



Revista Boliviana de Química

ISSN: 0250-5460

ISSN: 2078-3949

revbolquim@outlook.com

Universidad Mayor de San Andrés

Estado Plurinacional de Bolivia

Castañeta, Grover; Huayhua-Llusco, Aleyda; Tarqui, Santiago; F. Gutiérrez, Abel
CHARACTERIZATION OF TERPENOIDS FROM PSEUDOGNAPHALIUM
GAUDICHAUDIANUM (DC) ANDERB, WIRA-WIRA BY GC/MS, ACTIVE
PRINCIPLES WITH POSSIBLE USE IN COVID-19 INFECTION PREVENTION
Revista Boliviana de Química, vol. 39, núm. 1, 2022, Enero-, pp. 19-25
Universidad Mayor de San Andrés
La Paz, Estado Plurinacional de Bolivia

Disponible en: <https://www.redalyc.org/articulo.oa?id=426371936003>

- Cómo citar el artículo
- Número completo
- Más información del artículo
- Página de la revista en redalyc.org

redalyc.org

Sistema de Información Científica Redalyc

Red de Revistas Científicas de América Latina y el Caribe, España y Portugal
Proyecto académico sin fines de lucro, desarrollado bajo la iniciativa de acceso
abierto



CHARACTERIZATION OF
TERPENOIDS FROM
PSEUDOGNAPHALIUM
GAUDICHAUDIANUM (DC) ANDERB,
WIRA-WIRA BY GC/MS, ACTIVE
PRINCIPLES WITH POSSIBLE USE IN
COVID-19 INFECTION PREVENTION

Received 04 19 2022
Accepted 04 28 2022
Published 04 30 2022

Vol. 39, No.1, pp. 19-25, Ene./Abr. 2022
Revista Boliviana de Química

39(1), 19-25, Jan./Apr. 2022
Bolivian Journal of Chemistry
DOI: 10.34098/2078-3949.39.1.3



Short report

Peer-reviewed

Grover Castañeta*, Aleyda Huayhua-Llusco, Santiago Tarqui, Abel F. Gutiérrez

Instituto de Investigaciones Químicas IIQ, Facultad de Ciencias Puras y Naturales FCPN, Universidad Mayor de San Andrés UMSA, P.O. Box 303, Calle Andrés Bello s/n, Ciudad Universitaria Cota-Cota, La Paz, Bolivia, gcastaneta1@gmail.com, aleydahuayhua.419@gmail.com, starquit@fcpn.edu.bo, gabelfranz.afge@gmail.com, www.umsa.bo

Keywords: *α -Pinene, Asteraceae, Covid-19, Essential oil, Terpenoids, Wira-wira*

Palabras clave: *α -Pineno, Asteraceae, Covid-19, Aceite esencial, Terpenoides, Wira-wira*

ABSTRACT

Pseudognaphalium gaudichaudianum (DC.) Anderb., (Asteraceae) is a small herbaceous plant that grows in the heights and in mountainous places. Known by the vernacular name "Wira Wira", it is well reputed in traditional medicine by aymara communities to treat respiratory diseases like cough, common cold, bronchitis, and pneumonia in the highlands of Bolivia. Due of its expectorant properties, *P. gaudichaudianum* has been proposed as a phytodrug to prevent infection by COVID-19, in infusions and vaporization. In this study, the terpenoids from its essential oil were characterized by Gas Chromatography Coupled to Mass Spectrometry (GC/MS). The analysis showed the presence of 1 monoterpenoid, 11 sesquiterpenoids, 2 diterpenoids and 4 minor unidentified compounds. The major compounds identified were β -Eudesmene (16.35%), Rosifoliol (15.29%), Guaia 1(10), 11-diene (15.20%), Guaia 6,9 diene (14.46%), α -Pinene (11.32%) and α -Guaiene (6,16%).

*Correspondent autor: governeoaxel@gmail.com

RESUMEN

Pseudognaphalium gaudichaudianum (DC.) Anderb., (Asteraceae) es una pequeña planta herbácea que crece en las alturas y en lugares montañosos, conocida con el nombre vernacular de "Wira Wira". Tiene buena reputación en la



medicina tradicional de las comunidades aimaras de las tierras altas de Bolivia para tratar enfermedades respiratorias como tos, resfriado común, bronquitis y neumonía. Por sus propiedades expectorantes, *P. gaudichaudianum* se ha propuesto como fitofármaco para prevenir la infección por COVID-19, en infusiones y vaporización. En este estudio, los terpenoides de su aceite esencial se caracterizaron por cromatografía de gases acoplada a espectrometría de masas (GC/MS). El análisis mostró la presencia de 1 monoterpeneoide, 11 sesquiterpenoides, 2 diterpenoides y 4 compuestos menores no identificados. Los principales compuestos identificados fueron β -Eudesmene (16,35%), Rosifoliol (15,29%), Guaia 1(10), 11-dieno (15,20%), Guaia 6,9 dieno (14,46%), α -Pineno (11,32%) y α -Guaieno (6,16%).

