Methylpyrazine	0.63	35.02	9	124.14	3	0	0	1	117.84
7.	Beta-Pinene	3.33	0.00	10	136.24	0	0	0	0	152.37
8.	Safranal	2.95	17.07	11	150.22	1	0	0	1	158.60
9.	Terpinene	3.36	0.00	10	136.24	0	0	0	1	156.74
10.	Cineole	2.72	9.23	11	154.25	1	0	0	0	166.6

Table 5: Drug likeness score for compounds Black cumin (Nigella sativa):

Sr. No.	Compounds	milog P	TPSA	n atoms	MW	n ON	N OHNH	n violations	n rotb	Volume
1.	Thymohydroquinone	3.26	40.46	12	166.22	2	2	0	1	166.59
2.	P-cymene	3.90	0.00	10	134.22	0	0	0	1	150.55
3.	Carvacrol	3.81	20.23	11	150.22	1	1	0	1	158.57
4.	4-terpineol	2.62	20.23	11	154.25	1	1	0	1	171.20
5.	T-Anethole	3.57	9.23	14	240.37	1	0	0	2	190.28
6.	Sesquiterpenelongifolene	4.95	0.00	15	204.36	0	0	0	0	225.02
7.	Thymol	3.34	20.23	11	150.22	1	1	0	1	158.57
8.	Carvone	2.51	17.27	11	150.22	1	0	0	1	159.48
9.	Citronellol	3.15	20.23	11	156.27	1	1	0	5	181.79

Table 6: Drug likeness score for compoundsBitterCumin(C. Nigrum):

Sr. No.	Compounds	milog P	TPSA	n atoms	MW	n ON	N OHNH	n violations	n rotb	Volume
1.	Gallic acid	0.59	97.98	12	070.12	5	4	0	1	135.10
2.	Protocatechiuc acid	-1.56	121.13	15	234.19	7	3	0	3	167.50
3.	Caffeic acid	0.94	77.75	13	180.16	4	3	0	2	154.50
4.	Ellagic acid	0.94	141.33	22	302.19	8	4	0	0	221.78
5.	Ferulic acid	1.25	66.76	14	194.19	4	2	0	3	172.03
6.	Quercetin	1.68	131.35	22	302.24	7	5	0	1	240.08
7.	Kaempferol	2.17	111.12	21	286.24	6	4	0	1	232.07

Table 7: Biological activity of taken compounds with the reference of receptor mechanism Cumin (C. Cyminum):

Sr. No.	Compounds	GPCR Ligand	Ion Channel Modulator	Kinase Inhibitor	NuclearReceptor Ligand	Protease Inhibitor	Enzyme Inhibitor
1.	Cuminaldehyde	-1.15	-0.44	-1.22	-0.86	-1.48	-0.64
2.	Cymene	-1.18	-0.61	-1.40	-1.21	-1.42	-0.78
3.	Cuminic alcohol	-0.73	-0.16	-0.98	-0.68	-0.78	-0.24
4.	2-Ethoxy-3-Isopropylpyrazine	-0.59	-0.22	-0.53	-0.95	-0.98	-0.38
5.	Beta-Pinene	-0.53	-0.32	-1.45	-0.50	-0.80	-0.34
6.	Safranal	-1.18	-0.61	-1.40	-1.21	-1.42	-0.78
7.	Terpinene	-0.90	-0.24	-1.37	-0.33	-1.55	-0.07
8.	Cineole	-0.93	0.01	-1.60	-1.07	-0.90	-0.15

Table 8: Biological activity of taken compounds with the reference of receptor mechanism Black cumin (Nigella sativa):

