RJC

RASĀYAN *J. Chem.*
Vol. 15 | No. 2 |853-860| April - June | 2022
ISSN: 0974-1496 | e-ISSN: 0976-0083 | CODEN: RJCABP
http://www.rasayanjournal.com
http://www.rasayanjournal.co.in

THE ROLE OF NATURAL PRODUCTS AGAINST COVID-19: A REVIEW

D. Dutta, B. R. Chhetri, J. Biswas and N. K. Bhattacharyya✉
Department of Chemistry, Sikkim Manipal Institute of Technology (Sikkim Manipal University), Majitar-737136, Rangpo (Sikkim), India
✉Corresponding Author: nkamalbhatt@gmail.com

ABSTRACT

The pandemic COVID-19 is an infectious respiratory illness caused by SARS CoV-2 (severe acute respiratory syndrome coronavirus-2) and it spreads human-to-human. Due to the COVID-19 outbreak, the world is facing an unprecedented loss of lives around the globe and highlighted an effective treatment to deal with the virus. Natural products have historically been utilized for respiratory disease and display promising toxicity. Natural products have been reported for several antiviral activities of viruses, like influenza, HIV and some coronaviruses SARS-CoV and MERS-CoV. Therefore, natural products could be a vital resource for developing efficient and safe antiviral drugs against COVID-19. This review summarized the inhibition of isolated compounds from medicinal plants against different coronaviruses which could lead to the development of effective antiviral drugs to counter COVID-19.

Keywords: COVID-19, CoVs, Plant, Compound, IC_{50}/EC_{50}.

RASĀYAN *J. Chem.*, Vol. 15, No.2, 2022

INTRODUCTION

COVID-19 is a communicable respiratory illness affected by the latest class of coronavirus (CoV), recognized as SARS CoV-2, in the Coronaviridiae family. It has spread around the globe in a short duration and this pandemic, according to WHO, affects more than four hundred million people with over 5 million deaths.[1] Because of this virus, symptoms like fever, dry cough, loss of smell and tiredness are shown by mild infected COVID-19 patients. In severe infected patients, the symptoms like shortness of breath, dry cough and pneumonia are observed. However, in case of critical situation, patients show the complete failure of respiratory and multiple organ dysfunction.[2] This virus spreads person-to-person mainly due to contact with symptomatic patients of this virus, as well as via respiratory droplets released by patients.[2-4] In 1931, first diagnosed was performed related to CoV and the first human CoV was identified in 1965.[36] Recently, few vaccines like Pfizer, BioNTech, Moderna, BBIBP-CorV, CoronaVac and Sputnik V are available for the treatment of COVID-19, however, they have few side effects.[3] Keeping this in mind we can think that natural products could be a vital resource for dealing with COVID-19, as they have displayed prominent antiviral activity towards other viruses, like HIV, MERS-CoV, SARS-CoV, HCoV-229E, TGEV, FCoV, SARS-CoV 3CL, HCoV-OC43, HCoV-NL63 and influenza.[35-43] The plant products have therapeutic benefits against infectious respiratory illnesses including pneumonia, septic shock, lung injury, pulmonary fibrosis, diffuse alveolar damage and kidney injury, all of which have symptoms correlated with COVID-19.[44-51] The present review intends to systematically evaluate the reported inhibition of molecules isolated from plants against different CoVs which could be lead towards effective drug entrants to hinder SARS-CoV-2 and results are discussed below. The authors reviewed and interpreted the articles on antiviral activities of naturally occurring compounds which have been already accounted effective against various CoVs. The diverse antiviral compounds isolated from various medicinal plants were searched extensively in online databases like PubMed, Science Direct etc. to collect data.

Natural Products against CoVs

Natural compounds belonging to chemical groups including alkaloid, coumarin, diarylheptanoid, flavonoid, polyphenol, saponin, and terpenes have shown promising antiviral activity (Table-1 & Fig. 1-8). More than 200 Chinese medicinal plants were studied against SARS-CoV using MTS assay in Vero E6 cells, and their results demonstrated that the alkaloid-rich fraction from *Artemisia*, *Lycoris*, *Pyrrosia* and *Lindera* species

http://doi.org/10.31788/RJC.2022.1526332a

were reported antiviral activity.[42] A study on 221 lignin- and terpene-derivatives of natural products for their antiviral activity reported that 20 compounds showed promising activity against SARS CoV using CPE assay in Vero E6 cell.[34] Over 312 plant species of Taiwan were studied against SARS-CoV by MTT assays in Vero E6 cells and found that the plants of the Polygonaceae family, *Rheum officinale* and *Polygonum multiform* exhibited effective antiviral activity.[32] Nine alkylated chalcones and four coumarins reported from the Apiaceae family against SARS-CoV3CL^{pro} and PL^{pro} reported they exhibited an effective inhibition against SARS-CoV3CL^{pro}. Some diarylheptanoid derivatives showed inhibition against SARS-CoVPL^{pro} compared with reference curcumin.[9] They also demonstrated that if catechol group with a α, β-unsaturated carbonyl group is present, these compounds showed greater inhibition, whereas mono hydroxyl substitution lower the inhibitory effect.