INTRODUCTION

Pseudognaphalium is a large genus being part of the tribe *Gnaphalieae* (Asteraceae) with about 90 to 95 % annual, biannual or perennial species distributed in America. It is also present in less quantity in Asia and Africa [1,2]. Previous studies about *Pseudognaphalium* genus reported the presence of flavonoids and their glycosylated derivatives, diterpenoids and sterols [3-9]. The composition of the essential oil of *Pseudognaphalium* species, include α -pineno, α -(z)-ocimeno, β -phellandreno, (*E*)-nerolidol, 1,8 cineol, β -felandreno, germacrene D, germacrene B, and spatulenol among others [10,11].

Pseudognaphalium gaudichaudianum (DC.) Anderb. is distinctive for being a flowery material that is found throughout the whole year, blooming intensively between January and May. It is distributed in Bolivia, Peru, Colombia, Ecuador, Argentina, Uruguay and Brazil [2,12]. In Bolivia, it can be found between 2500 and 4700 m.a.s.l. of altitude, mainly in La Paz, Oruro, Cochabamba, Tarija, and Santa Cruz departments. [12,13].

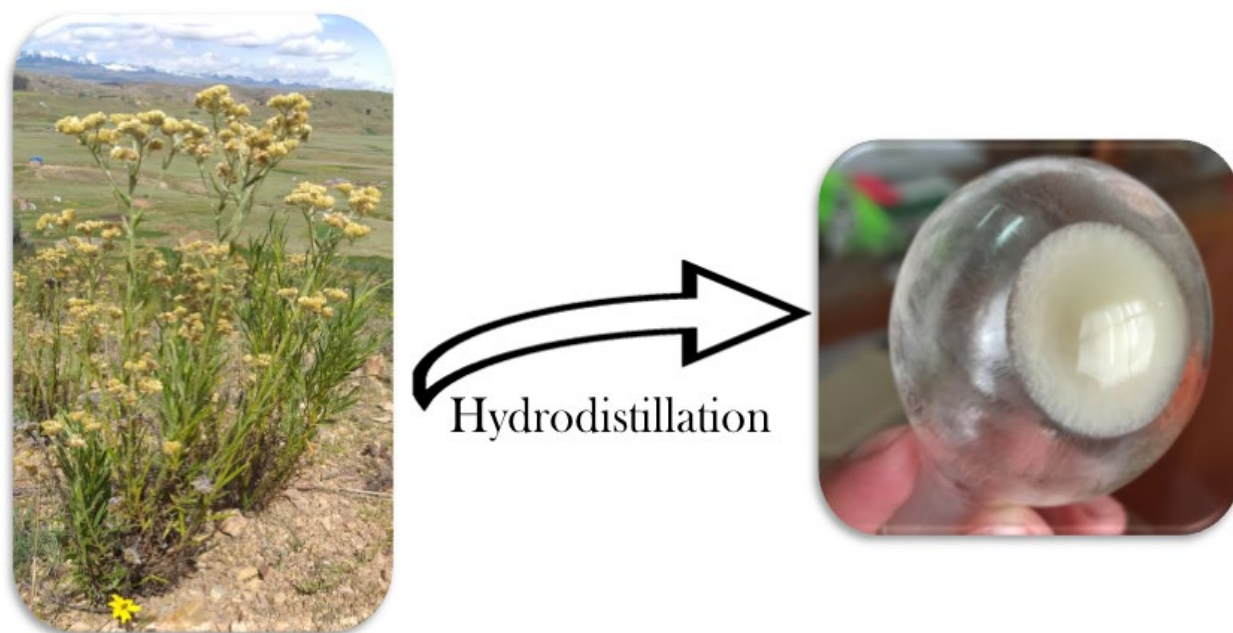


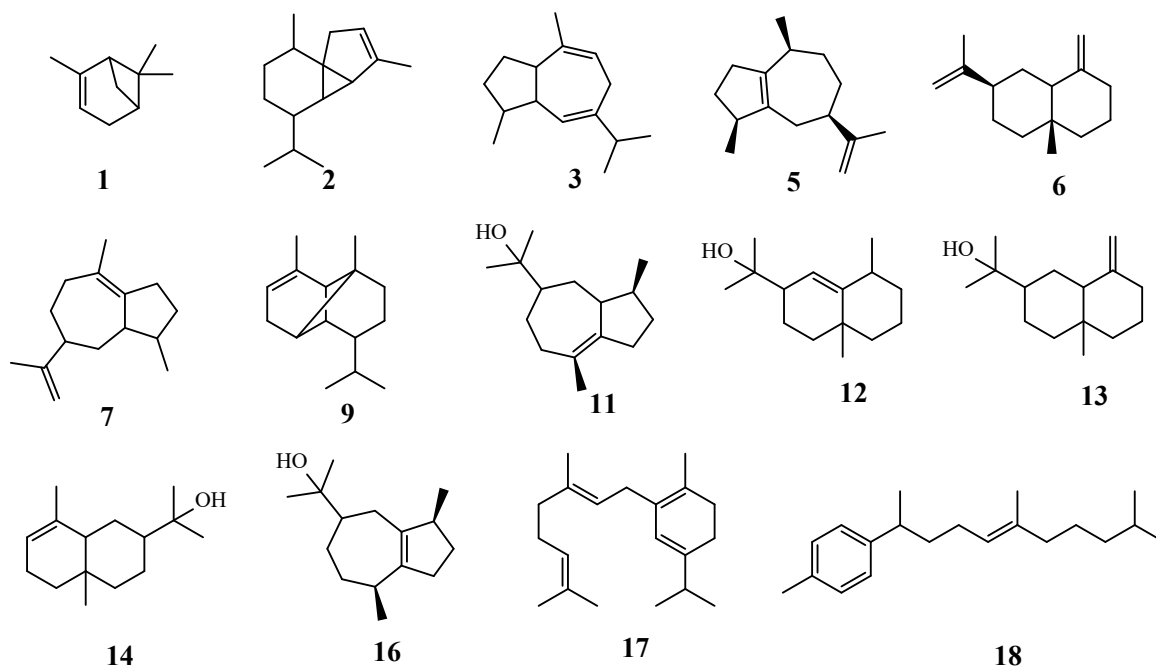
Figure 1. *Pseudognaphalium gaudichaudianum* (Left), essential oil obtained (Right)

RESULTS AND DISCUSSION

To the best of our knowledge, this is the first chemical study of *P. gaudichaudiannum* (DC.) Anderb from Bolivian highlands. This plant was collected from Apuvillque community that belongs to Omasuyos province in the department of La Paz during the rainy season. The essential oil was obtained by hydro-distillation technique with a 0,03% yield, and was analyzed by GC/MS. The results presented in Table 1 show that the essential oil contains 1 monoterpene, 11 sesquiterpenes, 2 diterpenes and 4 minor unidentified compounds. The structures are shown in figure 2. When the identified compounds were compared with common compounds from *Pseudognaphalium* genus, we found that α -Pinene was the only compound they have in common [11], which possesses an interesting antiviral activity [14].

**Table 1.** Compounds identified in the essential oil of the aerial parts from *P. gaudichaudianum*

Peak	Compound	T _R (min)	Area %
Monoterpene			
1	α -Pinene	8.09	11.32
