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# Phenolic Compounds: Promising Anti-Viral Agents A review

Mahmed sharaf



Photochemistry and Plant Systematic Department, National Research Centre, Dokki, Cairo, Egypt

### Abstract

Phenolic compounds are a class of the most widely distributed secondary metabolites and found in most plant tissues. They may function as pollination, pigment constituents and protection against UV radiation. Phenolics have been investigated for their biological activities. They showed great activity against various viruses such as herpes simplex, Epstein-Barr virus, equid herpes virus, hepatitis B virus, human immunodeficiency virus and respiratory syncytial. This review summarized some phenolic compounds which showed antiviral activities, and expected to provide guides for rational design of antiviral drugs.

Keywords: Medicinal plants, Phenolic compounds, Antiviral activit

## **1. INTRODUCTION**

Natural products have long been the major source of lead compounds for the development of a great variety of therapeutics including anticancer and antiviral agents. According to the WHO (World Health Organization), more than 80% of the world's population relies on traditional medicine for their primary healthcare needs [1]. Plant phenolics are the major source of compounds for the development of a great variety of antiviral agents [2]. Many studies revealed that a large number of phenolics has been isolated from medicinal plants. Medicinal plants synthesize and preserve a variety of biochemical products possessing potential inhibition of viruses. Table 1 showed some medicinal plants which reported to have antiviral activity against different viruses and their chemical constituents. The tabulated plants are found to be rich in phenolic compounds.

			tannins	
Psidium guajava	Myrtaceae	HSV-1	Polyphenols , tannins.	[5,6]
Moringa oleifera	Moringaceae	H1N1	Flavonoids, phenolic acids	[7,8]
Aloe barbadensis	Asphodelacea e	HIV, HSV, HBV, EBV, FMDV, NDV.	Polyphenols , Flavonoids, phenolic acids	[9-12]
Curcuma longa	Zingiberaceae	HCV, EBV, HIV-1, H1N1, H6N6, parainfluenza viruses 1, 2, 3 , VSV, RV	Phenolics (Curcumin)	[13,14]
Camellia sinensis	Theaceae	HIV, HSV-I, IAV, HCV.	Catechins, quercetin,	[15-18]
Euphorbia hirta	Euforbiacee	HIV-1, HIV-2	Flavonoids	[19]
Table 1(	cont.):			

acids.

Table 1	cont.).			
Glycyrrhiz	Fabace	HCV,	Glycycoumarin,	[20,21]
a uralensis	ae	Rotavirus diarrhea	Liquiritigenin, glabridin	
			isoliquiritigenin,	
			licochalcone A,	
Panax	Araliac	RSV,	Epigallocatechin	[22,23]
ginseng	eae	influenza	gallate,	
		virus,	theaflavin	
		HIV,	digallate,	
		HSV, HBV,	genistein,	
		enterovir	diosmin	

Table 1: Some medicinal plants with antiviral activity against numerous viruses

Plant name	Family	Virus name	Isolated	Reference
			compounds	s
Zataria	Labiate	HSV-1	Rosmarinic	[3]
multiflora			acid	
Spondias	Anacardiaceae	Human	Flavonoids,	[4]
lutea		rotavirus,	phenolic	

\*Corresponding author e-mail: <a href="mailto:sharafali1589@gmail.com">sharafali1589@gmail.com</a>.; (Mahmed sharaf).

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		s,	hesperidin,	
		norovirus	neohesperidin	
		,	neonesperium	
		coxsackie		
		-virus.		
Citrus	Rutace	DENV,	Polyphenols	[24,25]
aurantium	ae	HIV-1,	••	
		HSV-1		
		and 2,		
		influenza,		
		yellowfe		
		ver.		
Diospyros	Ebenac	Influenza	Licocoumarone,	[26,27]
kaki	ee	virus	apigenin,	
		H3N2,	licoflavonol,	
		H5N3,	luteolin, vitexin,	
		HSV-1, VSV,	glucoside, tannins	
		SEV,	tannins	
		HFMD,		
		ADV,		
		RSV,		
		NDV.		
Citrus	Rutace	HAV,SA	Flavonoids	[28]
sinensis	ae	RS-CoV-		
		2		
Ficus	Morace	HSV-1,	Flavonoids	[29]
benjamina	ae	HSV-2		
Vitis	Vitacea	(SA-11),	Resveratrol,	[30]
labrusca	e	human	piceatannol,	
		(HCR3)	trans-arachidin-	
		rotavirus	1, trans-	
		es	arachidin-3	
Allium	Amaryl	SARS-	Quercetin	[31]
сера	lidacea	COV		
Allium	e Amorril	DENV.	Quercetin	[32]
Allium sativum	Amaryl lidacea	DENV, common	Quercetin	[32]
suuvum	e	cold		
	C	virus,		
		influenza		
		virus		
		A,B,		
		HIV,		
		HSV-1,		
		HSV-2		