Table-1: Some Natural Compounds with Anti-CoVs Effects

Plant	Coronavirus	Compound	Coronavirus Type targeted	IC_{50}/EC_{50} Values	References
Aesculus hippocastanum	Saponin	Aescin **44**	SARS-CoV	3.4 µmol/L	[7]
Allium sativum	Alkaloid	Capsaicin **1**	SARS-CoV-2	-	[48]
Alnus japonica	Diarylheptanoid	Hirsutenone **40** Rubranoside **38** Curcumin **39**	SARS-CoV	4.1µmol/L 7.2±2.2 µM 5.7 µM	[9] [9] [9]
Angelica keiskei	Chalcone	Xanthoangelol **35**	SARS-CoV	11.4-130 µM	[10]
		Chalcones I–IX **37**			
Black tea	Polyphenol	Theaflavin **42**	SARS-CoV	-	[12]
Broussonetia papyrifera	Flavonoid	Isoliquiritigenin **18** Kaempferol **19**	SARS-CoV	61.9±11.0 µM 116.3±7.1 µM	[11]
		Kazinol F **20**		43.3±10.4 µM	
		Broussochalcone B **36**		57.8±0.5 µM	
		Papyrifavonol A **22**		103.6±17.4 µM	
Boenninghausenia sessilicarpa	Coumarin	Leptodactylone **68**	SARS-CoV	100 µg/mL	[13]
Bupleurum chinense	Glycoside	Saikosaponin A **46**	SARS-CoV	8.6 mmol/L	[14]
	Saponin	Saikosaponin B_2 **47**	HCoV-229E	1.7 µmol /L	
CalophylluBlancooi	Xanthone	Blancoxanthone **61**	HCoV 229E	3 µg/ml	[15]
		Pyranojacareubin **62**		15 µg/ml	
Cinnamomum Verum	Proanthocyanidin	Procyanidin A2 **70** Procyanidin B1 **71** CinnamtanninB1 **72**	wtSARS-CoV	29.9 µM 41.3 µM 32.9 µM	[46]
Cynanchum genus	Alkaloid	Tylophorine **5**	TGEV	58±4 µM	[5]
		7-Methoxy cryptopleurine **8**		20±1 µM	
Euphorbia neriifolia	Terpenoid	3β-friedelanol **56** 3β-acetoxy- friedelane **57** Friedelin 58 Epitaraxerol **59**	HCoV	132.4% at 5µg 80.9% at 5µg 109.0% at 5µg 111.0% at 5µg	[47]
Ginkgo biloba	Flavonoid	Quercetin-3-β-galactoside **32**	SARS-CoV	42.79µmol/L	[14]
Galanthus nivalis	Alkaloid	Agglutinin	FCoV	0.0088 nM	[17]
		Nelfinavir **9**	FCoV	8.19 µM	

Isatis indigotica	Polyphenol Flavonoid Alkaloid	Sinigrin **43** β-Sitosterol **63** Hesperetin **21** Indirubin **2** Indican **3**	SARS-CoV SARS-CoV 3CL	217 µM 1210 µM 8.3µM 217 and 8.4 M	[18]
Licorice Root	Saponin	Glycyrrhizin **45**	SARS-CoV	364.5 µM	[19]
Lycoris Radiata	Alkaloid	Lycorine **4**	SARS-CoV	15.7 nmol/L	[42]
Myrica rubra	Alkaloid	Myricetin **64**	SARS-CoV	2.71 µmol/L	[20]
Polygonum cuspidatum	Stilbenoid	Resveratrol **65**	MERS-CoV	-	[27]
Panax ginseng	Ginsenoside	Ginsenoside-Rb1 **60**	SARS-CoV	100 µmol/L	[7]
Psoraleacorylifolia	Chalcone	Isobavachalcone **34**	SARS-CoV	7.3±0.8 µM	[28]
Psoralea corylifolia	Flavonoid	Psoralidin **26**	SARS-CoV	4.2±1.0 µM	[28]
Paulownia tomentosa	Flavonoid	Tomentin A **23** Tomentin B **24**	SARS-CoV	6.2±0.04 µM 6.1±0.02 µM	[33]
		Tomentin E **25**		5.0±0.06 µM	
		3′-O-Methyl diplacol **33**		9.5±0.10 µM	
Rauvolfia serpentina	Alkaloid	Reserpine **13**	SARS-CoV	6.0 µmol/L	[7]
Rheum palmatum	Anthraquinone	Emodin **66**	SARS-CoV	200 µmol/L	[32]
Salvia miltiorrhiza	Diterpenoid	Dihydrotanshinone I **48**	MERS-CoV	1 µg/mL	[29]
Stephania tetrandra	Alkaloid	Tetrandrine **11**	HCoV-OC43	0.33µmol/L	[30]
Stephania japonica	Alkaloid	Cepharanthine **14**	SARS-CoV-2	0.98 µmol/L	[31]
Salvia miltiorrhiz		Tanshinone **67**	SARS-CoV	0.7–30 µmol/L	[8]
Strobilanthes cusia	Alkaloid	Indirubin **10** Tryptanthrin **12** Indigodole A-B **15-16**	HCoV-NL63	0.32 µM	[17]
Scutellaria baicalensis	Flavone	Scutellarein **27**	SARS-CoV	0.86 µmol/L	[20]
Triterygiumregelii	Triterpenoid	Celastrol **51**	SARS-CoV	10.3 µmol/L	[21]
		Pristimerin **52**		5.5 µmol/L	[21]
		Tingenone **53**		9.9 µmol/L	[21]
		Iguesterin **54**		2.6 µmol/L	[21]
	Polyphenol	Tetra-O-galloyl-β-D-glucose **41**		4.5 µM	[23]
	Flavonoid	Luteolin **28**		10.6 µM	[23]
Torreyanucifera	Flavonoid	Amentoflavone **31**	SARS-CoV	8.3 µM	[22]
		Luteolin **28**		20.2 µM	
		Quercetin **29**		23.8 µM	
		Apigenin **30**		280.8 µM	
Salvia miltiorrhiza	Diterpene	Dihydrotanshinone I **48**	SARS-CoV	4.9±1.2 µM	[8]
		Cryptotanshinone **50**		0.8±0.2 µM	
		Tanshinone IIA **49**		1.6±0.5 µM	
	Triterpene	Schimperinone **55**	PEDV	0.28±0.09 µM	
Torreya Nucifera	Triterpene	Tingenone **53**	SARS-CoV	9.9±0.1 µM	[22]
		Iguesterin **54**		2.6±0.3 µM	
Tribulus terrestris	Cinnamic amide	Terrestrimine **69**	SARS-CoV	15.8±0.6 µM	[24]
Ziziphus jujuba	Alkaloid	Jubanine G **6**	PEDV	13.41±1.13µM	[25]
		Jubanine H **7**		4.49±0.67 µM	
		Nummularine B **16**		6.17±0.50 µM	