Sesquiterpenes			
2	α -Cubebene	19.18	3.84
3	Guaia 6,9 diene	19.81	14.46
5	α -Guaiene	21.20	6.16
6	β -Eudesmene	21.57	16.35
7	Guaia 1(10),11-diene	21.71	15.20
9	α -Ylangene	22.02	0.76
11	Bulnesol	23.70	3.40
12	Rosifoliol	24.08	15.29
13	β -Eudesmol	24.50	2.12
14	α -epi-7-epi-5-Eudesmol	24.87	1.66
16	Champacol (Guaiol)	25.05	0.89
Diterpenes			
17	Geranyl α -terpinene	28.73	0.70
18	(E)-1-(6,10-Dimethylundec-5-en-2-yl)-4-methylbenzene	30.00	4.08
Unidentified			
4	Unknow	20.60	0.71
8	Unknow	21.80	0.81
10	Unknow	22.10	1.59
15	Unknow	24.96	0.65

**Figure 2.** Chemical structures of the compounds present in the essential oil from *P. gaudichaudianum*. The names of each numbered compound are presented in Table 1.



SARS-COV-2 infection process and possible prevention

Viruses unlike bacteria, need host cells to survive, because they cannot carry out metabolic processes on their own. The mechanism of viruses begins with productive infection, where they use the cell as a viral expression machine. In the end, the host cell could have produced between 10 and 10,000 viruses, depending mainly on the type of cell affected [15,16]. The entire sequence of viral infections occurs in eight definite steps. It begins with the entry of the virus into living organisms to give rise to infection, but an essential step is the incubation period. During this stage the symptoms of viral illness may or may not be present. However, the contagious period can occur in the next step by releasing the virus. The final step is resolution of the infection [17].

SARS-Cov-2 has been a viral respiratory illness originated in Wuhan, China (2019), and its expansion in the world increased exponentially [18]. Its contagious mechanism is similar to that described before, because it begins with the virus entry into the organism. Then, when it comes into the host cell, it is recognized by ACE2 receptor in the epithelial cells from lung alveoli (figure 3.A). Later, the virus links with TMPRSS2 that allows the fusion of virus-cell membrane (figure 3.B). The last step is the release of viral genetic material to the host cell (Figure 3C) for its expression, replication and virus incubation [19,20].

