Estimation of drug-likeness properties of GC-MS separated bioactive compounds in rare medicinal *Pleione maculata* using molecular docking technique and SwissADME *insilico* tools

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Research Article

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Abstract

The main aim of present paper is to determine bioactive compounds in *Pleione maculata* extracts using Gas chromatographic technique and to investigate their drug-likeness potential using molecular docking algorithm and ADME studies on the recent intractable disease for example; SARS-CoV-2. *P. maculata* sample was prepared for GC-MS analysis. The peak components are identified based on NIST Library. Molecular docking was performed using PatchDock and energy refinement was carried out using FireDock algorithm followed by drug-likeness analysis using Swiss ADME tool. Mass spectrum revealed various pharmacologically important compounds and novel compounds 8-oxatetracyclo{5.2.1.1(2,6). 1(4,10)}Dodecane, 7-tert-Butyl-1,9,9-Trimeth, Cholesterol Isocaproate, Docosane, 2,4-Dimethyl, 7.dehydrocholesterol isocaproate, Kryptogenin 2,4-dinitrophenyl hydrazine, N-decyl-Alpha,D-2-Deoxyglycoside, pyrimidine-2,4,6(1H,3H,5H)-Trione-1-octadecyl) which are reported for the first time. Molecular docking using PatchDock illustrates GC-MS compounds Nor-diazepam,3-{N-hydroxymethyl}aminocarbonyloxy a good docking and high binding affinity with Atomic contact energy -10.95 kcal/mol against SARS-CoV-2 Spike protein S2 subunit. ADME analysis predict Nor-diazepam,3-{N-hydroxymethyl}aminocarbonyloxy and andrographolide showed very high drug-likeness parameters with no metabolism disturbances. The random control anti-viral drug arabidiol revealed a lower binding energy and lower solubility compared to bioactive compounds of *P. maculata*. The study depicts the first and novel report on various pharmaceutical important GC-MS bioactive compounds and molecular docking study of *Pleione maculata* having potential against various intractable diseases.

Introduction

Plants are the main source of medicines as they produce various secondary metabolites which are biologically active. These secondary metabolites provide nutritional and beneficial effect to the human health (Lakshmi and Rajalakshmi 2011). Orchids are one large kingdom of plants which are over exploited, climatic changes and their illegal trading led to extinction, biodiversity loss (Pant B 2003). Epiphytic orchid growing on other living or non-living for physical supports tend to release bioactive secondary metabolites when they are exposed to disturbance (Lindley and Paxton 1851).. *Pleione maculata* commonly known as the peacock orchid is a rare unexplored epiphyte on the verge of extinction (Chauhan and Sharma 2017) growing on topmost of trees at very high elevation of about 600-1600 meters (Lindley and Paxton 1851). The epiphyte is well-known medicinal plants in few of the Northeastern region of India were the local people use either the pseudobulbs or rhizome to treat liver problems, stomach ailments and headache (Pant 2003; Teoh 2016). Gas chromatography is an instrumental technique coupled with mass spectrometry applied for separation, identification and quantification of organic compounds and chemical mixtures study. An inert gas such as Helium is used as mobile phase (carrier gas). The samples to be analyze will be injected and will interact with the glass or metal column coated with stationary phase which will elute different compounds at different time called Retention time (Ghosal and Srivastava 2013). The GC-MS method is highly sensitive, reproducibility and high speed resolution (Dua and Garg 2013). A random control anti-viral drug Arabidiol was used in severe cases of COVID-19 as it was observed to reduce the viral disease (Wang et al. 2020).

A worldwide viral outbreak of dreadful disease COVID-19 arose during the month of December 2019 in Wuhan, China (Yang and Wang 2020;Yang et al. 2020).. Severe Acute Respiratory Syndrome - Coronavirus-2 (SARS-CoV-2) as named by the International Committee on Taxonomy of Viruses (ICTV) and the disease cause was named coronavirus disease 2019 (COVID-19). COVID-19 is no new virus but a possible mutation of the long known SARS-CoV-1. A genome variation analysis was analyzed using detective genome computational tool were it revealed SARS-CoV-2 shares nearly 80% similarities with the SARS-CoV gene pool (Zhang et al., 2017) with nearly 17% variation which is a mutation occurring in spike protein, envelope protein and other respective proteins of SARS-CoV (Sardar et al. 2020) . The viral genome analysis of SARS-CoV-1 open reading frame (orf) has been observed to have a potential mutation to adapt to new environment (Groneberg et al. 2005) and recombination (Li Fang 2016) which might cause severe virulence of the virus. The Severe Acute Respiratory Syndrome (SARS) is a crown-like virus or Coronavirus which was spread widely in the late 2000 over 25 countries causing thousands of cases and death (Wen et al. 2011). Since 2003, anti-viral research has been evaluated for anti-SARS-COV activity in order to prevent the re-emergence of the deadly disease. The genome of SARS-CoV encodes various vital target proteins: the spike protein (S), 3CL Protease, the NTPase/Helicase, RNA-dependent RNA polymerase, membrane protein (M), envelope protein (E) and nucleocapsid phosphoprotein (N) which are involve in the virus replication, transcription and translation (Yang and Wang 2020). The main molecule that mediates coronavirus entry into host cell is their Spike protein (S) which is multi-functional (Li Fang 2016) were attachment is initiated by S1 subunit and conformation changes takes place from pre-fusion to post-fusion or membrane fusion form. The incorporation of the virus is initiated by the S2 subunit of spike glycoprotein through membrane fusion with host receptor (Rane et al. 2020). The viral 3-Chymotrypsin like protease responsible for replication complex (Anand et al. 2003) is considered highly conserved between the SARS-CoV and SARS-CoV-2 (Zhang et al. 2017; Donald and Hai-Feng 2020) The SARS-CoV spike protein has a strong binding affinity towards human receptor

Angiotensin-converting enzyme 2 (ACE2) based on structure and interaction (Zhang et al. 2020). The main agent for transmission is through respiratory droplets and can be transmitted from human to human through contact with the droplets (Yang and Wang 2020). For early diagnosis of SARS-CoV, improved RT-PCR assays can be carried out which is worldwide used for virus identification and high specificity (Shen et al. 2020). The symptoms of SARS-CoV -1 were persistent fever, chills, dry cough, dizziness, headache, sore throat, sputum production, vomiting or nausea, special attention given for watery diarrhea. But the primary target for infection is the respiratory epithelial cells. The viral effect the immune-mediated mechanism and molecular studies showed epithelial cells of gastrointestinal tract seems to be major target cells (Groneberg et al. 2020). In 2019, various health authorities of the Hubei province in China reported the novel COVID-19 disease as pneumonia (Wu et al. 2020) or COVID-19 pnuemonia (Tian et al. 2020). Pnuemonia are a type of fatal respiratory tract infections which are caused by bacteria (Streptococcus pneumonia) or viruses on inhaling them and the symptoms of Pneumonia are no different from the deadly virus SARS-CoV-2 such as high fever, shortness of breath, rapid breathing and cough (Zafar 2016). Earlier SARS-CoV patient was treated with anti-inflammatory steroidal compound such as methylprednisolone (Groneberg et al. 2005; Wu et al. 2017) and a metabolite profiling for SARS-CoV survivors using Ultra-high performance liquid chromatography-mass spectrometry (UPLC-MS) and Gas chromatography-mass spectrometry (GC-MS) were carried out after 12 years of recovery, were a significant portion (64%) of the recovered patients were prone to lung infections and various serum metabolic disorders associated with lipid metabolism including hyperlipidemia (HL), Cardiovascular abnormality (CVA), and abnormality in glucose metabolism (AGM). Single-stranded antisense as an anti-viral compound has been a vital therapeutic area for emerging viruses (Gulam et al. 2016). Antisense therapy (Anti-sense antivirals) treats diseases using single-stranded antisense-oligo-nucleotides to target specific mRNA sequences and blocks the translation of viral protein (Gulam et al. 2016) or by modifying the protein expression (Sharad 2019). Today, In Silico studies are more favored for drug target identification in order to find the interaction of pharmaceutically important compound with their target. The most commonly known computational tool for drug-target is molecular docking using various algorithms. PatchDock is highly efficient (Prabhu and Rajeswari 2016) accurate (Doss et al. 2014), fast transformational search and free-online server in comparison to other computational molecular docking server. PatchDock is a molecular docking algorithm based on the principle of shape complementarity. A complementarity molecular shaped is yield forming a conformational transformation of each docking molecule known as induced fit. The transformed molecules can be further evaluated based on the scoring function which involves geometric-fit and atomic contact energy (ACE). PatchDock algorithms contain three stages, (a) Molecular shape representation based on geometric patches (Concave, convex and flat surface pieces) (b) Surface patch matching and (c) Filtering and scoring (Duhovny et al. 2002). Various parameters are involved for running a docking interaction between molecules such as the Root Mean Square Deviation (RMSD) and a complex type. The RMSD is applied to prevent redundant solution of molecule and is exact (Duhovny et al. 2002). PatchDock uses technique such as geometry hashing and pose clustering which are advance data structures and spatial pattern detection. In Docking, energy refinement is required for further development of drug compound using FireDock (Andrusier et al. 2007; Surana et al. 2018). The FireDock (Fast iteration refinement in molecular docking) refinement of energy uses Monte Carlo minimization of binding score and it is highly efficient, easy to understand and requires no prior knowledge in docking (Lipinski et al. 1997). The score are Atomic Contact Energy (ACE), softened Van der Waals interaction, partial electrostatics and additional estimation of the binding energy. FireDock algorithm includes three refinement steps (1) Side-chain optimization (2) Rigid-body minimization and (3) Scoring and ranking (Lipinski et al. 1997).The docking analysis can be predicted base on the highest binding affinity and lowest docked energy (Iyamah et al. 2017). Prior to clinical studies which are time consuming and not cost effective, drug-likeness of compounds can be primarily analyzed using computational tools. Swiss ADME a free web tool to evaluate pharmacokinetics based on different drug-likeness parameters are predicted such as physicochemical properties, solubility and pharmacokinetics of molecule (Daina et al. 2003).

To-date, there has been a lot of controversies regarding vaccine or drug development against SARS-CoV-2 pnuemonia, therefore a compound separation technique using Gas chromatography-Mass spectrophotometry was performed for the epiphytic medicinal orchid *Pleione maculata* with the intention to provide a preliminary basic ideas on different bioactive compounds present in medicinal plants which might have potential against dreadful diseases. A phytochemical studies and anti-microbial activity of *Pleione maculata* was also reported to have distinct zone of inhibition against *Streptococcus pneumonia* (Sympli et al. 2019)· With prior knowledge using steroidal compound and antisense target for treatment of other viral disease in the earlier years, a few of the GC-MS compounds of *Pleione maculata* were known to have steroidal anti-viral bioactive compound as well as an antisense target compound. Based on the symptoms and side-effects after recovery from SARS-CoV patient, various bioactive compounds which might have the potential for the following were preliminary investigated for their drug-likeness using Molecular docking algorithm using PatchDock. A random control anti-viral treatment of COVID-19 arabidol was used for comparison with the bioactive compounds.

The present paper analyzed different bioactive compounds present in *Pleione maculata* using GC-MS technique and to evaluate their drug-likeness potential having multi-target bioactivity using molecular docking algorithm to observe the binding energy as well as the conformational fit between the bioactive compounds of *P. maculata* against target proteins, SARS-CoV-2.

Materials And Methods

2.1 Collection and extract preparation of plant material

Pleione maculata samples were collected from top tree trunks in the dense forest of Khliehriat, East Jaintia Hills regions of Meghalaya for the processing. The parts of *P. maculata* was washed under running tap water, followed by surface sterilization with distilled water, 1% sodium hypochlorite and re-washed with distilled water. The samples were shade dried until use. The samples were crushed and each plant part was soaked in three different solvents such as ethanol, methanol and acetone followed by incubation 24-48 hours. The crude extract was filtered using Whatman filter paper No 1 (Vijisaral and Arumugam 2014). The solvent extracts are then evaporated by using open-air evaporation in the laminar air flow hood for 24 hours and centrifuged at 12,000 rpm for about 15 minutes at 4˚C. The concentrated extracts was the transferred into micro-centrifuge tube for GC-MS analysis.