Abbreviations: HSV herpes simplex virus, VSV vesicular stomatitis virus, HBV hepatitis B virus, HIV human immunodeficiency virus, ADV adenovirus, FMDV foot and mouth disease virus, HCV hepatitis C virus, DENV dengue virus, RSV respiratory syncytial virus, EBV Epstein–Barr virus, RV rhinovirus, SEV Sendai Virus, HFMD hand, foot, and mouth disease,

Phenolic compounds are a class of plant secondary metabolites which are characterized by an aromatic ring system bonded with one or more hydroxyl groups. The structures vary in terms of complexity, from simple molecules to polymers of high molecular weight [33]. According to Harbone and Simmonds, these compounds can be classified into different groups according to carbon numbers [34]. **Table 2** showed the different class of phenolic compounds.

Table 2: Groups of phenolic compounds						
Number	Basic	Class	Example			
of	Skeleton					
Carbon						
6	C6	Simple phenols,	Catechol,			
		benzoquinone	hydroquinone,			
			2,6-dimethoxy-			
			benzoquinone			
7	C <sub>6</sub> -C <sub>1</sub>	Phenolic	Gallic acid,			
		acids	salicylic acid			
8	C6-C2	Acetophenones, tyrosine	3-Acetyl-6-			
		derivatives,	methoxy-			
		phenylacetic acids	benzaldehyde,			
			tyrosol, p-			
			hydroxyphenyl-			
			acetic acid			
9	C <sub>6</sub> -C <sub>3</sub>	Hydroxycinnamic acids,	Caffeic acid,			
		phenylpropenes,	ferulic acid,			
		coumarins,	myristicin,			
		isocoumarins,	eugenol			
		chromones	umbelliferone,			
			aesculetin,			
			bergenon,			
			eugenin			
10	C <sub>6</sub> -C <sub>4</sub>	Naphthoquinones	Juglone,			
			plumbagin			
13	$C_{6}-C_{1}-C_{6}$	Xanthones	Mangiferin			
14	$C_6-C_2-C_6$	Stilbenes,	Resveratrol,			
		anthraquinones	emodin			
15	$C_{6}-C_{3}-C_{6}$	Flavonoids	Quercetin,			
			cyaniding,			
			genistein			
18	$(C_6 - C_3)_2$	Lignans, neolignans Pinoresinol,				
			eusiderin			
30	$(C_6 - C_3 - C_6)_2$	Biflavonoids	Amento-flavone			
N	$(C_6 - C_3)n$ ,	Lignins, condensed	Proantho-			
	(C <sub>6</sub> ) <sub>n</sub> ,	tannins	cyanidins,			
	(C6-C3-C6)n		phlobaphenes			

# 2. PLANT PHENOLICS WITH ANTI-VIRAL ACTIVITY

The antiviral activities of some isolated natural phenolics are tabulated in **Table 3**. The name of the natural phenolic compounds and the references are provided. Structures of some selected phenolic compounds are shown in **Fig. 1**.

Table 3: Ai	ntiviral act	ivity of	phenolic	compounds
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Com	pd	Compound	Virus	IC	50	E	C <sub>50</sub>	Ref.
No.			name	(μ	<b>M</b> )	(µ	ι <b>M</b> )	
1		Gallic acid	HSV	23	5.9			[35]
2		Methyl-	HSV	0.	20			[36]
		gallate						
3		Chloro-	HSV,			47	7.6	[37,38]
		genic acid	ADV,			13	3.3	
			HBV,	1.3	3			
			influenzza	84				
			virus	07	r			
4 Caffei		Caffeic acid	HSV,	3.	5			[39,40]
			ADV,			14	4.2	
			HBV,	0.2	70			
			influenzza	10	00			
		virus						
]	Table 3: Cont.							
5 Ferulic acid		HSV				>100	[41,42]	
			CDV		3.6			