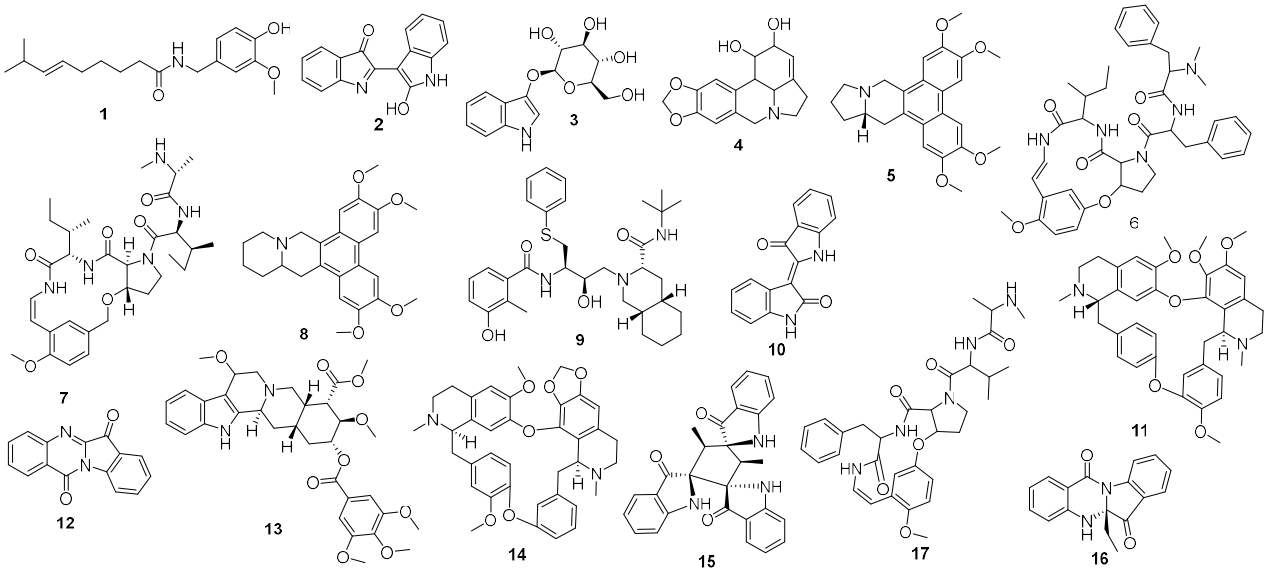

Fig.-1: Structures of Active Alkaloids Against Different CoVs

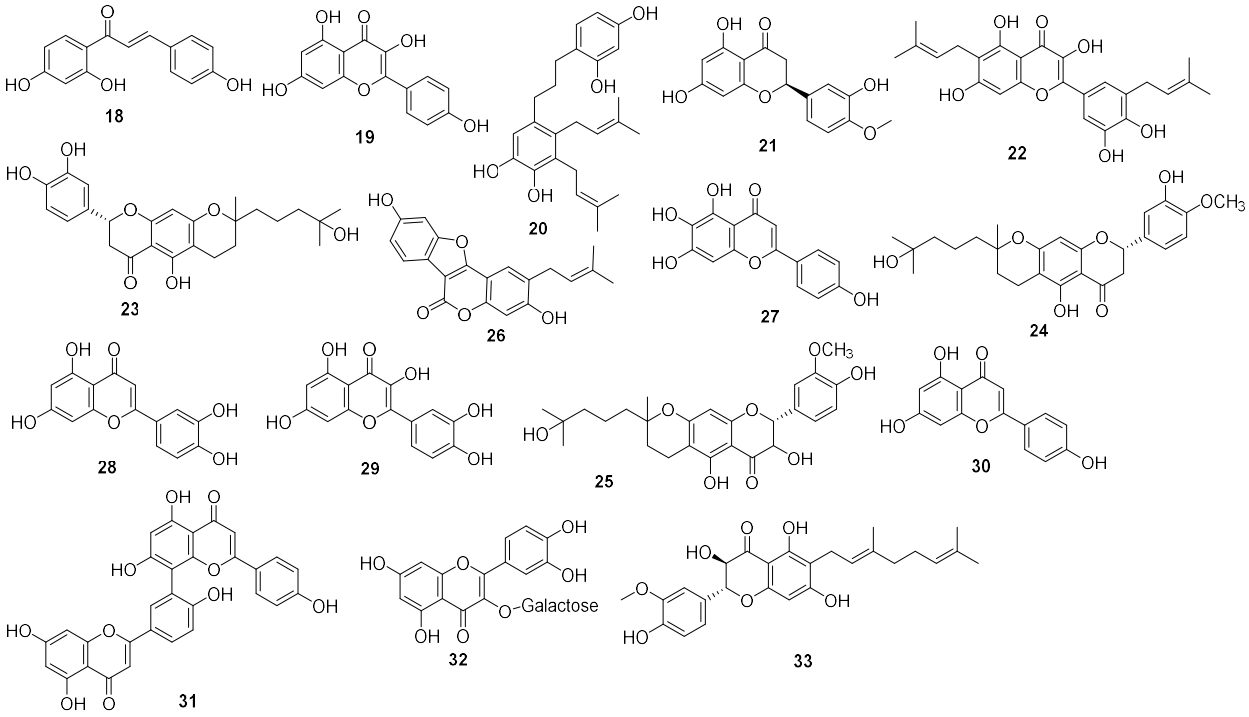

Fig.-2: Structures of Active Flavonoids Against Different CoVs