2.2 GC-MS analysis and Identification of compounds

In oven, the initial temperature was 110°C for 3 minutes (Thomas et al. 2013), then increased for 5°C/min to 200°C and held for 3 minutes and again increase for 5°C/min to 300°C and held 10 minutes (Darmasiwi et al. 2015). Injector and ion source temperature were 280°C and 180˚C, Injection volume was 1 µL, and the spilt ratio was 0:1. Carrier helium gas was used through the column. Solvent delay by 9.00 min and transfer temperature was 200°C. The sample was scan from 40 to 600Da. The chromatography was performed on a column of 60.0m x 250µm.

2.3 Identification of components by using NIST

The National Institute of Standards and Technology (NIST) are a mass spectral search databases for comparisons of acquired and unknown spectrum with the NIST/EPA (Environmental protection Agency)/NIH (National Institute of Health) Databases. The components are identified based on the standards employed by the National Institute Standards and Technology (NIST) Library (Darmasiwi et al. 2015). The detection is employed by comparing the peaks with that in the Mass spectral standard reference data of NIST having more than 62, 000 patterns.

2.4 Molecular docking using PatchDock

2.4.1. Input

Protein structures retrieval: Protein receptor target was retrieved from Protein Data Bank (PDB) in 3D structure as shown in Fig. 1. The following three target receptors are (1) SARS-CoV-2-3CL protease (PDB ID: 6M2Q), (2) SARS-CoV-2 RNA-dependent RNA-Polymerase (PDB ID: 6M71) and (3) SARS-CoV-2 spike glycoprotein receptor S2 subunit (PDB ID: 6LXT)

2.4.2 Ligand retrieval

A total of 19 ligand molecule ass shown in Fig. 2 was retrieved from PubChem database in SDF file format and using PyMol the small ligand was converted into PDB format (Prabhu and Rajeswari 2016; Yadav et al. 2017). The 3D-structures with compound CID: 6211 (2,4,6-Pyrimidinetrione), CID: 248856 (21-acetoxypregenelone), CID: 543946 (P-menth-8(10)-en-9-ol), CID: 541761 (Nor-diazepam, 3-N-hydroxymethyl,aminocarbonyloxy), CID: 441207 (Digitoxin), CID: 19089489 (DI-N-Decylsulfone), CID: 3893 (14-dodecanoic acid), CID: 13948 (Estra,13,5 (10)-trien-17-beta-ol), CID: 5283405 (Arachidonic amide, N-5-hydroxy-N-pentyl), CID: 572031 (1-methylsulfanyl-9,10-Dioxo-9,10-dihydro-anthracene-2-carboxylic acid), CID: 14077841 (Cholesterol margarate), CID: 8215 (Docosanoic acid), CID: 99470 (26-hydroxy cholesterol), CID: 5318517 (Andrographolide), CID: 135426867 (6H-purin-6-one-,1,7-dihydro-2-methylamino), CID: 261799 (Pseduosarsasapogenin), CID: 71360559 (Oxiraneundecanoic acid, 3-pentyl, methyl ester,cis), CID: 5486971 (Pregabalin), CID: 131411(Arabidol)

2.4.3 Molecular Docking analysis

Protein-Small ligand molecule docking was performed using PatchDock algorithm (Prabhu and Rajeswari 2016;Yadav et al. 2017;Surana et al. 2018). The parameters was set, were complex type was selected for protein-small ligand molecules, Clustering root mean square deviation (RMSD) was set to 1.5Å for protein-ligand interaction. The protein receptor was uploaded in PDB format also the small ligand molecule was uploaded followed by the form submission. The following output will be further sent by PatchDock to the given email ID. A 1000 docking candidate generated from PatchDock in their transformation form were refined and scored using FireDock. The result was then visualized using PyMoL a molecular visualization graphics system tool.

2.4.4 Drug-likeness analysis of bioactive compounds using Swiss ADME tool (Daina et al. 2003)

Chemical structure of compounds were downloaded from PubChem data bank in SDF (structure data format) and Swiss ADME web page was opened and the file was imported from the external file option and was converted into molecular sketcher based on ChemAxon's Marvin JS followed by ADME calculation using default parameters.

Results And Discussion

GC-MS analysis reported more than 146 hits and lead compounds from different parts of *P. maculata*. The compounds identified from the acetone leave extracts were more as compared to the other solvent extracts. The following hit and lead compounds of *P. maculata* with their bioactivity are listed on Table 1, Table 2 & Table 3. The GC-MS analysis of other orchids mostly focuses on the flower scent profile rather than medicinal profile, for example Vanda species (Darmasiwi et al. 2015), *Rhynchostylis gigantean Ridl, Rhynchostylis gigantean var. harrisonianum Holtt., Vanda coerulea and Dendrobium parishii Rchb*. F., (Julsrigival et al. 2013) and *Dendrophylax lindenii* (Sadler et al. 2011). The GC-MS report of *Pleione maculata* in the paper mainly focused on total medicinal important compounds present in different parts of the epiphyte. Compounds such as Phenol 4-(ethoxymethyl), Heptacosanoic acid methyl ester, 9-octadecanoic acid (Z)- 2-Hydroxy-1-(hydroxymethyl) ethyl ester (Vijisaral and Arumugam 2014; Rajalakshmi and Mohan 2016), Nonanoic acid 9(3-hexemyldenecyclopropylidene-2-hydroxy-1-1 (HYD) (Sahin et al. 2006) , Alpha-ketostearic acid ethyl ester, 1-naphthalenepropanol alpha-ethyl Decahydro-5-(hydroxymethyl), Cis Cis Cis-7,10,13-Hexadecatrienal (Prabhadevi et al. 2012; Abdulaziz et al. 2019), 1H-Purin-2-amine-6-methoxy, 4-cyanobenzoic acid Tridec-2-YNYL ester, Alpha-L-Fucopyranose 1,2.3,4-Bis (Benzeneboonate), cholesterol margarate, 2.pyridinecarboxylic acid 6-methoxy, 1-methyl sulfanyl -9-10-Dioxo-9,10-dihydro-anthracene-2-carbxylic acid, pyrimidine-2,4,6(1H,3H,5H)-Trione-1-octadecyl), E,E-1,9,17-Docasatriene Subavathy and Thilaga 2016; Kumaravel et al. 2019), N-decyl-Alpha D-2-Deoxyglycoside are few of the compounds which were identified but have no bioactivity reported before from other papers. Compounds 8-oxatetracyclo{5.2.1.1(2,6). 1(4,10)}Dodecane, 7-tert-Butyl-1,9,9-Trimeth, Cholesterol Isocaproate, Docosane, 2,4-Dimethyl, 7.dehydrocholesterol isocaproate, Kryptogenin 2,4-dinitrophenyl hydrazine, N-decyl-Alpha,D-2-Deoxyglycoside, pyrimidine-2,4,6(1H,3H,5H)-Trione-1-octadecyl) are some of the novel compounds which have not been reported earlier.

Molecular docking study was performed for nineteen GC-MS compounds using PatchDock with energy minimization and structure refinement using FireDock was analyzed. The selected compounds for docking were based on their bioactivity against symptoms related to the SARS-CoV-2 pneumonia such as anti-inflammatory activity, prevent cardiac insufficiency, prevent fatique, prevent shortness of breath, prevent gastrointestinal diseases, heart beat improvement, anti-viral activities and compound having repellent activity, larvicidal activity on the basis of earlier knowledge of using anti-malarial drug for reducing the viral load (Rane et al. 2020). The targets were docked properly as the binding energy was shown to be negative and the docked ligand RMSD value is 2.0Å (Singh et al. 2017). The binding residues and Atomic contact energy of ligands against the target proteins are listed in Table 4. The highest binding energy of docked molecule was considered below - 6.00 kcal/mol (higher negative value) higher binding energy then higher the binding potential between molecules. The different GC-MS compounds interacted with numbers of residues on the side-chain and backbone of the target protein as shown Fig. 4, Fig. 5 and Fig. 6. A non-covalent (polar) interaction was observed between the docking molecules at a closer distance of 1.5Å. All the docked molecules showed zero hydrogen bonding between them but formed a specific electrostatic, van der Waals interaction and some interacted with the positively charged functional groups of amino acid (Lysine, arginine, histidine) while some interacted with the hydroxyl groups of amino acid Serine, Threonine and Tyrosine. Amino acid residues such as Serine, Threonine and tyrosine contribute rotating hydroxyl groups between docked molecules are considered rigid (Pantsar and Poso 2018).

3.1 Docking analysis of the SARS-CoV-2 RNA-dependent RNA – polymerase (PDB ID - 6M71)

The target protein RNA-dependent RNA-polymerase residues interacted with GC-MS compounds based on lowest binding energy, Digitoxin, cholesterol maragarate, Docosanoic acid, Pseduosarsasapogenin-5,20-dien, Arachidonic amide,N-{5-hydroxy-N-pentyl), DI-N-Decylsulfone, Oxiraneundecanoic acid,3-pentyl,methyl ester,cis, andrographolide, 21-acetoxypregenelone, p-menth-8(10)-en-9-ol, 26-hydroxycholesterol and Pregabalin with high atomic contact energies -22.96, -21.60, -13.13, -12.54, -12.04, -11.57, -11.38, -8.43, 8.38, -7.18, -7.11 and -6.85 kcal/mol. The most prominent and common amino acid residues binding to the target protein were Asn 414, Lys 411, Tyr 141, Val 12, Tyr 546 and Asn 781.

3.2 Docking analysis of ligands against target SARS-CoV-2 3CL Protease (3CL pro) (PDB ID - 6M2Q)

GC-MS compounds of *P. maculata* Digitoxin, 26-hydroxycholesterol, 1-methylsulfanyl-9,10-Dioxo-dihydro-anthracene-2-carboxylic acid, Arachidonic amide,N-{5-hydroxy-N-pentyl), cholesterol margarate, 21-acetoxypregenelone, pseduosarsasapogenin-5,20-dien, DI-N-decylsulfone,, Nor-diazepam,3-{N-hydroxymethyl}aminocarbonyl, Andrographolide, p-menth-8(10)-en-9-ol and pregabalin with high binding

energies -13,27, -12.61, -12.22, -10.86, -9.91, -9.22, -8.41, -7.39, 7.19, -7.17, 6.75 and -6.33 kcal/mol against the target SARS-CoV-2 3CL protease. The most commonly found amino acid residues binding to the target pocket are Gln 110, Phe 294 and Thr 111.

3.3 Docking analysis of ligands against the target SARS-CoV-2 post-fusion core structure of spike glycoprotein S2 subunit (PDB ID- 6LXT)

The target Spike glycoprotein-S2 subunit amino acid residues interacted with compounds, 1-methylsulfanyl-9,10-Dioxo-9,10-dihydro-Anthracene-2-carboxylic, Nor-Diazepam, 3-{N-hydroxymethyl} aminocarbonyloxy, andrographolide, Digitoxin, cholesterol margarate, 26-hydroxycholesterol, p-menth-8(10)-en-9-ol and pregabalin with high binding energies of -10.95, -9.23, -8.93, -8.23, -8.23, 6.68 and 6.29 kcal/mol. The most common residues binding to target proteins are Ser 943, Ser 940, Glu 1188, Ser 939, Asp 1184, Asp 936, Lys 1191, Gln 935, Asn 1187.