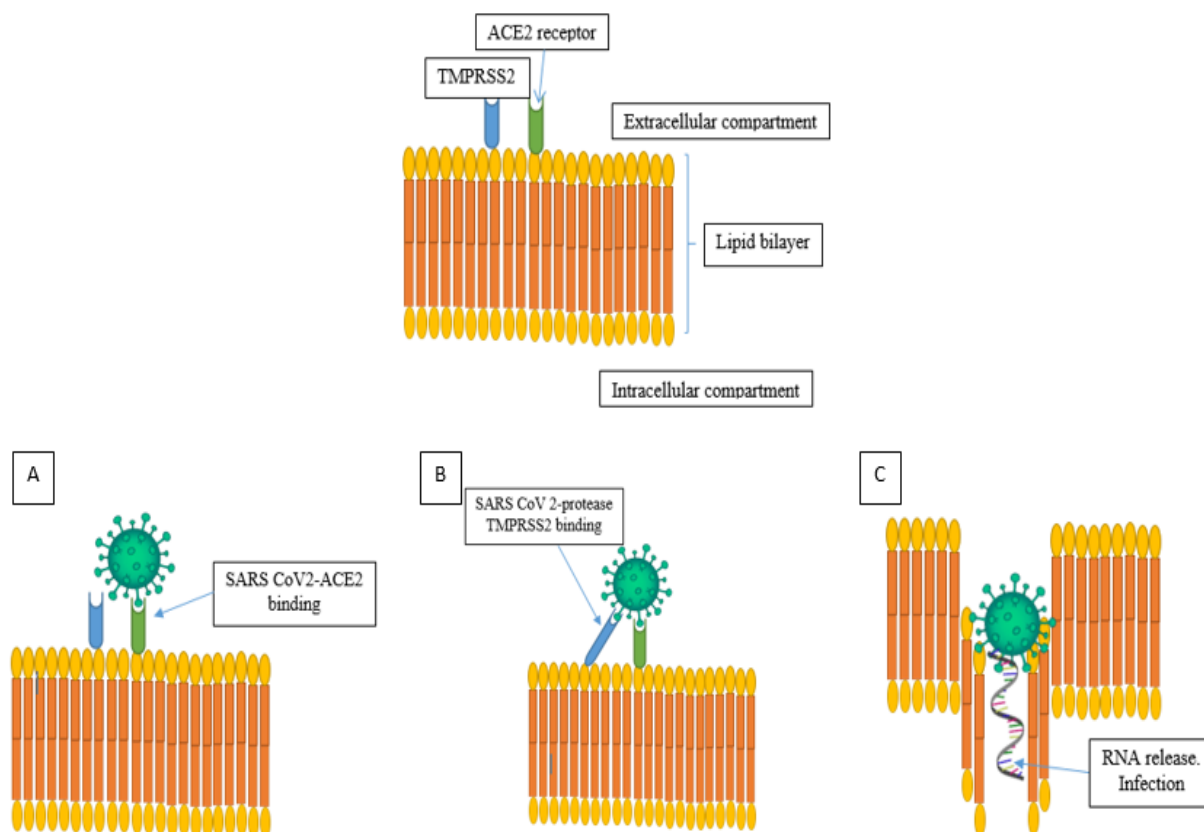


Figure 3. SARS-COV2 viral infection mechanism

For a long time, it has been known that essential oils have anti-inflammatory, immunomodulatory, bronchodilator and antiviral properties [21]. That is why we hypothesize, that it could help to treat COVID.19 infection. Because of the apolar nature of essential oils, it is estimated that these can come into the membrane cell to break it up and avoid entry of the virus to the cell [21] (Figura 4.A). While other authors claim that essential oils inhibit virus binding with ACE2 receptor through a competitive inhibition (Figure 4.B), these mechanisms must be studied deeply by molecular docking and experimental results [21,22].