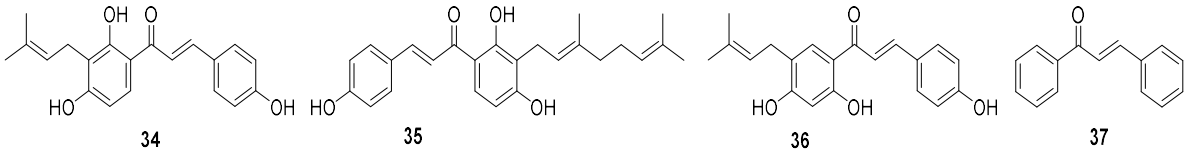

Fig.-3: Structures of Active Chalcones Against Different CoVs

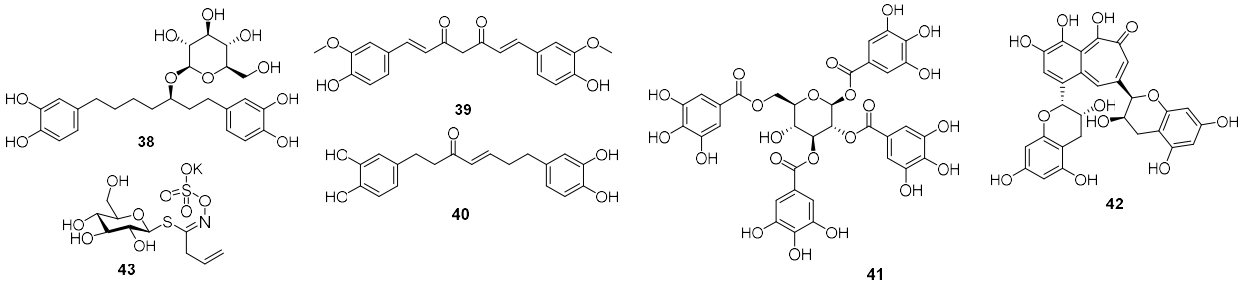

Fig.-4: Structures of Active Diaryl heptanoids And Polyphenols Against Different CoVs