3.4 Drug-likeness analysis of bioactive compound

Drug-likeness was analyzed to check whether they possess favorable ADME (Absorption, Distribution, metabolism, excretion) properties. Drug-likeness analysis of bioactive compounds is listed on Table 5 with their different parameters as shown in the bioavailibity radar Fig. 7. Nor-diazepam,3-{N-hydroxymethyl}aminocarbonyloxy, a bioactive compound which shows a good binging affinity against SARS-CoV-2 shows high drug-likeness parameters with good solubility property, no excretion problems as there is no pharmacokinetics P-gp (Permeability-glycoprotein) interference and non-inhibitor of CYP enzymes and compound is specific in nature as there is zero alerts for PAINS (pan assay interference compounds). 1-methylsulfanyl-9,10-Dioxo-9,10-dihydro-anthracene-2-carboxylic acid drug-likeness parameters is good since it follows the Lipinski, Ghose, Veber, Egan, Muegge rule and Bio-availability score 0.55 but the PAINS (Pan assay interference compounds) shows some interference with Quinone A compound therefore the compound is not specific in nature and is moderately soluble in nature. Digitoxin, might have shown good binding affinity but do not obey any of the drug-likeness parameters. Pregabalin and P-menth-8(10)-en-9-ol bioactive compound are highly soluble in nature but does not obey all the drug-likeness parameters due to molecular weight 160. 21-acetoxypregenolone an antisense target compound showing good binding affinity against SARS-CoV-2 shows moderate drug-likeness parameters, specific in nature and no excretion problems but is an inhibitor of CYP2C9 enzyme. Pseduosarsasapogenin-5,20-dien and Andrographolide drug-likeness activity is moderate with good solubility property. Compounds such as DI-N-decylsulfone, Arachidonic amide,N-{5-hydroxy-N-pentyl}, 26-hydroxycholesterol, Cholesterol margarate and Docosanoic acid showed poor solubility with low drug-likeness properties. Arabidiol an already marketed anti-viral drug does follow the Lipinski rule of five but does not obey the drug-likeness parameters and is poorly soluble compared to the bioactive compounds of *Pleione maculata* with high solubility in nature.

A phytochemical test for *P. maculata* also depicts the presence of various phytochemical compounds in different parts of the epiphyte (Sympli et al. 2019).Docking involves interaction of various polar and non-polar groups were both play a significant role in the stability of protein-ligand interactions. In Docking, water solvent is removed by most programs as they tend to form hydrogen bonds with molecules either as donor or acceptor (Pantsar and Poso 2018). Protein-ligand interactions are strong on removal of H-bond but in association with other non-covalent interactions such as electromagnetic interactions, ionic interactions, van der waal interaction and hydrophobic interactions plays an important role in protein-ligand stability (Yadav et al. 2017). Van Der Waals interactions are non-covalent intermolecular interactions which can be repulsive or attractive interaction, bonding energy decreases from zero to its negative value, when the distance of attraction between two molecules are close whereas repulsive forces occurs when the distance of separation decreases and bonding energy increases (Singh 2016). Van der Waals interaction may be considered weak but they play a vital role in structure and biomolecules interaction. Hydrogen bonds are also weak non-covalent bond which induces thermal fluctuation in energies and tend to form or break rapidly causing conformational changes during binding (Bronowska 2011). Drug-likeness compounds should have a good aqueous solubility which is predicted by three methods ESOL, (ALI) logS and (SILICOS-IT) logS (Mishra and Dahima 2019). Orally active drug should also obey the Lipinski five rule; Molecular weight (MW) not more than 500g/mol, Hydrogen bond acceptors should not be more than 10, hydrogen bond donors not more than 5, LogP value less than 5 and number of rotatable bonds not less than 10 (Lipinski et al. 1997).GC-MS bioactive compound Nor-diazepam,3-{N-hydroxymethyl}aminocarbonyloxy , Andrographolide, depicts a high binding energy -10.95, -9.23Kcal/mol and as well as very high drug-likeness properties when compared to the binding energies of Fisetin, quercetin, isorhamnetin, genistein, luteolin, resveratrol and apigenin with -8.5, -8.5, -8.3, -8.2, -8.2, -7.9,-7.7 Kcal/mol, respectively against S2 subunit spike glycoprotein (Rane et al. 2020). Compounds Nor-diazepam,3-{N-hydroxymethyl}aminocarbonyloxy, Andrographolide, pregabalin, P-menth-8(10)-en-9-ol, 21-acetoxypregenolone, 1-methylsulfanyl-9,10-Dioxo-9,10-dihydro-anthracene-2-carboxylic acid are few of the drug-likeness compounds which meets the characteristics to be a drug such as solubility, Lipophilicity (Log P) less than 5, hydrogen bond not more than 5. Most of the compounds predicted showed good solubility and good absorption. The drug-likeness parameters describe is the main criteria for primary drug development. The bioactive compounds of *P. maculata* screened using GC-MS has more potential as drug-

likeness against various intractable diseases for example here; SARS-CoV-2 pnuemonia (COVID-19) because of its stronger binding energies, closer interaction and abide by the ADME characteristics.

Conclusion

GC-MS analysis in methanol, ethanol and acetone extracts of different parts (Leaves, stem and roots) of *P. maculata* identified major peaks indicating the presence of phytochemical constituents such as Palmitic acid, Vitamin E, Vitamin A precursor, Cardiac glycoside, Ascorbic acid, Linoleic acid, oleic acid, stearic acid, alkaloid, di-terpenoid, flavonoid, phenolic and steroidal compound. Cholestenone compound which has the capability to suppress fat accumulation and anti-obesity activity is not commonly found in other medicinal plants but reported in the GC-MS study of *P. maculata*. The identified compounds were known to have various activities commonly antimicrobial, anti-inflammatory, antioxidant, cancer preventive, hypocholesterolemic, nematicide, antiasthma, anti-arrhythmic activity (improve heart beat), anti-viral activity, larvicidal activity, anti-convulsants and anti-obesity activities. Molecular docking analysis is one of the structure based designing of drugs. The compounds of *P. maculata* showed a highly effective binding affinity and high atomic contact energy. The spike glycoprotein S2 subunit of SARS-CoV-2 was one of the rigid target as it initiates membrane fusion with the host receptor but bioactive compound Nor-diazepam,3-{N-hydroxymethyl}aminocarbonyloxy showed a very good docking and high binding affinity with Atomic contact energy -10.95 kcal/mol and very high drug-likeness properties. For centuries, plants are the main source of medicinally important natural products. The paper represents the first report on the GC-MS analysis, molecular docking and drug-likeness study of *P. maculata*. The findings are expected to contribute a significant and major therapeutic impact in the pharmaceutical companies. An in-vitro and in-vivo analysis has to be implemented to know the mechanism of action, cytotoxicity studies of the above effective bioactive compounds. In conclusion, the study on rare *Pleione maculata* highlights their prospective therapeutic potentialities against various intractable diseases and their bioactive components will enhance a sustainable rural livelihood in both primary and secondary health care and also to save them from extinction and over-exploitation. The effective drug-likeness compound does not have to be separated or isolated directly from the sources plant but the study will provide a basic idea on the synthetic production of effective bioactive compounds.

Declarations

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Conflict of interest

The author declares no conflict of interest. The research work is original

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Tables

Table 1 GC-MS analysis of acetone extracts of *Pleione maculata*

Parts of *P. maculata*	Peak name	Molecular name	Molecular formula	Molecular weight	Activity
Leave	N-hexadecanoic acid	Palmitic acid	$C_{16}H_{32}O_2$	256	Anti-inflammatory, Antioxidant, hypocholesterolemic nematicide, pesticide, anti-androgenic flavor, hemolytic, 5-alpha reductase inhibitor Anti-carcinogenic (Aparna et al. 2012; Kumar et al. 2010; Shree 2012)
	Dodecanoic acid		$C_{12}H_{24}O_2$	200	Antibacterial, anti-viral, antioxidant, hypercholesterolemic (Gideon 2015)
	3-L- (+) Ascorbic acid 2, 6-dihexadecanoate		$C_{38}H_{68}O_8$	652	Anti-tumour and antibacterial activity (Babar et al. 2016)
	8,11,14 Eicosatrienoic acid, Methyl ester	Methyl dihomo-γ-linoleic acid	$C_{21}H_{36}O_2$	320	Tumoricidal (Das and Madhavi 2011)
	8, 11, 14-Docosatreienoic acid, Methyl ester		$C_{23}H_{20}O_2$		Anti-diabetic activity (George et al. 2018)
	Z,Z,-4,6-Nonadecadien-1-ol-acetate	Esters	$C_{21}H_{38}O_2$	322	Insecticidal activity (Hamada et al. 2018)
	Dichloroacetic acid, Tridec-2-YNYL ester		$C_{15}H_{24}C_{12}O_2$	306	Anti-mastitis (Dinesh et al. 2016)
	Octadecanoic acid, Methyl ester	Methyl stearate	$C_{19}H_{38}O_2$	298	Antifungal and antioxidant (Pinto et al. 2017)
	Nonanoic acid, 9(3-hexemyldenecyclopropylidene)-,2-hydroxy-1-1(HYD)	Nonanoic acid derivative			Not reported usually nonanoic acid have nematicidal activity components of biodegradable polyesters (Sahin et al. 2006)
	9,12,15-Octadecatrienoic acid, (Z,Z,Z)-	Linoleic acid	$C_{18}H_{30}O_2$	278	Anti-inflammatory, antihistaminic, cancer preventive, anti-acne, anti-coronory (Kumar et al. 2010)
	Octadecanoic acid	Stearic acid	$C_{18}H_{36}O_2$	284	Hypocholesterolemic, surfactant and softening agent, perfumery, flavor and in cosmetic Antibacterial activity (Rajashyamala and Elango 2015; Da Silva et al. 2003)
	Docosanoic acid/ Behenic acid	Fatty acid	$C_{23}SH_{44}O_2$	340	Anti-cancer potential against MCF7 and HeLa cell lines, Hair moisturizer (Lawal et al. 2015; Eswaraiah et al. 2020)
	Alpha-Ketostearic acid, ethyl ester		$C_{20}H_{38}O_3$	326	No activity reported
	Cyclopropaneoctanoic acid, 2-[[2-Ethylcyclopropyl)Methyl]cyclo	-	$C_{22}H_{38}O_2$	334	Anti-carcinogenic (Shree 2012)
	1-naphthaleneproponal, alpha-ethyl Decahydro-5-(hydroxymethyl)-		$C_{20}H_{36}O_2$	308	No activity reported
	Terpin hydrate		$C_{10}H_{22}O_3$	172	Expectorant commonly used to loosen mucus in patients presenting with acute or chronic bronchitis and related conditions (Jahan et al. 2015)
	Cis, Cis, Cis-7,10,13-Hexadecatrienal	aldehyde	$C_{16}H_{26}O$	234	No activity reported (Prabhadevi et al. 2012; Abdulaziz et al. 2019)
	Cholest-4-en-3-one	Cholestenone	$C_{27}H_{44}O$	384	Anti-obesity, suppress body weight and body fat accumulation (Suzuki 1993, 1998)
	Diazoprogesterone	Steroid, Nitrogen compound	$C_{21}H_{30}N_4$	338	Antimicrobial anti-inflammatory, Hepatoprotective, Duiretic, Anti-cancer Anti-HIV (Gopinath et al. 2013; Jothi et al. 2015)
	26-hydroxy cholesterol	steroid compound	$C_{27}H_{46}O_2$	402	Biomarkers in diagnosis of Alzheimers disease (AD) and other neurodegenerative disorders (De Kock 2016)
	pregn-4-ene-1,20-Dione, 12-hydroxy-16,17-dimethyl-	Steroid compound	$C_{23}H_{34}O_3$	358	Sexual disorders, baldness, anti-psioriatic, anti-pyretic, anti-allergic (Ansarali et al. 2018)