Sr. No.	Compounds	GPCR Ligand	Ion Channel Modulator	Kinase Inhibitor	NuclearReceptor Ligand	Protease Inhibitor	Enzyme Inhibitor
1.	Thymohydroquinone	-0.92	-0.44	-1.06	-0.54	-1.17	-0.46
2.	P-cymene	-1.18	-0.61	-1.40	-1.21	-1.42	-0.78
3.	Carvacrol	-1.02	-0.51	-1.15	-0.70	-1.25	-2.56
4.	4-terpineol	-0.63	0.23	-1.60	-0.21	-0.92	-0.07
5.	T-Anethole	-1.48	-1.18	-1.39	-1.40	-1.61	-0.04
6.	Sesquiterpenelongifolene	-0.43	-0.03	-0.77	0.03	-0.67	0.34
7.	Thymol	-1.05	-0.53	-1.29	-0.78	-1.34	-0.57
8.	Carvone	-1.23	-0.30	-2.51	-0.54	-1.21	-0.45
9.	Limonene	----	----	----	----	----	----
10.	Citronellol	-0.81	-0.24	-1.16	-0.61	-0.83	-0.12

Table 9: Biological activity of taken compounds with the reference of receptor mechanism Bitter Cumin (C. Nigrum):

Sr. No.	Compounds	GPCR Ligand	Ion Channel Modulator	Kinase Inhibitor	NuclearReceptor Ligand	Protease Inhibitor	Enzyme Inhibitor
1.	Gallic acid	-0.77	-0.26	-0.88	-0.52	-0.94	-0.17
2.	Protocatechiuc acid	-0.04	-0.21	-0.65	-0.30	-0.12	-0.71
3.	Caffeic acid	-0.48	-0.23	-0.81	-0.10	-0.79	-0.09
4.	Ellagic acid	-0.29	-0.27	-0.01	0.11	-0.18	0.17
5.	Ferulic acid	-0.47	-0.30	-0.72	-0.14	-0.81	-0.12
6.	Quercetin	-0.06	-0.19	0.28	0.36	-0.25	0.28
7.	Kaempferol	-0.10	-0.21	0.21	0.32	-0.27	0.26

chemistry proceedings

MDPI

Bioactivity score of Cumin (*C. Cyminum*)

GPCR ligand property

In the constituents of **Cumin (*C. Cyminum*),** compounds Cuminic alcohol, 2-Ethoxy-3-Isopropylpyrazine, Beta-Pinene shows good ligand property on GPCR receptor.

Ion channel modulation

In all taken constituent of table Cuminic alcohol, 2-Ethoxy-3-Isopropylpyrazine and Terpinene and Cineole shows good ion channel modulation property. They helps to regulate and promote ion channels modulation activity.

Kinase inhibition

Cuminic alcohol and 2-Ethoxy-3-Isopropylpyrazine are the constituent of table data which shows kinase inhibition property.

Nuclear receptor ligand property

In the constituents compounds Cuminic alcohol, Cuminaldehyde, Beta-Pinene and Terpinene shows good nuclear receptor ligand property.

Protease Inhibitor

Beta-Pinene shows good protease inhibition activity.

Enzyme Inhibitor

Terpinene, Cineole, Cuminic alcohol, 2-Ethoxy-3-Isopropylpyrazine, shows good enzyme inhibition activity.

Bioactivity score of Black cumin (*Nigella sativa*)

GPCR ligand property

In the constituents of Cumon (Nigella sativa) compounds 4-terpineol , Sesquiterpenelongifolene , Citronellol shows good ligand property on GPCR receptors.

Ion channel modulation

In all taken constituent of table 4-terpineol, Sesquiterpenelongifolene and Citronellol shows good ion channel modulation property.

Kinase inhibition

Sesquiterpenelongifolene is posseses kinase inhibition property.

Nuclear receptor ligand property

In the constituent of table data Carvacrol , Sesquiterpenelongifolene and Citronello shows good Nuclear receptors ligand property.

Protease Inhibitor

4-terpineol and Sesquiterpenelongifolene shows good protease inhibition activity

Enzyme Inhibitor

In the constituent of table data 4-terpineol, T-Anethole and Citronellol shows good enzyme inhibition property.

Bioactivity score of Bitter Cumin (*C. Nigrum*)

GPCR ligand property

In the constituent of Cumin(C.Nigrum) componds Protocatechuuc acid , Quercetin and kampferol shows good ligand property of GPCR receptor.

Ion channel modulation

In all taken constituent of Protocatechuuc acid , Quercetin and kampferol shows good ion channel modulation property.