6       Resveratrol       EBV, HCMV, YZV, HRV, SO, VACV, BRV, VACV, SS, MPXV       52.20 19,0 52.5       [43- 48] 19,0 52.5         7       Epicatechin       HSV, RABV, influenza virus       2.5 85.4       [49] 85.4         8       Curcumin       HSV, HRV       33.0 HIV       [50- 52]         9       Catachin       HSV, HRV       33.0 HIV       [51- 52]         10       Theaflavin       ADV, HBV       13.6 HIV, S3, RSV, 68.5       [53]         11       Epigallocatechin 3- gallate       BSV, EBV, ADV, S7.6 HEV, 4.56       5.7 ADV, S7.6 HEV, 4.56       [54]         11       Epigallocatechin 3- gallate       EBV, EBV, ADV, S7.6 HEV, 4.56       5.7 ADV, S7.6 HEV, 4.56       [55,56]         12       Luteolin       EBV, EEV 4.56       6.8 JEV 4.56       [57- 60]         13       Baicalein       HSV- ZIKV       8.5       [51- 60]         14       Hesperetin       CHIKV 2KV 342.9       6.18 2.00       [51- 60]         15       Naringenin       CHIKV 2KV 4.56       8.5       [61]         16       Apigenin       HSV-2 ADV-3 FIC       9.7 11.1 7.1       [63]         16       Apigenin       HSV-2 ADV-3 FIC       9.7 11.1 7.1       [65]         17       Geraniin       HSV-1 HEV						
VZV, HIV, HV, NXCV, X.CV, MEXV, S.S. MEXV, S.S. MEXV, S.S. MEXV, S.S. MEXV, S.S. MEXV, S.S. MEXV, S.S. MEXV, S.S. MEXV, S.S. MEXV, S.S. MEXV, MEXV	6	Resveratrol	EBV,		52.20	[43-
Introduct of the section of the sec				1.70		48]
Image: base of the section of the s						
VACV, MPXV3.5 MPXVI.2.31I.4Final energy restrict restrict virusEpicatechin RABV, influenza virus2.5 85.4[49] 85.48CurcuminHSV HIV HBV33.0 40.0 HIV HBV13.6 68.5[50] 52]9CatachinHSV, HIV, S.3 (68.5)4.0[53]10Theaflavin alleADV, HIV, S.3 (68.5)13.6 (62.2)[53]11Epigallocatechin 3- gallateHSV, EBV, ADV, S.76 (100) 2.538.6 (7.6)5.712LuteolinEBV, ADV, S.76 (100) 2.55.7[55]13Baicalein MCV PEV (13.5)155.76] (100) (2.5)[57.6]14Hesperetin ApigeninCHIKV CVB3 (2.5) (2.7)5.7[61]15Naringenin (2.10) (2.10)CHIKV (2.10) (2.10)5.7[61]16Apigenin acidCHIKV (2.10) (2.10)5.7[61,62]17Gerantin (2.10) (2.10)EV1 (1.11) <b< th=""><th></th><th></th><th></th><th></th><th>&gt;2.5</th><th></th></b<>					>2.5	
MPXV15.23MMFpicatechinHSV, RABV, influenza virus145.12.5 85.4[49] 85.48CurcuminHSV, HIV40.0[50- 52]9CatachinHSV, HIV, BSV, influenza virus13.6 (8.5) (8.5)[51]10TheaflavinADV, HIV, S.3 (8.5)13.6 (8.5) (16.2)[54]11Epigallocatechin 3- galateHSV, EBV, ADV, BSV, EBV, BSV, EBV, HIV, 9.9 S7.6 (10.0) 2.55.7[54]12LuteolinEBV EBV, HSV, 2.506.8 (5.7)[57- 60] (2.5)[57-13BaicaleinHSN2 EDEV, (2.58)4.66 (10.0) (2.5)[57- 60] (2.5)[57-14HesperetinCHIKV ZLKV HCV8.51.61 (11.1) (1.1) (1.1)[61.62] (2.6)15NaringeninCHIKV ZLKV HCV8.51.61 (1.1) (1.1) (1.1)[61.62] (2.6)16ApigeninSHV-2 ADV-3 (1.6)9.7 (1.1) (1.7)[63.64] (1.1) (1.1) (1.1)[61.62] (2.6)16ApigeninSHV-2 (1.6) (1.6)3.0[65] (3.6)[65] (3.6)17GeraniinEV71 (10 (1.6)10.3±1.5 (1.6)[65] (3.9±1.2)[66, (7]18Nordihydroguaiaretic (1.6)HIV (2.8) (2.6)3.0[65] (3.9±1.2)[66, (7]19SalidrosideRSV (1.6)3.3 (1.62)[66, (7] (1.6)			HRV,			
7         Epicatechin         HSV, RABV, influenza virus         2.5         [49]           8         Curcumin         HSV HIV         33.0 HIV         145.1         55.1           9         Catachin         HSV, HIV, BV         150.0         52]           9         Catachin         HSV, HIV, BV, influenza virus         1.0         5.3 (68.5)         [50- 52]           10         Theaflavin         ADV, HV, BV, avirus         1.3.6 HV, BV, ADV, 57.6 HBV, ADV, 57.6 HBV, ADV, 57.6         5.7         [54]           11         Epigallocatechin 3- gallate         EBV, ADV, BV, BV, BV, BNV, BNV, HV, SN, EEV         5.7         [54]           