	Spiro[Androst-5-ene-17,1-cyclobutan]-2-one,3-hydroxy-, (3,beta,17,beta)		$C_{22}H_{32}O_2$	328	Anti-inflammatory and anti-microbial Antiarthritic, anticancer, antiasthma, Hepatoprotective (Sathiyabalan et al. 2014; Okereke 2017)
	Andrographolide	Diterpenoid	$C_{20}H_{30}O_5$	350	cell signaling, Immunomodulator, used in stroke (Selvan and Velavan 2015)
	8-oxatetracyclo {5.2.1.1(2,6). 1(4,10)}Dodecane, 7-tert-Butyl-1, 9,9-Trimeth			262	compound not reported
	Ergosta-7,22-dien-3-ol,(3.Beta, 22E)		$C_{28}H_{46}O$	398	Anti-inflammatory effect (Pereira et al. 2014)
	Stigmastan-6,22-dien,3,5-dedihydro		$C_{29}H_{46}$	394	Antimicrobial Antiasthma, Anti-inflammatory Diuretic, Anticancer, Antiarthritic Antioxidant, insecticidal activity (Sujatha and Vijayalakshmi 2013; Rajeswari et al. 2013; Asaraja and Sahayaraj 2013)
	Cholest-5-en-3-ol(3,beta)-,carbonochloridate		$C_{28}H_{45}ClO_2$	448	Antibacterial (Agboke and Attama 2016)
	Cholesterol Isocaproate				Compound not reported
	Octadecane,3-ethyl-5-(2-ethylbutyl)-		$C_{26}H_{54}$	366	Antimicrobial, antioxidant (Chandrasekar et al. 2015)
	Docosane, 2,4-Dimethyl				compound not reported
	DL-alpha-tocopherol	Vitamin E	$C_{29}H_{50}O_2$	430	Anti-oxidation effects, protects human skin against cytotoxic effect of UVB and dietary supplement (Kondo et al. 1990;Jialal and Grundy 1992)
	Vitamin E	Vitamin E	$C_{29}H_{50}O_2$	430	Analgesic, anti-cataract, anti-coronary, anti-diabetic, antioxidant, Hepatoprotective, Vasodilator, protein-kinase-c-inhibitor, anticancer, Lipoxygenase inhibitor, Anti-bronchitic, anti-coronary (Jothi et al. 2015; Rajalakshmi and Mohan 2016)
	6h-Purin-6-one,1,7-dihydro-2(methylamino)	imidazole derivatives	$C_7H_8N_{4O}$	164	Acts as anti-viral (active against HSV-1 and HSV-2) (Kumar et al. 2017)
	1H-Purin-2-amine-6-methoxy		$C_6H_7N_{5O}$	165	No activity reported
	26-nor-5-cholesten-3,beta,-ol-25-one		$C_{26}H_{42}O_2$	386	Anti-tumor, anti-inflammatory, anti-oxidant and anti-bacterial (Yuvaraj and Arul 2014)
	21-Acetoxypregnenolone		$C_{25}H_{36}O_5$	416	Anti-microbial, antioxidant, targets antisense strands (targets single stranded RNA complimentary to protein coding mRNA which hybridizes and block translation of protein) mainly use in gene knockdown Antiproliferative activity against melanoma cells (Chidambaram et al. 1996; Kim et al. 2009; Chen et al. 2014)
Stem	Hexadecanoic acid, methyl ester		$C_{17}H_{34}O_2$	270	Antioxidant, hypocholesterolenic, flavor, hemolytic 5-alpha reductase inhibitor, nematicide, antiandrogenic (Easwaran and Ramani 2014)
	N-hexadecanoic acid	Palmitic acid	$C_{16}H_{32}O_2$	256	Anti-inflammatory, Antioxidant, hypocholesterolemic nematicide, pesticide, anti-androgenic flavor, hemolytic, 5-alpha reductase inhibitor (Kumar et al. 2010; Aparna et al. 2012)
	Isopropyl palmitate		$C_{19}H_{38}O_2$	298	Anti-proliferative activity (Saxena et al. 2007)
	8,11,14 Eicosatrienoic acid, methyl	Methyl dihomo-γ-	$C_{21}H_{36}O_2$	320	Tumoricidal (Das and Madhavi

ester	linoleic acid			2011)
10-undecynoic acid, methyl ester		$C_{12}H_{20}O_2$	196	Anti-oxidant (Palakkal et al. 2017)
Octadecanoic acid, methyl ester	Methyl stearate	$C_{19}H_{38}O_2$	298	Antifungal and antioxidant (Pinto et al. 2017)
9,12-octadecadienoyl chloride, (Z,Z)-	Linoleoyl chloride	$C_{18}H_{31}ClO$	298	Anticancer, Anticoronary, Antieczemic, Antihistamic (Kumar et al. 2015)
Octadecanoic acid	Stearic acid	$C_{18}H_{36}O_2$	284	Hypocholesterolemic, surfactant and softening agent, perfumery, flavor and in cosmetic Antibacterial activity (Da Silva et al. 2003; Rajashyamala and Elango 2015)
Hexadecanoic acid, 1-(hydroxymethyl)-1,2-ethanediyl ester	Glyceryl 1,2-dipalmitate	$C_{35}H_{68}O_5$	568	Antimicrobial, Antioxidant (Kumar et al. 2013)
2-piperidinone,N-(4-Bromo-N-butyl)-	Alkaloid	$C_9H_{34}O_7S$	370	Anti-inflammatory, anti-microbial, anti-cancer (Jothi et al. 2015)
oleic acid	Carboxylic acid	$C_{18}H_{34}O_2$	282.468	Anti-inflammatory, cancer preventive, antimicrobial, anti-tumour activity (Padma et al. 2018; Karunanithi and Venkatachalam 2019)
Hexadecanoic acid, 3-[(trimethylsilyl)oxy]propyl ester	3-Trimethylsilyloxypropyl hexadecanoate	$C_{22}H_{46}O_3Si$	386	Antimicrobial, Antioxidant (Chandrasekar et al. 2015)
4-cyanobenzoic acid, Tridec-2-YNYL,ester		$C_{21}H_{27}NO_2$	325	No activity reported
Bisnor-7-desoxycholic acid		$C_{22}H_{36}O_4$	364	Antimicrobial, Antioxidant, Anticancer (Wei et al. 2011)
26-hydroxycholesterol	LDL	$C_{27}H_{46}O_2$	402	Inhibition of cholesterol synthesis (Javitt 1990)
pseduosarsasapogenin-5,20-dien		$C_{27}H_{42}O_3$	414	Treatment of Amyotrophic lateral sclerosis (Sulthanabegam et al. 2019)
1-napthalenepropanol, Alpha-ethyl decahydro-5(hydroxymethyl)		$C_{20}H_{36}O_2$	308	No activity reported
Cholest-5-en-3-ol (3.beta)., carbonochloridate		$C_{28}H_{45}ClO_2$	448	Antibacterial (Agboke and Attama 2016)
Spiro[Androst-5-ene-17,1-cyclobutan]-2-one, 3-hydroxy-, (3.beta.,17.bet		$C_{22}H_{32}O_2$	328	Anti-inflammatory and anti-microbial Antiarthritic, anticancer, antiasthma, Hepatoprotective (Sathiyabalan et al. 2014; Okereke et al. 2017)
Serverogenin acetate		$C_{29}H_{36}O_{10}$	544	Anti-insect, anti-microbial, anti-oxidant, anti-cancer, and anti-ulcerogenic activity (Karunanithi and Venkatachalam 2019)
pseduosarsasapogenin-5,20-dien		$C_{27}H_{42}O_3$	414	Treatment of Amyotrophic lateral sclerosis (Sulthanabegam et al. 2019)
Trans-Z-Alpha-Bisabolene epoxide		$C_{15}H_{24}O$	220	Anti-bacterial activity Anti-inflammatory effects (Hameed et al. 2016)
Limonene-6-ol,Pivalate		$C_{15}H_{24}O_2$	236	Anti-inflammatory and antioxidant anti-stress activity (Hadi et al. 2015; Hussein 2016)
Arachidonic amide,N-(5-Hydroxy-N-pentyl)		$C_{25}H_{43}NO_2$	389	COX enzyme expression for catalysis of prostalglandins (plays a significant role in health and disease in the gastrointestinal tract (GI), in renal, skeletal and ocular system (Barry et al. 1997; Autore et al. 2010)
Spiro[Androst-5-ene-17,1-cyclobutan]-2-one,3-hydroxy-, (3.beta.,17.bet		$C_{22}H_{32}O_2$	328	Anti-inflammatory and anti-microbial Antiarthritic, anticancer, antiasthma, Hepatoprotective (Sathiyabalan et al. 2014; Okereke et al. 2017)
7.dehydrocholesterol isocaproate				compound not reported
Kryptogenin 2,4-dinitrophenyl				compound not reported

	hydrazine				
	Beta-Carotene	Vitamin A precursor	$C_{40}H_{56}$	536	used in leukaemia therapies, cardiovascular disease protective (Dreosti 1996; Zaini et al. 2012)
	Coprostan-3. Beta, 16. Beta-Diol				compound not reported
Roots	Pentadecanoic acid, 14 methyl ester-, methyl ester	Palmitic acid methyl ester	$C_{19}H_{34}O_2$	270	Antioxidant, antifungal and antimicrobial (Vijisaral and Arumugam 2014; Elaiyaraja and Chandramohan 2016)
	N-hexadecanoic acid	Palmitic acid	$C_{16}H_{32}O_2$	256	Anti-inflammatory, Antioxidant, hypocholestero lemic nematicide, pesticide, anti-androgenic flavor, hemolytic, 5-alpha reductase inhibitor (Kumar et al. 2010; Aparna et al. 2012)
	Undecanoic acid	carboxylic acid	$C_{11}H_{22}O_2$	186.295	Anti-mycotic activity (Padma et al. 2018)
	8,11,14- Eicosatrienoic acid, methyl ester	Methyl dihomo-ɣ-linoleic acid	$C_{21}H_{36}O_2$	320	Tumoricidal (Das and Madhavi 2011)
	(Z)6,(Z)9-Pentadecadien-1-ol		$C_{15}H_{28}O$	224	Antifungal (Umaiyambigai et al. 2017)
	P-menth-8(10)-en-0-ol, cis		$C_{10}H_{18}O$	154	Sedative effect, depressant effect in the CNS, such as anti-convulsants and anxiolytics, increase the time of sleep, larvicidal and repellant activity against dengue fever (De Sousa et al. 2007; Balasubramani et al. 2018)
	Propylure		$C_{18}H_{32}O_2$	280	Sex pheromone (Jacobson 1969)
	Octadecanoic acid	Stearic acid	$C_{18}H_{36}O_2$	284	Hypocholesterolemic, surfactant and softening agent, perfumery, flavor and in cosmetic Antibacterial activity (Da Silva et al. 2003; Rajashyamala and Elango 2015)
	Alpha-Ketostearic acid, ethyl ester		$C_{20}H_{38}O_3$	326	No activity reported
	Z,Z,Z-1,4,6,9-Nonadecatetraene		$C_{19}H_{32}$	260	Antioxidant (Naidu et al. 2012; Suffo et al. 2016)
	1-Dodecen-3-yne				Anti- skin pathogen, Anti-oxidant (Kim et al. 2011)
	Hexadecanoic acid, 1-(hydroxymethyl)-1,2-ethanediyl ester	Glyceryl 1,2-dipalmitate	$C_{35}H_{68}O_5$	568	Antimicrobial, Antioxidant (Kumar et al. 2013)
	2-piperidinone,N-(4-Bromo-N-Butyl)-	Alkaloid	$C_9H_{16}BrNO$	233	Anti-inflammatory Anti-microbial Anti-cancer (Jothi et al. 2015)
	Oxiraneundecanoic acid, 3-pentyl, methyl ester, cis		$C_{19}H_{36}O_3$	312	Larvicidal activity Antioxidant activity (Elumalai et al. 2015; Al-Marzoqi et al. 2016)
	9-octadecanoic acid (Z)-, 2-Hydroxy-1-(hydroxymethyl)ethyl ester	Fatty acid ethyl ester, Oleic acid compound	$C_{21}H_{40}O_4$	356	No activity reported (Vijisaral and Arumugam 2014; Rajalakshmi and Mohan 2016)
	Spiro[Androst-5-ene-17, 1'-cyclobutan]-2'-one, 3-hydroxy-, (3.beta.,17.bet		$C_{22}H_{32}O_2$	328	Anti-inflammatory and anti-microbial Antiarthritic, anticancer, antiasthma, Hepatoprotective (Sathiyabalan et al. 2014; Okereke et al. 2017)
	Serverogenin acetate		$C_{29}H_{36}O_{10}$	544	Anti-insect, anti-microbial, anti-oxidant, anti-cancer, and anti-ulcerogenic activity (Karunanithi and Venkatachalam 2019)
	pseduosarsasapogenin-5,20-dien		$C_{27}H_{42}O_3$	414	Treatment of Amyotrophic lateral sclerosis (Sulthanabegam et al. 2019)
	Trans-Z-Alpha- bisabolene epoxide		$C_{15}H_{24}O$	220	Anti-bacterial activity Anti-inflammatory effects (Hameed et al. 2016)
	Arachidonic amide, N-(5-hydroxy-N-pentyl)		$C_{25}H_{43}NO_2$	389	COX enzyme expression for catalysis of prostalglandins (plays a significant role in health and