Kinase inhibition

Ellagic acid , Quercetin and kampferol shows good kinase inhibition property.

Nuclear receptor ligand property

In the constituent compounds Caffeic acid , Ellagic acid , Ferullic acid , Quercetin and kampferol shows good Nuclear receptors ligand property.

Protease Inhibitor

Protocatechuuc acid , Quercetin and kampferol shows good Protease inhibition property.

Enzyme Inhibitor

Ellagic acid, Caffeic acid , ferulic acid shows good Enzyme inhibition activity.

In-silico ADME T properties

The selected molecules were examined for their in-silico ADME T properties. The results of pharmacodynamics studies revealed that most of the compounds have normal level of mutagenic, tumurogenic, eye and skin irritation and reproductive effects except few which has high irritation effects. Few compounds, on the other side has high level of mutagenic,

tumurogenic, eye and skin irritation and reproductive effects. Based on Pharmacodynamics and pharmacokinetics properties ascorbic acid has got a highest drug score of 0.74, while citric acid and cysteine have got a moderate drug score of 0.58 and 0.48 respectively and urea with a least drug score of 0.08 among the studied molecules. The results are shown in table 10.

Table 10: *In-silico*ADME-Tstudies

Molecules	Pharmacodynamics				Pharmacokinetics			Drug-likeliness	Drug score
	Mutagenic	Tumorigenic	Eye and skinIrritation	Reproductive effect	Solubility	Human Intestinal Absorption	Blood Brain Barrier		
Cuminaldehyde	N	N	H	N	-2.81	2.78	17.07	-11.1	0.27
cymene	N	M	H	N	-2.83	3.19	0.0	-5.63	0.21
cuminic alcohol	N	N	H	N	-2.37	2.25	20.23	-6.67	0.28
2-ethoxy-3-isopropylpyrazine	N	N	N	N	-1.76	1.59	35.01	-3.44	0.49
2-methoxy-3-sec butylpyrazine	N	N	N	N	-1.73	1.63	35.01	-0.86	0.62
2-methoxy-3-methylpyrazine	N	N	N	N	-0.94	0.34	35.01	-1.8	0.56
beta-pinene	N	N	H	N	-2.69	2.8	0.0	-7.56	0.27
safranal	N	N	H	N	-1.99	1.84	17.07	-4.39	0.29
terpinene	N	N	H	N	-2.54	3.13	0.0	-7.74	0.27
Cineole	H	N	N	H	-2.48	2.11	9.23	-3.21	0.17
Thymohydroquinone	H	M	N	N	-2.24	2.5	40.46	-6.33	0.22
P-cymene	N	M	H	N	-2.83	3.19	0.0	-5.63	0.21
Carvacrol	N	N	H	N	-2.53	2.84	2.23	-2.59	0.29

4-terpineol	N	N	H	N	-2.19	2.34	20.23	-7.41	0.28
t-anethole	H	H	N	H	-2.54	2.68	9.23	-3.42	0.1
Sesquiterpenelongifolene	N	N	N	N	-3.81	4.06	0.0	-7.76	0.37
Thymol	H	N	N	H	-2.53	2.84	20.23	-3.02	0.17
Carvone	H	H	H	N	-2.19	2.65	17.07	-18.99	0.1
Limonene	H	H	H	H	-2.54	3.36	0.0	-21.85	0.06
citronellol	N	N	H	H	-2.15	3.35	20.23	-8.68	0.16
Gallic acid	H	N	N	H	-0.74	0.11	97.99	0.12	0.27
Protocatechiuc acid	N	N	N	N	-0.36	-1.16	129.5	-0.89	0.63
Caffeic acid	H	H	N	H	-1.14	0.78	77.76	1.62	0.19
Ellagic acid	N	N	N	N	-3.29	1.28	133.5	-1.6	0.51
Ferulic acid	H	H	N	H	-1.72	1.06	66.76	1.12	0.18
Quercetin	H	H	N	N	-2.49	1.49	127.4	1.6	0.3
Kaempferol	H	N	N	N	-2.79	1.84	107.2	0.9	0.46

*H-HighM-MediumN-Normal

Conclusion

The in silico screening and evaluation parameters of *different varieties of cumin* were performed and it showed the presence of many pharmacological active phyto-constituents. Effective formulations to be developed using indigenous medicinal plants, with proper pharmacological experiments and clinical trials. The manufacture of Herbal products should be governed by standards of safety and efficacy. So finally we concluded that these in silico phytochemical screening data and phytochemical investigation of *different varieties of cumin* will be useful for further studies of pharmacological parameters. The seeds of *different varieties of cumin* contain different types of active constituents in varying amounts.