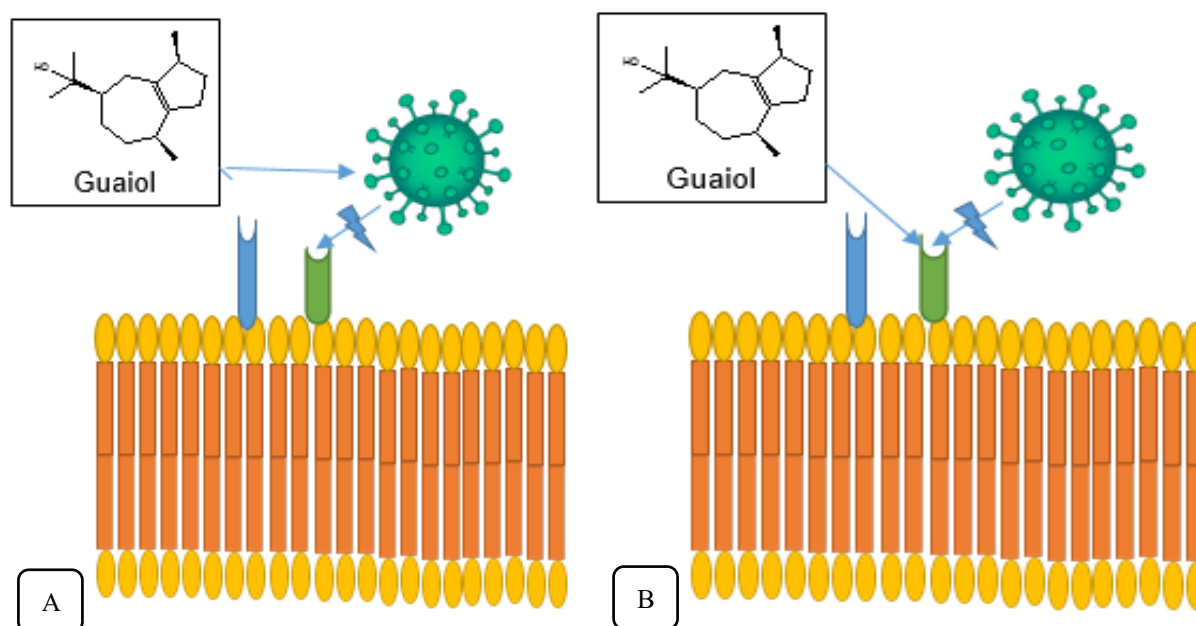


Figure 4. Mechanisms of viral inhibition by SARS-CoV-2 A) Destruction of the viral wall by the interaction of essential oils. B) Competitive inhibition by essential oil and virus to the SARS-Cov-2 receptor ACE2 protease binding site.

Various research groups made *in silico* studies about compounds present in essential oils that could prevent COVID-19 effects. Compounds like (*E,E*)- α -farnesene, ϵ - β -farnesene, (*E,E*)-farnesol [18], anethole, cinnamaldehyde, carvacrol [23], allyl disulfide and allyl trisulfide [24] could possess an activity inhibitory of the receptor proteins and enzymes that intervene in COVID-19 infection process. Previous *in silico* studies played an important role in accelerating the drug discovery process. In Parallel, an *in vitro* study of different kinds of essential oils shows that geranium (Citronellol, Geraniol anderyl acetate) and lemon (Limonene, γ -Terpinene and β -Pinene) inhibit the Angiotensin-converting enzyme 2 (ACE2), that acts as a transmembrane receptor. Thus, this fact could block the Coronavirus entry into the host cell [25].

A study made using molecular docking by My et al. [22], evaluated the binding of *Melaleuca cajuputi* essential oil components on ACE2 human receptor proteins and PDB6LU7 protease from SARS-Cov-2. This study showed that 10 of 22 essential oil compounds were active as pure components, but their activities increased by synergism against proteases, inhibiting and preventing the virus-host cell interactions. The compounds that have activity in *M. cajuputi* essential oil are Guaiol and β -Eudesmol. They are also present in *P. gaudichaudianum*, as well as other major compounds like β -Eudesmene, Rosifoliol, β -Eudesmol and γ -Eudesmol, which are eudesmane sesquiterpenes. Other eudesmane derivatives, guaiol and α -Pinene (present in several essential oils) through *in vitro* and *in silico* experiments, showed a promising anti-SARS-CoV-2 activity due to a potential inhibitory effect on the protease Mpro of the virus [26-30]. These compounds could suggest that the essential oil from *P. gaudichaudianum* may have inhibitory activity—Further studies will be needed to confirm their potential activity.

To prevent COVID-19, many aromatic plants have been used in Bolivia by the population such as: Eucalipto (*Eucalyptus globulus*), wira wira (*Achyrocline alata*, *A. satuireioides*, *A. venosa*, *Gnaphalium cheiranthifolium*, *Gamochaeta spp.*), manzanilla (*Matricaria chamomilla*) [31], and also the use of Mentisan®, a commercial product that contains α -Pinene, β -Pinene and 1,8-Cineol [32,33]. Medicinal plants, as *P.gaudichaudianum*, have been used safely for generations which support its use as potential treatment for diseases as COVID-19, but more scientific research is needed to prove their efficacy, effectiveness and safety.

EXPERIMENTAL

Plant material

The sample was collected approximately at 3800 m.a.s.l. in Apuvillque community, in Omasuyos province, department of La Paz, GPS coordinates were 16°07'31.9"S-68°37'40.5"W, on December 2020. The material was



identified by Alfredo Fuentes Ph.D. A specimen voucher is deposited in National Herbarium of Bolivia (LPB) under the code AF-1.

Extraction of essential oil

The essential oil was extracted from fresh plant material (3.9 kg of aerial parts), using hydro-distillation technique. The parameters used were: 3.5 hours for the extraction, after that time the oil was obtained as a yellow solid, with a yield of 0,03%. The oil was stored at 4°C until analysis by GC/MS.

GC/MS parameters and characterization

The gas chromatography instrument (GC2010 PLUS) was coupled to a mass spectrometer (QP 2020), both from SHIMADZU Scientific (Japan), with a Sil MS RESTEK 5% diphenyl and 95% dimethyl polysiloxane column with a size of 30 m x 0.25 mm and 0.25µm film thickness dimensions.