				disease in the gastrointestinal tract (GI), in renal, skeletal and ocular system (Barry et al. 1997; Autore et al. 2010)
Cholest-5-en-3-ol (3.beta)-,carbonochloridate		$C_{28}H_{45}ClO_2$	448	Antibacterial (Agboke and Attama 2016)
Stigmastan-3,5-diene		$C_{29}H_{48}$	396	Antimicrobial and Antioxidant (Khan et al. 2016)
Beta-Sitosterol acetate		$C_{31}H_{52}O_2$	456	Anti-inflammatory, inducing apoptosis, chemoprotective or chemoprotective effects, angiogenic effect, prostatic cancer treatment (Saeidnia et al. 2014)
Digitoxin	cardiac glycoside	$C_{41}H_{64}O_{13}$	764	used for chronic cardiac insufficiency (fatigue, shortness of breath and edema) (Vardanyan and Hruby 2006)
Ergosta-4,6,22-Trien-3, alpha-ol	steroid	$C_{28}H_{44}O$	396	Anti-microbial, anti-inflammatory, anti-cancer, anti-arthritic, anti-asthma, diuretic (Lalithi et al. 2015)
Ascorbyl palmitate	Ascorbic acid ester	$C_{22}H_{38}O_7$	414	Food additive and cosmetic ingredient (Tufino et al. 2019)
D-mannitol, 1-Decylsulfonyl	Sulfur compound	$C_{16}H_{34}O_7S$	370	antimicrobial antidiabetic (Muthukrishnan and Thinakaran 2012; Alagammal et al. 2012; Jothi et al. 2015; Ezekiel et al. 2018)
DI-N-Decylsulfone		$C_{20}H_{42}O_2S$	346	Anti-microbial and anti-cancer Larvicidal activity (Vijayakumari and Raj 2019; Karthi et al. 2020)
Alpha-L-Fucopyranose 1,2.3,4-Bis (Benzeneboonate)		$C_{18}H_{18}B_2O_5$	336	No activity reported
cholesterol margarate		$C_{44}H_{78}O_2$	639	No activity reported
N-decyl-Alpha,D-2-Deoxyglycoside				Compound not reported

Table 2 GC-MS analysis of ethanol extracts of *Pleione maculata*

Parts of *P. maculata*	Peak name	Molecular name	Molecular formula	Molecular weight	Activity
Leaves	Phenol, 4-(ethoxymethyl)	4-(Ethoxymethyl) Phenol	$C_9H_{12}O_2$	152	No activity reported
	2.pyridinecarboxylic acid, 6-methoxy		$C_8H_9NO_3$	153	No activity reported
	1-methyl sulfanyl -9-10-Dioxo-9,10-dihydro-anthracene-2-carbxylic acid		$C_{23}H_{17}NO_3S$	387	No activity reported
	N-hexadecanoic acid	Palmitic acid	$C_{16}H_{32}O_2$	256	Anti-inflammatory, Antioxidant, hypocholesterolemic nematicide, pesticide, anti-androgenic flavor, hemolytic, 5-alpha reductase inhibitor (Kumar et al. 2010; Aparna et al. 2012)
	N-hexadecanoic acid	Palmitic acid	$C_{16}H_{32}O_2$	256	Anti-inflammatory, Antioxidant, hypocholesterolemic nematicide, pesticide, anti-androgenic flavor, hemolytic, 5-alpha reductase inhibitor (Kumar et al. 2010; Aparna et al. 2012)
	Ethyl tridecanoate		$C_{15}H_{30}O_2$	242	Antioxidant (Qurzeddine et al. 2017)
	Octadecanoic acid, 2-(2-hydroxyethoxy) ethyl ester	Diethylene glycol stearate	$C_{22}H_{44}O_4$	372	Used in cosmetic, textile, serve as plasticizer, lubricant, binding and thickening agent (Oduje et al. 2015)
	N-butyl myristate		$C_{18}H_{36}O_2$	284	used as plasticizers anti-microbial activity (Sujatha et al. 2014)
	Guanidine acetic acid	Glycocyamine	$C_3H_7N_3O_2$	117	Antibacterial activity Biosynthesis of creatine as a suitable food and feed supplement Beneficial effect on the stamina (US 8, 501, 810 B2) (Gastner and Krimmer 2013)
Stem	Phenol,4-(ethoxymethyl)	4-(Ethoxymethyl) Phenol	$C_9H_{12}O_2$	152	No activity reported
	1,2-benzenedicarboxylic acid, butyl octyl ester	Phthalic acid, butyl octyl ester, Plasticizer BOP	$C_{20}H_{30}O_4$	334	Antimicrobial, Antifouling (Lakshmi and Rajalakshmi 2011; Khalil et al. 2014)
	N-hexadecanoic acid	Palmitic acid	$C_{16}H_{32}O_2$	256	Anti-inflammatory, Antioxidant, hypocholesterolemic nematicide, pesticide, anti-androgenic flavor, hemolytic, 5-alpha reductase inhibitor (Kumar et al. 2010; Aparna et al. 2012)
	Hexadecanoic acid, ethyl ester	Palmitic acid ester	$C_{18}H_{36}O_2$	284	Antioxidant, Hemolytic, hypocholesterone, Flavor, Nematicide, Anti-androgenic (Tyagi and Agarwal 2016)
	9,12-octadecadienoic acid (Z,Z)-	Conjugated Linoleic acid	$C_{18}H_{32}O_2$	280	Anti-Inflammatory, hypocholesterolic, cancer preventive, Hepatoprotective, nematicide, antihistaminic, antieczemic, antiacne, 5-α reductase inhibitor, anti-coronary, antimicrobial (Adeoye-Isijola et al. 2018)
	Linoleic acid ethyl ester		$C_{20}H_{34}O_2$	308	Hypocholesterolemic, nematicide, anti-arthritic, hepatoproctective, anti-androgenic, hypycholesterolemic, 5-alpha reductase inhibitor, anti-histaminic, anti-coronary, insectifuge, anti-eczemic, anti-acne (Chidambarampillai and Mohan 2013; Tyagi and Agarwal 2016)
	Isopropyl linoleate		$C_{21}H_{38}O_2$	322	Antioxidant, antidiabetic, anti-inflammatory Formulation of skin and hair care products, facial makeup (Rajendra et al. 2017; Rautela et al. 2018)
	Dichloroacetic acid, dodec-9-YNYL		$C_{14}H_{23}ClO_2$	292	Acidifier, arachidonic acid inhibitor, increase aromatic amino acid decarboxylase activity, inhibit production of uric acid (Mohammad et al. 2019)
	Oleic acid		$C_{18}H_{34}O_2$	282	Antibacterial activity (Abubakar and Majinda 2016)
	Estra-1,3,5 (10)-Trien-17-Beta-ol		$C_{18}H_{24}O$	256	Anti-arrhythmic activity (Al-Gara'awi 2019)
	9-Oxononanoic acid (9-ONA)		$C_9H_{16}O_3$	172	Lipid peroxidation (treats disorder such as inflammation, atherosclerosis and other degenerative diseases) induces phospholipase A2 activity and thromboxane A2 production in human blood (Ren et al. 2013)
Roots	Phthalic acid, butyl hexyl ester	Butyl hexyl phthalate	$C_{18}H_{26}O_4$	306	Antimicrobial (Ingole 2016)
	1,2-benzenedicarboxylic	Phthalic acid, butyl octyl ester,	$C_{20}H_{30}O_4$	334	Antimicrobial, Antifouling (Lakshmi and Rajalakshmi 2011; Khalil et al. 2014)

	acid, butyl octyl ester	Plasticizer BOP		
	Ethyl tridecanoate	$C_{15}H_{30}O_2$	242	Antioxidant (Qurzeddine et al. 2017)

Table 3 GC-MS analysis of methanol extracts of *Pleione maculata*

Parts of *P. maculata*	Peak name	Molecular name	Molecular formula	Molecular weight	Activity
leaves	Phenol, 4-(methoxymethyl)-		$C_8H_{10}O_2$	138	Anti-diabetic Balamurugan et al. 2017)
	Pentadecanoic acid, 14-methyl-, methyl ester	Palmitic acid methyl ester	$C_{19}H_{34}O_2$	270	Antioxidant (Vijisaral and Arumugam 2014)
	N-hexadecanoic acid	Palmitic acid	$C_{16}H_{32}O_2$	256	Anti-inflammatory, Antioxidant, hypocholesterolemic nematicide, pesticide, anti-androgenic flavor, hemolytic, 5-alpha reductase inhibitor (Kumar et al. 2010; Aparna et al. 2012)
	9-octadecyne	Alkene compound	$C_{18}H_{34}$	250	Antioxidant, Antimicrobial (Upgade and Bhaskar 2013)
	Isopropyl linoleate		$C_{21}H_{38}O_2$	322	Antioxidant, antidiabetic, anti-inflammatory Formulation of skin and hair care products, facial makeup (Rajendra et al. 2017; Rautela et al. 2018)
	6-octadecenoic acid, methyl ester, (Z)-	*Trans*-13-octadecanoic acid, methyl ester 7	$C_{19}H_{36}O_2$	296	Anti-inflammatory, antiandrogenic, cancer preventive, dermatitigenic irritant, antiluekotriene-D4, Hypocholesterolemic, 5-alpha reductase inhibitor, anemiagenic, insectifuge, flavor (Abubakar and Majinda 2016)
	Oxiraneundecanoic acid, 3-pentyl, methyl ester, cis		$C_{19}H_{36}O_3$	312	Larvicidal activity Antioxidant activity (Elumalai et al. 2015;Al-Marzoqi 2016)
	Octadecanoic acid, methyl ester	Methyl stearate	$C_{19}H_{38}O_2$	298	Antifungal and antioxidant (Pinto et al. 2017)
	N-hexadecanoic acid	Palmitic acid	$C_{16}H_{32}O_2$	256	Anti-inflammatory, Antioxidant, hypocholesterolemic nematicide, pesticide, anti-androgenic flavor, hemolytic, 5-alpha reductase inhibitor (Kumar et al. 2010; Aparna et al. 2012)
	Heptacosanoic acid, methyl ester	Methyl heptacosanoate	$C_{28}H_{56}O_2$	424	No activity reported
Stem	Hexadecanoic acid, methyl ester		$C_{17}H_{34}O_2$	270	Antibacterial and antifungal (Abubakar and Majinda 2016)
	N-hexadecanoic acid	Palmitic acid	$C_{16}H_{32}O_2$	256	Anti-inflammatory, Antioxidant, hypocholesterolemic nematicide, pesticide, anti-androgenic flavor, hemolytic, 5-alpha reductase inhibitor (Kumar et al. 2010; Aparna et al. 2012)
	(2s,3s)-(-)-3-propyloxirane methanol		$C_6H_{12}O_2$	116	Anti-oxidant (Yusufzai et al. 2019)
	pyrimidine-2,4,6(1H,3H,5H)-Trione-1-octadecyl)				compound not reported 2,4,6-trisubstituted pyrimidine were evaluated as anti-malaria drug (Agrawal et al. 2005)S
	2,3-anhydro-D-galactosan	Sugar moeity	$C_6H_8O_4$	144	preservative (Paulpriya rt al. 2014)
	9,12-octadecadienoic acid, methyl ester		$C_{19}H_{34}O_2$	294	Anticancer, anti-inflammatory, antileukotriene, flavor (Abubakar and Majinda 2016)
	9-octadecenoic acid (Z)-, methyl ester	*Trans*-13-octadecanoic acid, methyl ester 7	$C_{19}H_{36}O_2$	296	Anti-inflammatory, antiandrogenic, cancer preventive, dermatitigenic irritant, antiluekotriene-D4, Hypocholesterolemic, 5-alpha reductase inhibitor, anemiagenic, insectifuge, flavor (Abubakar and Majinda 2016)
	Octadecanoic acid, methyl ester	Methyl stearate	$C_{19}H_{38}O_2$	298	Antifungal and antioxidant (Pinto et al. 2017)
	Triacontanoic acid, methyl ester	Methyl triacontanate	$C_{31}H_{62}O_2$	466	Antimicrobial Kumar et al. 2015)
Roots	Hexadecanoic acid, methyl ester		$C_{17}H_{34}O_2$	270	Antibacterial and antifungal activity (Abubakar and Majinda 2016)
	9,12-octadecadienal		$C_{18}H_{32}O$	264	Antimicrobial and antioxidant (Gurnani et al. 2015)
	E,E-1,9,17-Docasatriene	alkene compound	$C_{22}H_{40}$	304	No activity reported (Subavathy and Thilaga 2016; Kumaravel et al. 2016, 2019)
	9-octadecenoic acid, methyl ester	*Trans*-13-octadecanoic acid, methyl ester 7	$C_{19}H_{36}O_2$	296	Anti-inflammatory, antiandrogenic, cancer preventive, dermatitigenic irritant, antiluekotriene-D4, Hypocholesterolemic, 5-alpha reductase inhibitor, anemiagenic, insectifuge, flavor (Abubakar and Majinda 2016)
	Nonanal	aldehyde	$C_9H_{18}O$	142	Anti-aging use in cosmetics