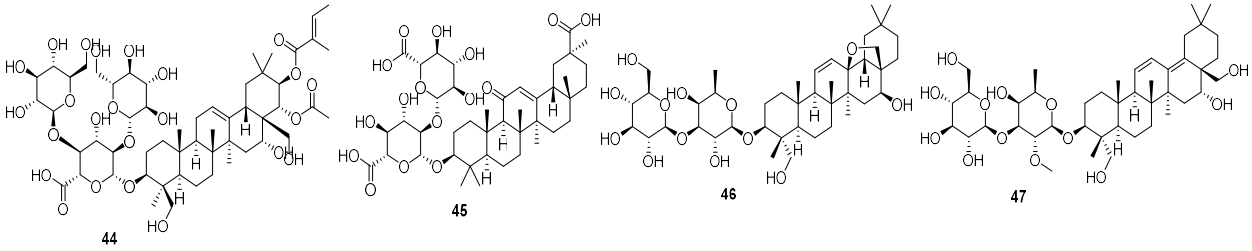

Fig.-5: Structures of Active Saponins Against Different CoVs

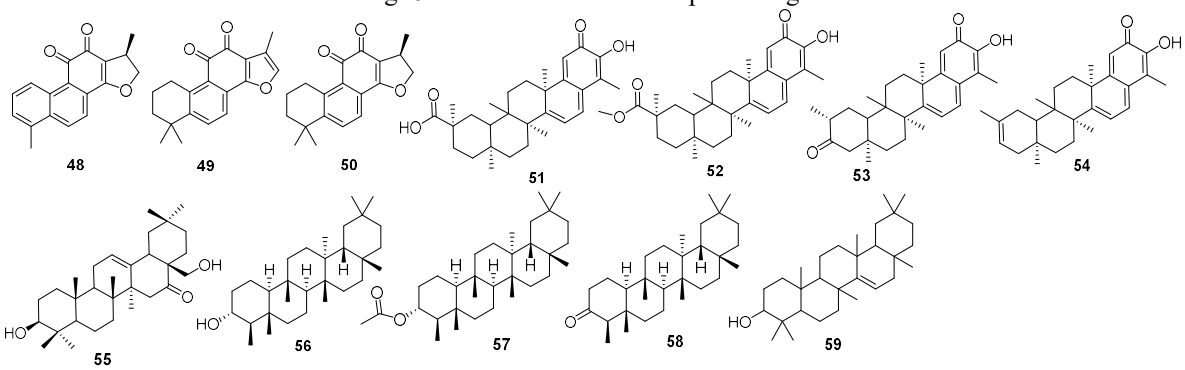

Fig.-6: Structures of Active Terpenoids Against Different CoVs

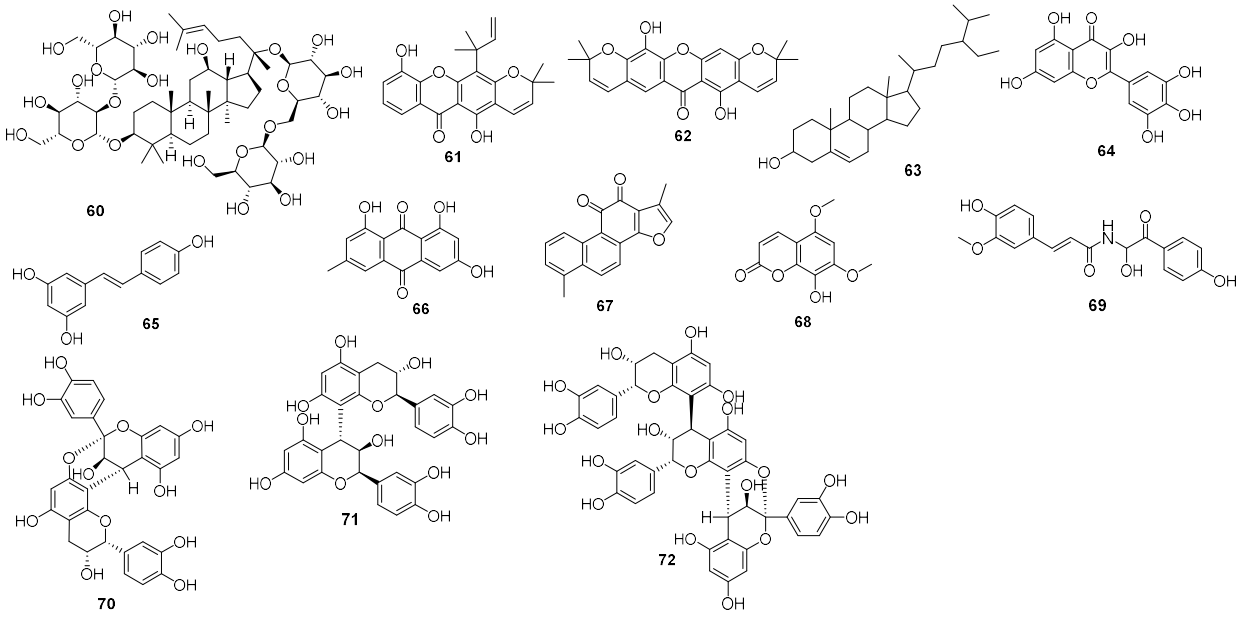

Fig.-7: Structures of Miscellaneous Molecules Against Different CoVs

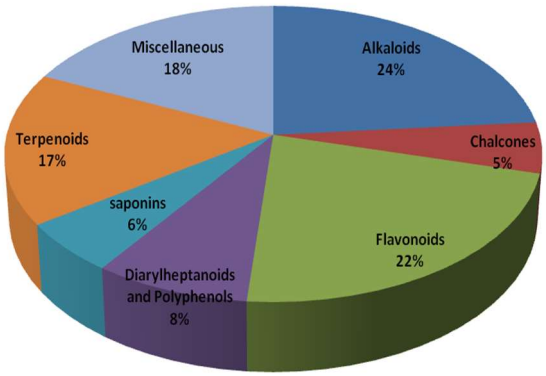

Fig.-8: Various Classes of Molecules from Plants Towards Different CoVs

CONCLUSION

In recent years, CoVs are associated with several infectious respiratory illness outbreaks in humans. Due to the side effects of the vaccine or drug to treat COVID-19, there is a requirement for effective treatment to deal with the virus. In present review, we discussed several naturally occurring compounds that have exhibited significant anti-CoV agents and potential for COVID-19 treatment. Diverse phytochemicals belonging to the classes including alkaloids, flavonoids, chalcones, diarylheptanoids, polyphenols, terpenoids, and saponins were reported inhibition towards several CoVs. Therefore, natural products could be a vital resource for the treatment of COVID-19, as they have been shown to promise antiviral inhibition against various viruses.

ACKNOWLEDGEMENT

The authors would like to acknowledge the Director, Sikkim Manipal Institute of Technology, Sikkim in executing this review article.

REFERENCES

1. World Health Organization, Health emergencies Programme, Weekly operational update on COVID-19 (2022), https://www.who.int/publications/m/item/weekly-operational-update-on-covid-19---15-february-2022 (accessed 15.02.22)
2. R. Chakravarti, R. Singh, A. Ghosh, D. Dey, P. Sharma, R. Velayutham, S. Roy, D. Ghosh, *RSC Advance*, **11**, 16711(2021), https://doi.org/10.1039/d1ra00644d