12         Luteolin         EBV, CVB3         4.9.6         [57- 60]         [57- 60]           13         Baicalein         HSN- 2.0         13.5         [56]         [57- 60]           14         Hesperetin         CHIKV         8.5         [61]         [61.62]           15         Naringenin         CHIKV         8.5.7         [63.64]         [61.62]           16         Apigenin         HSV-2 HCV         18.8 (ADV-3 HBV         10.1 (ADV-3 S.7)         [63.64]           11.1         T.1.1 (BSV         10.3 ±1.5 (ADV-3 (BSV)         [65]         [65]			VACV,			
Prime influenza virusRABV, influenza virusHSC 145.185.4F17 influenza influen			MPXV	15.23		
influenza virus145.1 virusImage: second seco	7	Epicatechin	HSV,		2.5	[49]
image: constraint of the section of			RABV,		85.4	
8         Curcumin         HSV HIV         33.0 40.0 HBV         [50.0] 52]           9         Catachin         HSV. HBV         4.0. (53)           10         Theaflavin         ADV. HIV. S.3. (62.0)         13.6 (68.5) (68.5) (61.0)         [53]           11         Epigallocatechin 3- gallate         HSV. HV. ADV. (70.0)         38.6 (70.0)         5.7 (70.0)         [54]           11         Epigallocatechin 3- gallate         HSV. HV. (70.0)         38.6 (70.0)         5.7 (70.0)         [54]           12         Luteolin         EBV. (70.0)         38.6 (70.0)         5.7 (70.0)         [57.0)           13         Baicalein         HSV. (70.0)         49.6 (70.0)         [57.0)         [57.0)           14         Hesperetin         CHIKV         8.5         [61.0]         [61.0]           15         Naringenin         CHIKV         8.5         [61.0]         [61.0]           15         Naringenin         HSV-2 (ADV-3)         9.7 (ADV-3)         [63.64]           160         Apigenin         HSV-2 (HVV)         33.1 (70.0)         [61.0]           16         Apigenin         HSV-2 (HVV)         33.1 (70.0)         [61.0]           18         acid         HSV-1 (HCV)         13.5 (7			influenza	145.1		
HIV HBV         40.0 150.0         Image selection         S21 selection           9         Catachin         HSV, MSV, sinfluenza virus         1.0         S3.6 S.7 (5.7)         [53]           10         Theaflavin         ADV, HIV, sinfluenza virus         3.8.6 S.7 (5.7)         5.7 (5.7)         [54]           11         Epigallocatechin 3- gallate         HSV, HBV, ADV, NDV, S7.6 HBV, 2.5         38.6 S.7 (10.0)         5.7 (10.0)         [54]           12         Luteolin         EBV ADV, NDV, NDV, S7.6 HBV, 2.5         6.8 (10.0)         5.7 (10.0)         [55.66]           13         Baicalein         HSN2 (S.7)         49.6 (13.1)         [57- 60]         [57- 60]           14         Hesperetin         CHIKV (CVB) JEV         8.5         I.1 (11.1)         [61.62]           15         Naringenin         CHIKV (CVB) JEV         8.7 (20.0)         [61.62]           16         Apigenin         CHIKV (CVB) JEV         8.7 (20.0)         [61.62]           16         Apigenin         CHIKV (CVB) ADV-3 (BV)         8.7 (21.1)         [61.62]           17         Geraniin         CHIKV (CVB) ADV-3 (BV)         6.18 (S.7)         [61.62]           18         Nordihydroguaiaretic acid         HV         1.1 (S.7)         [65] <th></th> <th></th> <th>virus</th> <th></th> <th></th> <th></th>			virus			