					Fungicides (Plainfosse et al. 2017; Zhang et al. 2017)
	pregabalin		$C_8H_{17}NO_2$	159	Adjunctive treatment of partial seizures, use in neuropathic pain, neuralgia, use in alcohol withdrawal syndrome, restless leg syndromes, migraine and vasomotor symptoms of menopause (World Health Organization (WHO) 2018)
	Octadecanoic acid, methyl ester	Methyl stearate	$C_{19}H_{38}O_2$	298	Antifungal and antioxidant (Pinto et al. 2017)
	Tetracosanoic acid, methyl ester	Methyl lignocerate	$C_{25}H_{50}O_2$	382	Antibacterial, Antimicrobial (Valiei et al. 2011;Ukil et al. 2015)
	Vor-Diazepam,3-{(N-hydroxymethyl)aminocarbonyloxy}		$C_{18}H_{16}CIN_3O_4$	373	No activity reported

Table 4: Docking analysis depicting the binding residues and their binding energy

Protein Name	Drug-likeness ligands	Polar contact binding residues	Other intermolecular contact binding residues	Global energy (kcal/mol)	Attractive Vdw (kcal/mol)	Repulsive Vdw (kcal/mol)	ACE (kcal/mol)
RNA dependent RNA-pol (6M71)	2,4,6-Pyrimidinetrione	Cys 780, Arg 467, Leu 470, Arg 305	all side bonded by polar contacts	-23.59	-10.00	0.72	-5.79
	21- Acetoxypregenelone	Ala 706, Leu 707, Asn 705	Gly 774, Asp 135, Ala 130, Ser 709	-34.15	-20.12	10.12	-8.38
	P- menth-8(10)-en-9-ol	Thr 141, Leu 142	Ala 130, Asp 126	-31.56	-12.13	0.87	-7.18
	Nor-diazepam, 3{n-hydroxymethyl}aminocarbonyloxy	Thr 556, Arg 555, Arg 624	all side bonded by polar contact	-35.35	-23.08	4.90	-3.16
	Digitoxin	Lys 267, Ser 255, Thr 252	Ser 255, Tyr 265, Thr 319	-79.90	-36.74	12.20	-22.96
	DI-N-Decylsulfone	Tyr 546, Val 410, Lys 141	Lys 411, Asn 414, Gln 408	-44.31	-19.74	2.12	-11.57
	14-dodecanoic acid	Lys 411, Val 410	Tyr 546, Ser 15, Asn 414	-29.99	-14.73	2.24	-6.96
	Estra-1,3,5(10)-trien-17-beta-ol	Gln 18, Gln 19	Ser 15, Asn 414	-36.68	-20.43	4.20	-6.57
	Arachidonic amide,N-{5-hydroxy-N-Pentyl}	Tyr 268	Lys 267	-46.08	-21.29	4.04	-12.04
	1-methylsulfanyl-9-10-Dioxo-9,10-dihydro-Anthracene-2-carboxylic acid	Asp 218, Thr 206	Tyr 217, Ile 37, Tyr 38	-37.97	-20.97	3.26	-6.72
	Cholesterol margarate	Lys 391	Thr 393, Lys 395, Asn 136	-70.69	-31.28	9.37	-21.60
	Docosanoic acid	no polar contact	Ser 15, Asn 414, Tyr 546, Lys 411	-47.59	-23.22	8.71	-13.13
	26-hydroxycholesterol	Asn 781, Asp 126	Ser 784, Lys 47, Thr 141, Lys 780	-42.36	-21.98	1.38	-7.11
	Andrographolide	Leu 142, Asp 140, Tyr 129, Asn 781, Ser 709, Leu 708	Cys 139, Asp 140, Thr 141, Lys 47	-37.42	-19.40	4.39	-8.43
	6H-purin-6-one,1,7-dihydro-2-(methylamino)	Tyr 530, Asn 534	Asn 360, Val 342	-29.00	-12.14	0.14	-6.92
	Pseduosarsasapogenin-5,20-dien	Ser 15	Val 12, Asp 846, Asn 414, Val 12	-56.41	-29.45	6.51	-12.54
	Oxiraneundecanoic acid,3-pentyl,methyl ester cis	no polar contact	Lys 411, Ser 15, Asn 414, Val 12	-46.14	-22.77	5.77	-11.38
	Pregabalin	Asn 356, Tyr 530, Asp 377	Thr 344, Ser 343	-30.35	-13.26	0.32	-6.85
	Arabidol	Asn 781, Tyr 129	Lys 780, Ser 709, Thr 710, Ser 784	-41.54	-20.55	5.40	-9.95
3CL Protease (6M2Q)	2,4,6-Pyrimidinetrione	Met 6, Asp 295, Gln 127, Val 296, Arg 298	all side bonded by Polar contacts	-16.68	-7.33	0.09	-4.42
	21- Acetoxypregenelone	Arg 188, Gln 184, Thr 190, Met 165, Glu 166, Leu 167, Ser 46, Thr 45	Thr 25, Thr 24, Thr 26	-28.57	-14.64	8.41	-9.22
	P- menth-8(10)-en-9-ol	Asn 142	Gly 143, Cys 145, His 163, Asn 143	-24.19	-11.51	2.27	-.6.75
	Nor-diazepam, 3{n-hydroxymethyl}aminocarbonyloxy	Met 165, Glu 166, Asn 142	Ser 46, Met 49	-25.73	-11.42	0.80	-7.19
	Digitoxin	Gly 116, Tyr 154	Asn 151, Asp 153, Tyr 154, Phe 305, Phe 294	-54.15	-27.23	6.90	-13.27
	DI-N-Decylsulfone	Phe 294, Gln 110, Thr 111, Thr 292	Asp 295, Pro 293	-28.23	-14.86	5.07	-7.39
	14-dodecanoic acid	Leu 253, Leu 250, Ile 249, Pro 252	Phe 294, Val 297, Asp 248, Asp 245	-18.11	-9.92	4.01	-5.98
	Estra-1,3,5(10)-trien-17-beta-ol	Phe 294, Pro 293, Thr 111, Gln 110, His 246	all side bonded by polar contacts	-19.00	-10.41	3.39	-5.43
	Arachidonic amide,N-{5-hydroxy-N-Pentyl}	Asn 142, Gly 143	Ser 144, Glu 166, Leu 167	-38.03	-17.95	5.31	-10.86
	1-methylsulfanyl-9-10-Dioxo-9,10-dihydro-Anthracene-2-carboxylic acid	Glu 166, Met 165	Ser 46, Thr 25, Glu 47	-39.16	-16.63	4.12	-12.29
	Cholesterol margarate	Gln 110, Gln 109	Pro 108, Gln 240	-40.95	-23.94	9.46	-9.91
	Docosanoic acid	no polar contacts	Phe 294, Gln 110, Thr 111, Asp 153	-28.31	-14.82	1.65	-6.51
	26-hydroxycholesterol	His 163, Met 165, Glu 166	Asn 142, Cys 145, Ser 46, Thr 45	-40.85	-17.40	4.98	-12.61

	Andrographolide	Thr 25, Ser 46, Glu 166, Met 165	Asn 142, His 41	-24.51	-13.53	7.31	-7.17
	6H-purin-6-one,1,7-dihydro-2-(methylamino)	Glu 166, Met 165, Leu 167, Cys 145	His 163, Asn 142, Gly 143	-21.58	-8.97	2.01	-6.60
	Pseduosarsasapogenin-5,20-dien	Thr 243, Phe 294, Thr 111, Gln 110	Thr 242, Asp 245	-34.40	-18.57	6.71	-8.41
	Oxiraneundecanoic acid,3-pentyl,methyl ester cis	Gln 110, Gly 109	Phe 294, Pro 293, His 246, Asr 153	-24.73	-12.67	1.46	-5.53
	Pregabalin	Arg 298, Met 6	Val 303, Thr 304, Arg 298, Gln 299	-20.69	-10.29	3.12	-6.33
	Arabidol	Glu 166, Met 165, His 164	Thr 26, Thr 25, Thr 24, Thr 45	-37.06	-16.29	10.23	-14.02
Spike glycoprotein (6LXT)	2,4,6-Pyrimidinetrione	Val 952, Asn 955, Asn 956, Asn 953	all side bonded by polar contact	-26.44	-10.31	0.16	-6.94
	21- Acetoxypregenelone	Ala 942, Ser 940, Arg 1185	Asn 1187, Ser 943, Lys 1181, Ile 183	-28.10	-19.75	5.74	-2.22
	P- menth-8(10)-en-9-ol	Leu 922	Ile 923, Ala 924, Asn 919, Gln 920	-24.89	-11.41	1.94	-6.68
	Nor-diazepam, 3{n-hydroxymethyl}aminocarbonyloxy	Ile 1198, Asn 928, Leu 1197	Asp 1199, Asn 925	-36.22	-17.30	4.48	-10.95
	Digitoxin	Ser 940, Arg 1185	Glu 1182, Ser 943, Asp 936, Lys 1191, Gln 935	-63.54	-42.37	17.15	-8.93
	DI-N-Decylsulfone	Ser 940	Ser 943, Ser 939, Lys 1181, Lys 947	-41.11	-26.75	5.32	-4.29
	14-dodecanoic acid	Ser 939	Asn 1194, Asn 1187, Glu 1188, Glu 1195, Gln 935	-23.19	-13.50	1.46	-3.08
	Estra-1,3,5(10)-trien-17-beta-ol	Ala 1190, Lys 1191	Arg 1185, Asn 1187, Gln 935	-32.36	-19.07	3.90	-4.34
	Arachidonic amide,N-{5-hydroxy-N-Pentyl}	Lys 947	Asp 1184, Glu 1188, Asn 1187, Asp 936, Lys 1191, Ser 939	-42.54	-27.63	3.87	-2.74
	1-methylsulfanyl-9-10-Dioxo-9,10-dihydro-Anthracene-2-carboxylic acid	Asp 184, Ser 940, Arg 1185, Lys 947	Ser 943, Ser 949	-31.67	-21.43	1.25	-0.52
	Cholesterol margarate	no polar contact	Asn 1184, Asn 1187, Asp 936, Gln 935	-54.12	-32.79	9.27	-8.23
	Docosanoic acid	Asn 1178, Lys 1181	Ser 943, Ser 939, Lys 947, Gln 935	-37.20	-26.13	3.97	-2.01
	26-hydroxycholesterol	Asn 925, Gln 926, Lys 1191	Gln 1195, Asp 936, Gly 932, Asn 928	-41.67	-20.53	2.58	-8.23
	Andrographolide	Gln 920, Lys 921, Tyr 917	Glu 1202, Val 915	-29.04	-21.14	20.25	-9.23
	6H-purin-6-one,1,7-dihydro-2-(methylamino)	Tyr 917	Leu 1200, Asp 1199, Tyr 917	-19.45	-8.27	0.66	-5.86
	Pseduosarsasapogenin-5,20-dien	Ser 939	Ser 940, Glu 1182, Lys 1181	-41.80	-28.41	2.51	-2.20
	Oxiraneundecanoic acid,3-pentyl,methyl ester cis	Lys 1181	Arg 1181, Asp 936, Ser 943, Ser 939	-34.65	-25.21	6.80	-2.26
	Pregabalin	no polar contacts	Leu 1200, Ile 923, Ala 924	-27.07	-13.01	2.00	-6.29
	Arabidiol	Arg 1185, Leu 1186, Asp 1184	Lys 1181, Asn 1187, Ser 943	-29.82	-22.67	4.74	0.13