3. D.S. Chauhan, S. Yadav, M.A. Quraishi, *Current Research in Green and Sustainable Chemistry*, **4**, 100114(2021), https://doi.org/10.1016/j.crgsc.2021.100114
4. A.R. Noviyanti, D.R. Eddy, Rukiah, Y. Deawati, *Rasayan Journal of Chemistry*, **14(2)**, 1006(2021), https://doi.org/10.31788/ RJC.2021.1426255
5. F.M. Ibrahim, H.A. Holik, A. Achmad, *Rasayan Journal of Chemistry*, **14(3)**, 1469(2021), https://doi.org/10.31788/ RJC.2021.1436172
6. R. Pemmereddy, K.S. Chandrashekhar, S.R.K. Pai, v. Pai, A. Mathew, B.V. Kamath, *Rasayan Journal of Chemistry*, **15(1)**, 1(2022), http://dx.doi.org/10.31788/RJC.2022.1516421
7. C.Y. Wu, J.T. Jan, S.H. Ma, C.J. Kuo, H.F. Juan and Y.S. Cheng, *Proceedings of National Academy of* Sciences, USA, **101**, 10012(2004), https://doi.org/10.10.1073/pnas.0403596101
8. J.Y. Park, J.H. Kim, Y.M. Kim, H.J. Jeong, D.W. Kim, K.H. Park, *Bioorganic and Medicinal Chemistry*, **20**, 5928(2012a), https://doi.org/10.1016/j.bmc.2012.07.038
9. J.Y. Park, H.J. Jeong, J.H. Kim, Y.M. Kim, S.J. Park, D. Kim, K.H. Park, W.S. Lee, Y.B. Ryu, *Biological and Pharmaceutical Bulletin*, **35**, 2036(2012b), https://doi.org/10.1248/bpb.b12-00623
10. J.Y Park, J.A. Ko, D.W. Kim, Y.M. Kim, H.J. Kwon, H.J. Jeong, C.Y. Kim, K.H. Park, W.S. Lee, Y.B. Ryu, *Journal of Enzyme Inhibition and Medicinal Chemistry*, **31**, 23(2016), https://doi.org/10.3109/14756366.2014.1003215
11. J.Y Park, H.Y. Yuk, H.W. Ryu, S.H. Lim, K.S. Kim, K.H. Park, Y.B. Ryu, W.S. Lee, *Journal of Enzyme Inhibition and Medicinal Chemistry*, **32**, 504(2017), https://doi.org/10.1080/14756366.2016.1265519
12. J. Lung, Y.S. Lin, Y.H. Yang, Y.L. Chou, L.H. Shu, Y.C. Cheng, H.T. Liu, C.Y. Wu, *Journal of Medical Virology*, **92**, 693(2020), https://doi.org/10.1002/jmv.25761