One milligram of the solid sample obtained from hydrodistillation of the plant was dissolved in 2 ml of n-hexane with 98% purity. Later, it was filtered through a PTFE filter of 0.2 µm of pore size, in order to be injected to the GC/MS. The injection volume was 1 µL, the total flow was 15.6 mL/min, the column flow was 0.60 mL/min, the injector temperature was 210°C. The temperature began at 40°C for 2 minutes then increased to 210°C at a speed of 2°C/min during 5 minutes. The ionization temperature was 23°C, and the temperature of the interface was 280°C. The compounds' characterization was obtained comparing the samples' mass spectrum with the ones in the library database (NIST14).

CONCLUSION

This is the first chemical study of the essential oil from aerial parts of *P. gaudichaudianum* species, which shows interesting terpenoids reported for the first time in this genus. Considering its traditional use and its recent applications for COVID-19 prevention, we propose that the essential oil of this species could help prevent COVID-19 infection due to the presence of bioactive terpenoids and the synergy between them, which must be validated by *in vitro* and *in vivo* studies.

ACKNOWLEDGEMENT

A cordial thanks to Dr. Giovanna Almanza, (Laboratory of Bioorganic, Chemical Research Institute IIQ - UMSA) for making the hydrodistiller available. Special thanks to Ruth Quispe Pilco (University of Colorado Boulder) for fruitful comments on the manuscript.

REFERENCES

- Freire, S.E., Bayón, N.D., Baeza, C.M., Giuliano, D.A., Monti, C. **2014**, Revision of the genus *Pseudognaphalium* (Asteraceae, Gnaphalieae) in Chile, *Gayana Botánica*, 71(1), 68-107. DOI: <http://dx.doi.org/10.4067/S0717-66432014000100010>
- Paz Deble, L., Cardozo Marchiori, J.N. **2006**, O gênero *Pseudognaphalium* Kirp. (Asteraceae-Gnaphalieae) no sul do Brasil, *Balduinia*, 6, 1-13. DOI: <https://doi.org/10.5902/2358198014026>
- Mendoza, L., Urzúa, A. **1998**, Minor flavonoids and diterpenoids in the resinous trichome exudates from *Pseudognaphalium cheiranthifolium*, *P. heterotrichum*, *P. vira vira* and *P. robustum*, *Biochemical Systematics and Ecology*, 26(4), 469-471. DOI: [https://doi.org/10.1016/S0305-1978\(97\)00117-8](https://doi.org/10.1016/S0305-1978(97)00117-8)
- Mendoza, L., Wilkens, M., Urzúa, A. **1997**, Antimicrobial study of the resinous exudates and of diterpenoids and flavonoids isolated from some Chilean *Pseudognaphalium* (Asteraceae). *Journal of Ethnopharmacology*, 58(2), 85-88. DOI: [https://doi.org/10.1016/S0378-8741\(97\)00084-6](https://doi.org/10.1016/S0378-8741(97)00084-6)
- Urzúa, A., Mendoza, L., Tojo, E., Rial, M.E. **1999**, Acylated flavonoids from *Pseudognaphalium* species, *Journal of Natural Products*, 62(2), 381-382. DOI: <https://doi.org/10.1021/np9804031>
- Cotoras, M., García, C., Lagos, C., Folch, C., Mendoza, L. **2001**, Antifungal activity on *Botrytis cinerea* of flavonoids and diterpenoids isolated from the surface of *Pseudognaphalium* spp., *Boletín de la Sociedad Chilena de Química*, 46(4), 433-440. DOI: <http://dx.doi.org/10.4067/S0366-16442001000400007>
- Cotoras, M., Mendoza, L., Muñoz, A., Yáñez, K., Castro, P., Aguirre, M. **2011**, Fungitoxicity against *Botrytis cinerea* of a flavonoid isolated from *Pseudognaphalium robustum*, *Molecules*, 16(5), 3885-3895. DOI: <https://doi.org/10.3390/molecules16053885>
- Aderogba, M.A., McGaw, L.J., Bagla, V.P., Eloff, J.N., Abegaz, B.M. **2014**, In vitro antifungal activity of the acetone extract and two isolated compounds from the weed, *Pseudognaphalium luteoalbum*, *South African Journal of Botany*, 94, 74-78. DOI: <https://doi.org/10.1016/j.sajb.2014.06.003>
- Rezende, M.C., Urzúa, A., Bortoluzzi, A.J., Vásquez, L. **2000**, Variation of the antimicrobial activity of *Pseudognaphalium vira vira* (Asteraceae): isolation and X-ray structure of ent-3β-hydroxy-16-kauren-19-oic acid, *Journal of Ethnopharmacology*, 72(3), 459-464. DOI: [https://doi.org/10.1016/S0378-8741\(00\)00239-7](https://doi.org/10.1016/S0378-8741(00)00239-7)