Table 5 Drug-likeness analysis of bioactive compounds showing good binding energy against SARS-CoV-2 proteins

ess compounds	Physicochemical properties (Lipinski rule of Five)					Solubility			Pharmacokinetics	
	MW	HB donors	HB acceptors	No of rotatable bond	consensus log P	Log S (ESOL)	Log S (Ali)	Log S (SILICOS-IT)	GI absorption	CYP enzymes inhibitors
	764	5	13	7	2.61	moderately soluble	moderately soluble	moderately soluble	low	no
cholesterol	402	2	2	6	5.86	poorly soluble	poorly soluble	moderately soluble	high	no
lfanyl-9,10-Dioxo-9,10-thracene-2-carboxylic	387	1	3	4	4.10	moderately soluble	poorly soluble	poorly soluble	high	yes
c amide,N-{5-hydroxy-	389	2	2	20	6.27	moderately soluble	poorly soluble	poorly soluble	high	no
l margarate	639	0	2	22	12.43	insoluble	insoluble	insoluble	low	no
pregenolone	374	1	4	4	3.77	moderately soluble	soluble	soluble	high	only CYP2C9 inhibitor
sulfone	346	0	2	18	6.68	poorly soluble	poorly soluble	poorly soluble	low	CYP2C9, CYP1A2 inhibitor
asapogenin-5,20-dien	414	2	3	4	4.86	moderately soluble	moderately soluble	moderately soluble	high	no
am,3-{N-thyl}aminocarbonyloxy	373	2	5	5	2.16	soluble	soluble	soluble	high	no
holide	350	3	5	3	2.33	soluble	soluble	soluble	high	no
	159	2	3	5	0.56	highly soluble	highly soluble	soluble	high	no
10)-en-9-ol	154	1	1	2	2.55	soluble	soluble	soluble	high	no
acid	340	1	2	20	7.40	poorly soluble	insoluble	poorly soluble	low	CYP1A2 inhibitor
	444	2	2	7	6.97	poorly soluble	poorly soluble	poorly soluble	low	no

Figures

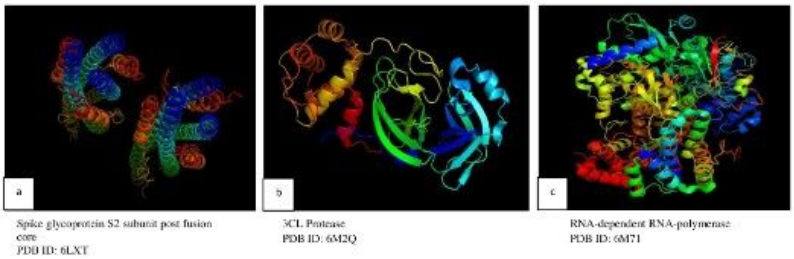

Figure 1

The 3D ribbon structures representation of SARS-CoV-2 target proteins (a) spike glycoprotein S2 subunit post-fusion core (b) 3CL protease and (c) RNA-dependent RNA polymerase visualized using PyMol

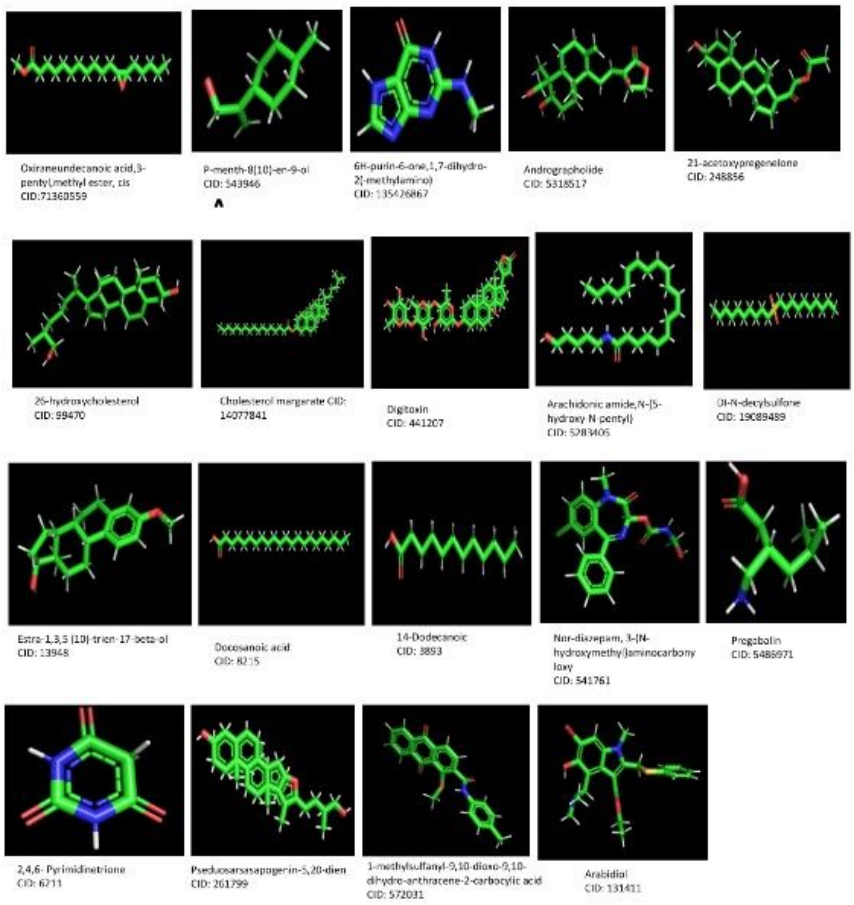

Figure 2

GC-MS compounds and positive control Arabidol ligands downloaded from PubChem data bank with compound ID and visualized using PyMol for molecular docking

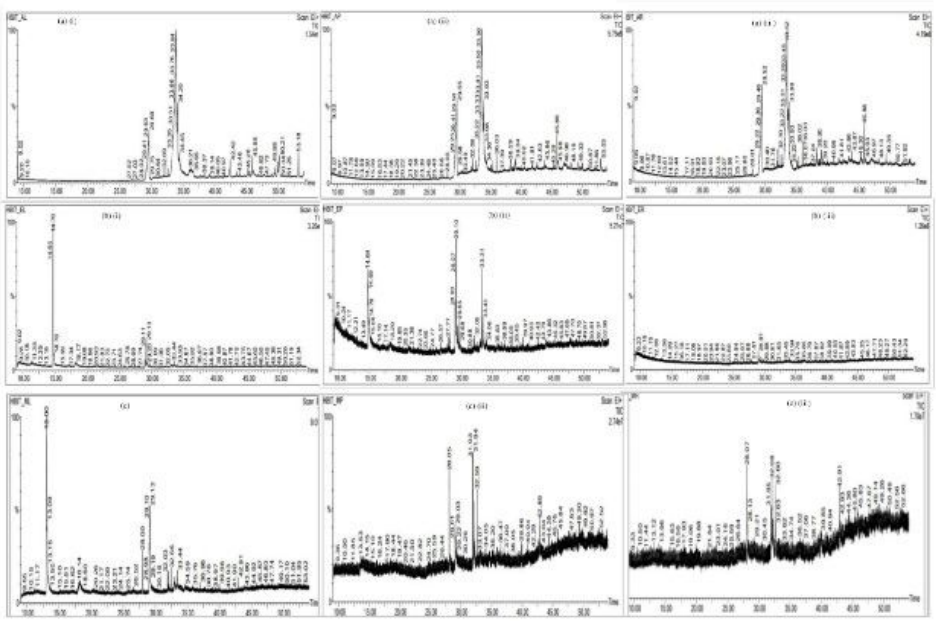

Figure 3

GC-MS spectrograms showing peaks of compounds of Pleione maculata extracts (a) acetone (b) ethanol (c) methanol extracts of (i) leave (ii) stem and (iii) root

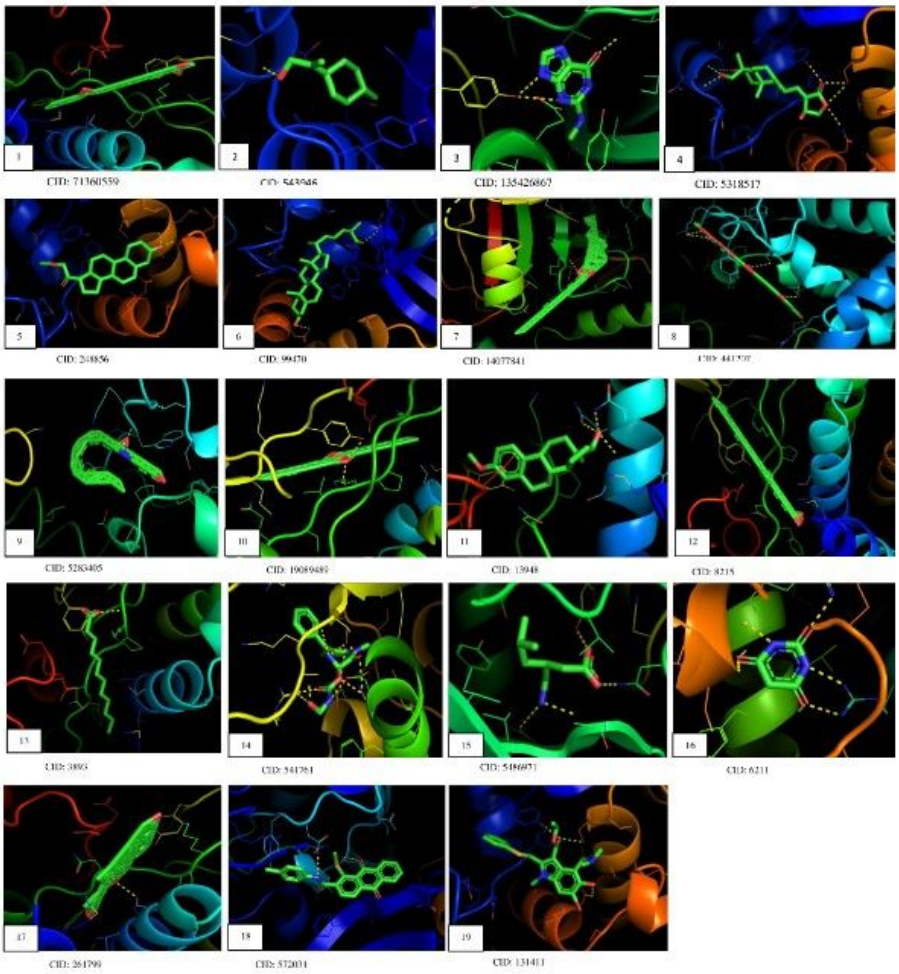

Figure 4

Molecular docking of target SARS-CoV-2 RNA-dependent RNA-polymerase (PDB ID- 6M71) with the S-CoV-2 RNA-dependent RNA polymerase (PDB ID-6M71) with the GC-MS bioactive compounds of Pleione maculata (1) Oxiraneundecanoic acid,3-pentyl,methyl ester, cis (2) p-menth-8(10)-en-9-ol (3) 6H-purin-6-one,1,7-dihydro-(2-methylamino) (4) Andrographolide (5) 21-acetoxypregenelone (6) 26-hydroxycholesterol (7) Cholesterol margarate (8) Digitoxin (9) Arachidonic amide, N-{5-hydroxy-N-pentyl} (10) DI-N-decylsulfone (11) Estra-1,3,5(10)-trien-beta-ol (12) Docosanoic acid (13) 14-dodecanoic acid (14) Nor-diazepam,3-{N-hydroxymethyl}aminocarbonyloxy (15) Pregabalin (16) 2,4,6-pyrimidinetrione (17) pseudosarsasapogenin acid, 3-pentyl, methyl ester cis, (18) 1-methylsulfanyl-9,10-dioxo-9, 10-dihydro-anthracene-2-carboxylic acid and positive control (19) arabidiol