References:

1. Xia X. Bioinformatics and drug discovery. Curr Top Med Chem 2017;17(15): 1709–26. https://doi.org/10.2174/1568026617666161116143440.

2. Katara P. Role of bioinformatics and pharmacogenomics in drug discovery and development process. network modeling analysis in health informatics and bioinformatics 2013;2(4):225–30. https://doi.org/10.1007/s13721-013-0039-5.

3. Whittaker P. What is the relevance of bioinformatics to pharmacology? Trends Pharmacol Sci 2003;24(8):434–9. https://doi.org/10.1016/S0165-6147(03)00197-4.

4. Ortega S, Cara L, Salvador M. In silico pharmacology for a multidisciplinary drug discovery process. Drug Metabol Drug Interact 2012;27(4). https://doi.org/10.1515/dmdi-2012-0021.

5. Shevtsova ON. Wound healing management bioinformatics approach. Biostatic Biometric Open Access J 2018;7(2). https://doi.org/10.19080/BBOAJ.2018.07.555709.

6. Kim S, Thiessen P, Bolton E, Chen J, Fu G, Gindulyte A, et al. PubChem substance and compound databases. Nucleic Acids Res 2015;44(D1):D1202–13. https://doi.org/10.1093/nar/gkv951.

7. Wishart D, Feunang Y, Guo A, Lo E, Marcu A, Grant J, et al. DrugBank 5.0: a major update to the DrugBank database for 2018. Nucleic Acids Res 2017;46(D1):D1074–82. https://doi.org/10.1093/nar/gkx1037.

8. Wishart D. In silico drug exploration and discovery using DrugBank. Current Protocols in Bioinformatics 2007;18(1). https://doi.org/10.1002/0471250953.bi1404s18. 14.4.1-14.4.32.

9. Lipinski, C.A.; Lombardo, F.; Dominy, B.W.; Feeney, P.J. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Adv. Drug Del. Rev. 1997, 23, 4–25.

10. Veber, D.F.; Johnson, S.R.; Cheng, H.-Y.; Smith, B.R.; Ward, K.W.; Kopple, K.D. Molecular Properties That Influence the Oral Bioavailability of Drug Candidates. J. Med. Chem. 2002, 45, 2615–2623, doi:10.1021/jm020017n.

11. Venkatesh, S.; Lipper, R.A. Role of the Development Scientist in Compound Lead Selection and Optimization. J. Pharm. Sci. 2000, 89, 145–154, doi:10.1002/(sici)1520-6017(200002)89:23.0.co;2-6.

12. Gupta, I.; Gupta, V.; Parihar, A.; Gupta, S.; Lüdtke, R.; Safayhi, H.; Ammon, H.P. Effects of Boswellia serrata gum resin in patients with bronchial asthma: Results of a double-blind, placebo-controlled, 6-week clinical study. Eur. J. Med. Res. 1998, 3, 511–514.

11. S. Raghavendra, V. Kumar, C.k. Ramesh, M. Paramesh, M.H.M. Khan, Turk. J. Biol. 2011, 35, 0912.

12. B. Malstrom, L. Ryden, Biological Oxidations. T Singer, Interscience Publications., New York, 1968, pp 419.

13. G.M. Morris, D.S. Goodsell, R.S. Halliday, R. Huey, W.E. Hart, J Comput. Chem. 1998, 19, 1639-1662.

14. R. Huey, G.M. Morris, A. J. Olson, D.S. Goodsell, J. Comput. Chem. 2007, 28, 1145.