10. Urzúa, A. **2002**, Monoterpenes and sesquiterpenes in the headspace volatiles from intact plants of *Pseudognaphalium vira vira*, *P. heterotrichum*, *P. cheiranthifolium* and *P. robustum*: their insect repellent function, *Bol. Soc. Chil. Quím.*, 47(2), 99-104. DOI: <http://dx.doi.org/10.4067/S0366-16442002000200005>
11. Urzúa, A., Echeverría, J., Santander, R. **2011**, Comparative chemical composition of the essential oils from *Pseudognaphalium robustum*, *P. heterotrichum* and *P. cheiranthifolium*, *Journal of Essential Oil Bearing Plants*, 14(5), 600-604. DOI: <https://doi.org/10.1080/0972060X.2011.10643977>
12. Freire, S.E., Monti, C., Bayón, N., Migoya, M.A. **2018**, Taxonomic Studies in *Pseudognaphalium* Kirp.(Asteraceae, Gnaphalieae) from Peru, *Systematic Botany*, 43(1), 325-343. DOI: <https://doi.org/10.1600/036364418X696914>
13. Monti, C. **2016**, Revisión taxonómica y análisis cladístico de las especies sudamericanas del género *Pseudognaphalium* Kirp. (Asteraceae, Gnaphalieae), (PhD Tesis), Universidad Nacional de La Plata, Buenos Aires, Argentina, recuperado de <https://doi.org/10.35537/10915/56369>
14. Bravo, J.A., Vila, J.L., Bonté, F. **2021**, Eucalyptol and alpha-pinene, natural products with antiviral activity. Personal anti COVID-19 prevention method based on essential oils; nasal, oral and manual aqueous cleaning [3xal]. Coronavirus: environmental disinfection by Eucalyptus, *Revista Boliviana de Química*, 38(2), 95-103. DOI: <https://doi.org/10.34098/2078-3949.38.2.4>
15. Beale, J.M. Block, J.H., Antiviral Agents. In: Organic Medicinal and Pharmaceutical Chemistry, 12th ed., ed by Beale, J.M., Block, J.H., **2011**, Lippincott Williams & Wilkins, Philadelphia, USA, 330-354.
16. Elsevier Connect. **2019**, Inmunidad contra los virus y sus mecanismos de evasión, <https://www.elsevier.com/es-es/connect/medicina/inmunidad-contra-los-virus-y-sus-mecanismos-de-evasion>, Access date: 12/02/2022
17. Galán-Sánchez, F., Fernández-Gutiérrez del Álamo, C., Rodríguez-Iglesias, M. **2014**, Infecciones víricas, Medicine - Programa de Formación Médica Continuada Acreditado, 11(49), 2885-2892. DOI: [https://doi.org/10.1016/S0304-5412\(14\)70711-5](https://doi.org/10.1016/S0304-5412(14)70711-5)
18. Da Silva, J.K.R., Figueiredo, P.L.B., Byler, K.G., Setzer, W.N. **2020**, Essential Oils as Antiviral Agents, Potential of Essential Oils to Treat SARS-CoV-2 Infection: An In-Silico Investigation, *International Journal of Molecular Sciences*, 21(10), 3426. DOI: <https://doi.org/10.3390/ijms21103426>
19. Caravaca Pérez, P., Moran Fernández, L., García-Cosío, M.D., Delgado, J.F. **2020**, Sistema renina-angiotensina-aldosterona y COVID19. Implicaciones clínicas, *Revista Española de Cardiología Suplementos*, 20(E), 27-32. DOI: [https://doi.org/10.1016/S1131-3587\(20\)30032-7](https://doi.org/10.1016/S1131-3587(20)30032-7)
20. Mehta, N., Kalra, A., Nowacki, A. S., Anjewierden, S., Han, Z., Bhat, P., Carmona-Rubio, A.E., Jacob, M., Procop, G.W., Harrington, S., Milinovich, A., Svensson, L.G., Jehi, L., Young, J.B., Chung, M.K. **2020**, Association of Use of Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers with Testing Positive for Coronavirus Disease 2019 (COVID-19), *JAMA Cardiology*, 5(9), 1020-1026. DOI: <https://doi.org/10.1001/jamacardio.2020.1855>
21. Asif, M., Saleem, M., Saadullah, M., Yaseen, H.S., Al Zarzour, R. **2020**, COVID-19 and therapy with essential oils having antiviral, anti-inflammatory, and immunomodulatory properties, *Inflammopharmacology*, 28(5), 1153-1161. DOI: <https://doi.org/10.1007/s10787-020-00744-0>
22. My, T.T.A., Loan, H.T.P., Hai, N.T.T., Hieu, L.T., Hoa, T.T., Thuy, B.T.P., Quang, D.T., Triet, N.T., Anh, T.T. Van, Dieu, N.T.X., Trung, N.T., Hue, N. Van, Tat, P. Van, Tung, V. T., Nhung, N.T.A. **2020**, Evaluation of the Inhibitory Activities of COVID-19 of *Melaleuca cajuputi* Oil Using Docking Simulation, *ChemistrySelect*, 5(21), 6312-6320. DOI: <https://doi.org/10.1002/slct.202000822>