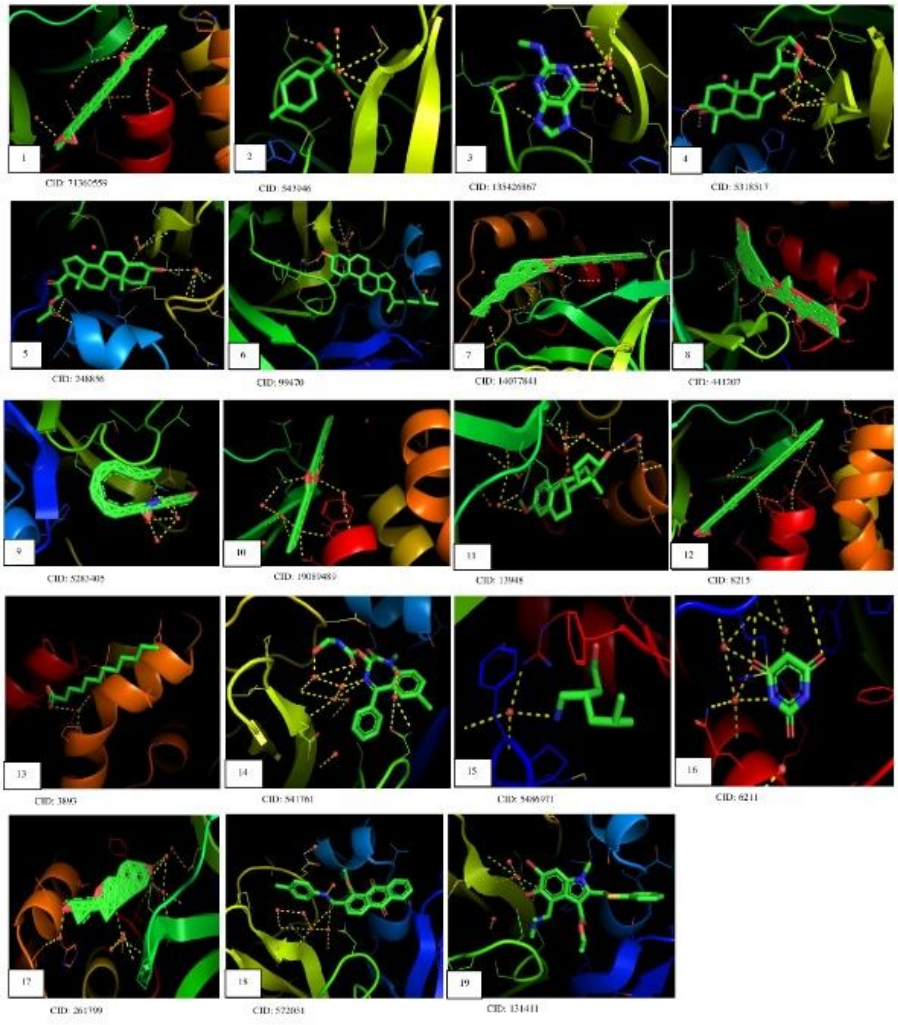

Figure 5

Molecular docking of target SARS-CoV-2 3CL Protease (PDB ID- 6M2Q) with the GC-MS bioactive compounds of Pleione maculata (1) Oxiraneundecanoic acid,3-pentyl,methyl ester, cis (2) p-menth-8(10)-en-9-ol (3) 6H-purin-6-one,1,7-dihydro-(2-methylamino) (4) Andrographolide (5) 21-acetoxypregenelone (6) 26-hydroxycholesterol (7) Cholesterol margarate (8) Digitoxin (9) Arachidonic amide, N-{5-hydroxy-N-pentyl} (10) DI-N-decylsulfone (11) Estra-1,3,5(10)-trien-beta-ol (12) Docosanoic acid (13) 14-dodecanoic acid (14) Nor-diazepam,3-{N-hydroxymethyl}aminocarbonyloxy (15) Pregabalin (16) 2,4,6-pyrimidinetrione (17) pseduosarsasapogenin acid, 3-pentyl, methyl ester cis, (18) 1-methylsulfanyl-9,10-dioxo-9, 10-dihydro-anthracene-2-carboxylic acid and positive control (19) arabidiol

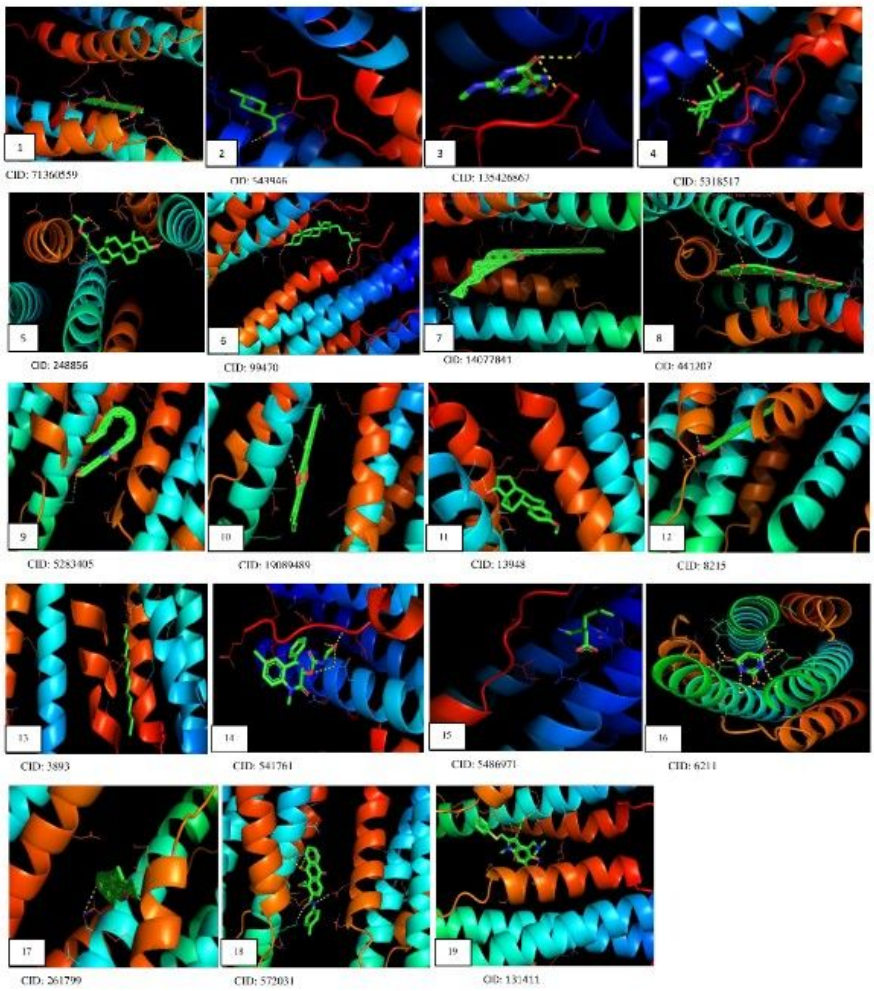

Figure 6

Molecular docking of target SARS-CoV-2 spike glycoprotein S2 subunit (PDB ID- 6LXT) with the GC-MS bioactive compounds of Pleione maculata (1) Oxiraneundecanoic acid,3-pentyl,methyl ester, cis (2) p-menth-8(10)-en-9-ol (3) 6H-purin-6-one,1,7-dihydro-(2-methylamino) (4) Andrographolide (5) 21-acetoxypregenelone (6) 26-hydroxycholesterol (7) Cholesterol margarate (8) Digitoxin (9) Arachidonic amide, N-{5-hydroxy-N-pentyl} (10) DI-N-decylsulfone (11) Estra-1,3,5(10)-trien-beta-ol (12) Docosanoic acid (13) 14-dodecanoic acid (14) Nor-diazepam,3-{N-hydroxymethyl}aminocarbonyloxy (15) Pregabalin (16) 2,4,6-pyrimidinetrione (17) pseduosarsasapogenin acid, 3-pentyl, methyl ester cis, (18) 1-methylsulfanyl-9,10-dioxo-9, 10-dihydro-anthracene-2-carboxylic acid and positive control (19) arabidiol

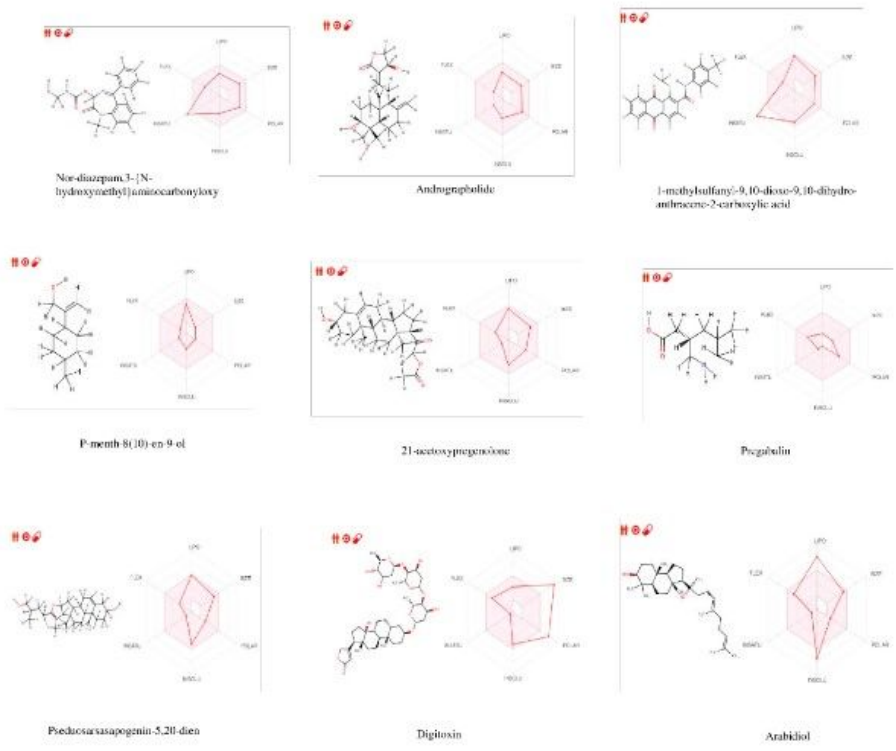

Figure 7

The bioavailibility radar of different bioactive drug-likeness molecules were the pink areas represents each properties (Lipophilicity, molecular weight, solubility, flexiibility)

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- FigureS1.jpg
- FigureS2.jpg