13. Q.Y. Yang, X.Y. Tian, W.S. Fang, *Journal of Asian Natural Products Research*, **9**, 59(2007), https://doi.org/10.1080/10286020500382397
14. P.W. Cheng, L.T. Ng, L.C. Chiang, C.C. Lin, *Clinical and Experimental Pharmacology and Physiology*, **33**, 612(2006), https://doi.org/10.1111/j.1440-1681.2006.04415.x
15. Y.C. Shen, L.T. Wang, A.T. Khalil, L.C. Chiang, *Chemical and Pharmaceutical Bulletin*, **53**, 244(2005), https://doi.org/10.1248/cpb.53.244
16. L. Chen, J. Li, C. Luo, H. Liu, W. Xu, G. Chen, *Bioorganic and Medicinal Chemistry*, **14**, 8295(2006), https://doi.org/10.1016/j.bmc.2006.09.014
17. Y.C. Tsai, C.L. Lee, H.R. Yen, Y.S. Chang, Y.P. Lin, S.H. Huang, C.W. Lin, *Biomolecules*, **10**, 366(2020), https://doi.org/10.3390/biom10030366
18. C.W. Lin, F.J. Tsai, C.H. Tsai, C.C. Lai, L. Wan, T.Y. Ho, C.C. Hsieh, P.D. Chao, *Antiviral Research*, **68**, 36(2005), https://doi.org/10.1016/j.antiviral.2005.07.002
19. J. Cinatl, B. Morgenstern, G. Bauer, P. Chandra, H. Rabenau, H.W. Doerr, *Lancet*, **361**, 2045(2003), https://doi.org/10.1016/s0140-6736(03)13615-x
20. M.S. Yu, J. Lee, J.M. Lee, Y. Kim, Y.W. Chin, J.G. Jee, *Bioorganic and Medicinal Chemistry Letters*, **22**, 4049(2012), https://doi.org/10.1016/j.bmcl.2012.04.081
21. Y.B. Ryu, S.J. Park, Y.M. Kim, J.Y. Lee, W.D. Seo, J.S. Chang, K.H. Park, M.C. Rho, W.S. Lee, *Bioorganic and Medicinal Chemistry Letters*, **20**, 1873(2010a), https://doi.org/10.1016/j.bmcl.2010.01.152
22. Y.B. Ryu, H.J. Jeong, J.H. Kim, Y.M. Kim, J.Y. Park, D. Kim, T.T. Nguyen, S.J. Park, J.S. Chang, K.H. Park, M.C. Rho, W.S. Lee, *Bioorganic and Medicinal Chemistry*, **18**, 7940(2010b), https://doi.org/10.1016/j.bmc.2010.09.035
23. L. Yi, Z. Li, K. Yuan, X. Qu, Chen, G. Wang, H. Zhang, H. Luo, L. Zhu, P. Jiang, L. Chen, Y. Shen, M. Luo, G. Zuo, J. Hu, D. Duan, Y. Nie, X. Shi, W. Wang, Y. Han, T. Li, Y. Liu, M. Ding, H. Deng, X. Xu, *Journal of virology*, **78**, 11334(2004), https://doi.org/10.1128/JVI.78.20.11334-11339.2004
24. Y.H. Song, D.W. Kim, M.J. Curtis-Long, H.J. Yuk, Y. Wang, N. Zhuang, K.H. Lee, K.S. Jeon, K.H. Park, *Biological and Pharmaceutical Bulletin*, **37**, 1021(2014), https://doi.org/10.1248/bpb.b14-00026
25. K.B. Kang, G. Ming, G.J. Kim, T.K. Ha, H. Choi, W.K. Oh, S.H. Sung, *Phytochemistry*, **119**, 90(2015), https://doi.org/10.1016/j.phytochem.2015.09.001
26. G. Hoever, L. Baltina, M. Michaelis, R. Kondratenko, L. Baltina, G.A. Tolstikov, *Journal of Medicinal Chemistry*, **48**, 1256(2005), https://doi.org/10.1021/jm0493008
27. S.C. Lin, C.T. Ho, W.H. Chuo, S. Li, T.T. Wang, C.C. Lin, *BMC Infect Disease*, **17**, 144(2017), https://doi.org/10.1186/s12879-017-2253-8
28. D.W. Kim, K.H. Seo, M.J. Curtis-Long, K.Y. Oh, J.W. Oh, J.K. Cho, K.H. Lee, K.H. Park, *Journal of Enzyme Inhibition and Medicinal Chemistry*, **29**, 59(2014), https://doi.org/10.3109/14756366.2012.753591
29. J.Y. Kim, Y.I. Kim, S.J. Park, I.K. Kim, Y.K. Choi, S.H. Kim, *International Journal of Antimicrobial Agents*, **52**, 730(2018), https://doi.org/10.1016/j.ijantimicag.2018.05.003
30. D.E. Kim, J.S. Min, M.S. Jang, J.Y. Lee, Y.S. Shin, C.M. Park, J.H. Song, H.R. Kim, S. Kim, Y.H. Jin, S. Kwon, *Biomolecules*, **9**, 696(2019), https://doi.org/10.3390/biom9110696
31. H.H. Fan, L.Q. Wang, W.L. Liu, X.P. An, Z.D. Liu, X.Q. He, *Chinese Medicinal Journal (Engl)* **133**, 1051(2020), https://doi.org/10.1097/CM9.0000000000000797
32. T.Y. Ho, S.L. Wu, J.C. Chen, C.C. Li, C.Y. Hsiang, *Antiviral Research*, **74**, 92(2007), https://doi.org/10.1016/j.antiviral.2006.04.014
33. J.K. Cho, M.J. Curtis-Long, K.H. Lee, D.W. Kim, H.W. Ryu, H.J. Yuk, K.H. Park, *Bioorganic and Medicinal Chemistry*, **21**, 3051(2013), https://doi.org/10.1016/j.bmc.2013.03.027
34. C.C. Wen, Y.H. Kuo, J.T. Jan, P.H. Liang, S.T. Wang, H.G. Liu, C.K. Lee, S.T. Chang, C.J. Kuo, S.S. Lee, C.C. Hou, P.W. Hsiao, S.C. Chien, L.F. Shyur, N.S. Yang, *Journal of Medicinal Chemistry*, **50**, 4087(2007), https://doi.org/10.1021/jm070295s
35. S. Panyod, C.T. Ho, L.Y. Sheen, *Journal of Traditional and Complementary Medicine*, **10**, 420(2020), https://doi.org/10.1016/j.jtcme.2020.05.004