23. Kulkarni, S.A., Nagarajan, S.K., Ramesh, V., Palaniyandi, V., Selvam, S.P., Madhavan, T. **2020**, Computational evaluation of major components from plant essential oils as potent inhibitors of SARS-CoV-2 spike protein, *Journal of Molecular Structure*, 1221, 128823. DOI: <https://doi.org/10.1016/j.molstruc.2020.128823>
24. Thuy, B.T.P., My, T.T.A., Hai, N.T.T., Hieu, L.T., Hoa, T.T., Thi Phuong Loan, H., Nhung, N.T.A. **2020**, Investigation into SARS-CoV-2 resistance of compounds in garlic essential oil, *ACS Omega*, 5(14), 8312-8320. DOI: <https://doi.org/10.1021/acsomega.0c00772>
25. Senthil Kumar, K.J., Gokila Vani, M., Wang, C.S., Chen, C.C., Chen, Y.C., Lu, L.P., Huang, C.H., Lai, C.S., Wang, S.Y. **2020**, Geranium and lemon essential oils and their active compounds downregulate angiotensin-converting enzyme 2 (ACE2), a SARS-CoV-2 spike Receptor-Binding Domain, in Epithelial Cells, *Plants*, 9(6), 770. DOI: <https://doi.org/10.3390/plants9060770>
26. Ebada, S.S., Al-Jawabri, N.A., Youssef, F.S., El-Kashef, D.H., Knedel, T.O., Albohy, A., Korinek, M., Hwang, T.L., Chen, B.H., Lin, G.H., Lin, C.Y., Aldalain, S.M., Disi, A.M., Janiak, C., Proksch, P. **2020**, Anti-inflammatory, antiallergic and COVID-19 protease inhibitory activities of phytochemicals from the Jordanian hawksbeard: identification, structure-activity relationships, molecular modeling and impact on its folk medicinal uses, *RSC advances*, 10(62), 38128-38141. DOI: [10.1039/D0RA04876C](https://doi.org/10.1039/D0RA04876C)
27. Pandey, P., Singhal, D., Khan, F., Arif, M. **2020**, An in silico screening on *Piper nigrum*, *Syzygium aromaticum* and *Zingiber officinale* roscove derived compounds against SARS-CoV-2: A drug repurposing approach, *Biointerface Res. Appl. Chem*, 11, 11122-11134. DOI: <https://doi.org/10.33263/BRIAC114.1112211134>
28. Mohamed, M.E., Tawfeek, N., Elbaramawi, S.S., Fikry, E. **2022**, *Agathis robusta* Bark Essential Oil Effectiveness against COVID-19: Chemical Composition, In Silico and In Vitro Approaches, *Plants*, 11(5), 663. DOI: <https://doi.org/10.3390/plants11050663>
29. Patne, T., Mahore, J., Tokmurke, P. **2020**, Inhalation of essential oils: could be adjuvant therapeutic strategy for COVID-19, *Int J Pharm Sci Res*, 11(9), 4095-4103. DOI: <https://doi.org/10.1007%2Fs10787-020-00744-0>
30. Tshibangu, D.S., Matondo, A., Lengbiye, E.M., Inkoto, C.L., Ngoyi, E.M., Kabengele, C.N., Bongo, G.N., Benjamin Z. Gbolo, B.Z., Kilembe, J.T., Mwanangombo, D.T., Mbadiko, C.M., Mihigo, S.O., Tshilanda, D.D., Ngbolua, K.T.N., Mpiana, P.T. **2020**, Possible effect of aromatic plants and essential oils against COVID-19: Review of their antiviral activity, *Journal of Complementary and Alternative Medical Research*, 11(1), 10-22. DOI: [10.9734/JOCAMR/2020/v11i130175](https://doi.org/10.9734/JOCAMR/2020/v11i130175)
31. Maldonado, C., Paniagua-Zambrana, N., Bussmann, R. W., Zenteno-Ruiz, F.S., Fuentes, A.F. **2020**, La importancia de las plantas medicinales, su taxonomía y la búsqueda de la cura a la enfermedad que causa el coronavirus (COVID-19), *Ecología en Bolivia*, 55(1), 1-5.
32. Bravo, J.A., Vila, J.L., Bonté, F. **2021**, Updates on coronavirus, covid-19, personal antiviral prevention method based on natural products, essential oils, eucalyptol, alpha-pinene: Mentisan®; nasal, oral and environmental disinfection by eucalyptus. No more deaths, *Revista Boliviana de Química*, 38(1), 1-13. DOI: [10.34098/2078-3949.38.1.1](https://doi.org/10.34098/2078-3949.38.1.1)
33. Bravo, J.A. **2020**, Coronavirus, COVID-19, preventing the spreading of viruses is easier than we think; biosafety protocols, guide for the reopening of the country and for reducing the risk of reactivation of the spreading, *Revista Boliviana de Química*, 37(2), 94-131. DOI: [10.34098/2078-3949.37.2.4](https://doi.org/10.34098/2078-3949.37.2.4)