36. I.E. Orhan, F.S.S. Deniz, *Natural Products and Bioprospecting*, **10**, 171(2020), https://doi.org/10.1007/s13659-020-00250-4
37. Y. Xian, J. Zhang, Z. Bian, H. Zhou, Z. Zhang, Z. Lin, H. Xu, Acta Pharmaceutica Sinica B, **10**, 1163(2020), https://doi.org/10.1016/j.apsb.2020.06.002
38. A.D.S. Antonio, L.S.M. Wiedemann, V.F. Veiga-Junior, *RSC Advance*, **10**, 23379(2020), https://doi.org/10.1039/D0RA03774E
39. T. Joshi, T. Joshi, P. Sharma, S. Mathpal, H. Pundir, V. Bhatt, S. Chandra, *European Review for Medical and Pharmacological Sciences*, **24**, 4529(2020), https://doi.org/10.26355/eurrev_202004_21036
40. M. Cascella, M. Rajnik, A. Cuomo, S.C. Dulebohn, D.R. Napoli, Features, evaluation and treatment coronavirus (COVID-19). StatPearls, Treasure Island (FL), (2020)
41. G. Kampf, A. Kramer, *Clinical Microbiology Reviews*, **17**, 863(2004), https://doi.org/10.1128/CMR.17.4.863-893.2004
42. S.Y. Li, C. Chen, H.Q. Zhang, H.Y. Guo, H. Wang, L. Wang, *Antiviral Research*, **67**, 18(2005), https://doi.org/10.1016/j.antiviral.2005.02.007
43. C.W. Yang, Y.Z. Lee, I.J. Kang, D.J. Barnard, J.T. Jan, D. Lin, C.W. Huang, T.K. Yeh, Y.S. Chao, S.J. Lee, *Antiviral Research*, **88**, 160(2010), https://doi.org/10.1016/j.antiviral.2010.08.009
44. M. Junaid, Y. Akter, A. Siddika, S.M.A. Nayeem, A. Nahrin, S.S. Afrose, M.M.A. Ezaj, M.S. Alam, *Mini Reviews in Medical Chemistry*, **22**, 498(2021), https://doi.org/10.2174/1389557521666210805113231
45. J.T. Ristovski, M.M. Matin, R. Kong, M.P. Kusturica, H. Zhang, *South African Journal of Botany*, (2021), https://doi.org/10.1016/j.sajb.2022.02.009
46. M. Zhuang, H. Jiang, Y. Suzuki, X. Li, P. Xiao, T. Tanaka, *Antiviral Research*, **82**, 73(2009), https://doi.org/10.1016/j.antiviral.2009.02.001
47. F.R. Chang, C.T. Yen, M. Ei-Shazly, W.H. Lin, M.H. Yen, K.H. Lin, *Natural Product Communication*, **7**, 1934(2012), https://doi.org/10.1177/1934578x1200701103
48. N. Mohammadi, N. Shaghaghi, *ChemRxiv Preprint,* (2020), https://doi.org/10.26434/chemrxiv.11987475.v1
49. D. Dutta, M. Bordoloi, N.K. Bhattacharyya, *Rasayan Journal of Chemistry*, **14(4)**, 2161(2021), http://doi.org/10.31788/RJC.2021.1446353
50. A.G. Omokhua-Uyi, J.V. Staden, *South African Journal of Botany*, **139**, 186(2021), http://doi.org/10.1016/j.sajb.2021.03.012
51. O.L. Erukainure, O. Atolani, A. Muhammad, R. Ravichandran, M.M. Abarshi, S.B. Katsayal, C.I. Chukwuma, R. Preissner, P. Bannerjee, M.A. Mesaik, *Computers in Biology and Medicine*, **139**, 104964(2021), https://doi.org/10.1016/j.compbiomed.2021.104964

[RJC-6332a/2021]