HIV HBV         40.0 150.0         521 (53)           9         Catachin         HSV, NSV, influenza virus         1.6         (53)           10         Theaflavin         AV (SV, influenza virus         1.6         (53)           11         Epigallocatechin 3- gallate         HSV, HSV, influenza virus         38.6         5.7         [54]           11         Epigallocatechin 3- gallate         HSV, HBV, ADV, S7.6         38.6         5.7         [55]           12         Luteolin         EBV (CV) ADV, VCV         57.6         1.6         [55,56]           12         Luteolin         EBV (CV) ADV, VCV         6.8         [57- 60]         [57- 60]           13         Baicalein         HSN2 (CV) ADV, YCV         49.6         [57- 60]         [61,62]           15         Naringenin         CHIKV (CV) ADV, YCV         58.79         [61,62]           16         Apigenin         HSV-2 (HCV)         58.79         [63,64]           15         Naringenin         CHIKV (CV)         58.79         [65]           16         Apigenin         HSV-2 (ADV, S0)         3.0         [65]           17         Geraniin         HV (HCV)         20.0         3.0           18         N	8	Curcumin	HSV	33.0		[50-
Image: Marrier of the state of the	-					-
9         Catachin         HSV, ADV, RSV, influenza virus         13.6 (5.3) (68.5) (16.2)         [53]           10         Theaflavin         ADV, RSV, influenza virus         13.6 (68.5) (16.2)         [53]           11         Epigallocatechin 3- gallate         HSV, RSV, Balte         38.6 (68.5) (16.2)         5.7 (7.6) (10.0)         [54]           12         Luteolin         EBV HCV         39.4 (10.0)         5.7 (7.6) (10.0)         [57- (7.5)           13         Baicalein         H3N2 HSV, PEnterovirus         49.6 (7.15)         [57- (7.5)           14         Hesperetin         CHIKV ADV-3 HCV         8.5         [61]           15         Naringenin         CHIKV ADV-3 HCV         6.18 (7.7) (7.7)         [61,62]           16         Apigenin         HSV-2 ADV-3 HCV         9.7 (7.1)         [63,64] (7.1)           16         Apigenin         HSV-2 (7.7)         9.7 (7.1)         [63,64] (7.1)           17         Geraniin         EV71 HSV HCV         10 (8.3)         [65]           18         Nordihydroguaiaretic acid         HIV HCV         20 (7.7)         30         [65]           19         Salidroside         RSV-1 (7.7)         13.0 (7.1)         [66, (7.1)         [66, (7.1)           10         <				150.0		· ·
10         Theaflavin         ADV, RSV, influenza virus         13.6 (5.3) (6.2         [53]           11         Epigallocatechin 3- gallate         HSV, EBV, ADV, HSV, Ballate         38.6 (5.7)         5.7         [54]           11         Epigallocatechin 3- gallate         HSV, HSV, BV, BV, HSV, S7.6 HBV, 39.4 HIV, RSV, Entervirus HCV         38.6 (5.7)         5.7         [54]           12         Luteolin         EBV ADV, RSV, Entervirus HCV         57.6 (10.0)         57.6 (10.0)         [57- (10.0)           13         Baicalein         H3N2 JEV ADV, RSV, ENCVB3 JEV A2.9         49.6 (13.5)         [57- (60]           14         Hesperetin         CHIKV ZIKV HCV         8.5         [61]           15         Naringenin         CHIKV ZIKV HCV         8.5         [61,62]           16         Apigenin         HSV-2 ADV-3 HBV HCV         9.7 (15.7)         [63,64] 11.1 (7.1)           16         Apigenin         HSV-2 HV HCV         9.7 (15.7)         [63,64] 15.7 (15.7)           18         Nordihydroguaiaretic acid         HIV HCV         10 (15.7)         [65]           19         Salidroside         RSV (CVB3         33 (15.7)         [65]           20         Genistein         BV HSV-1         33 (1.69)         [66, (71] (0.07) <t< th=""><th>9</th><th>Catachin</th><th></th><th></th><th>4.0</th><th>[53]</th></t<>	9	Catachin			4.0	[53]
HIV, RSV, influenza virus         5.3 (6.5) (1.2         Image: Constraint of the constraint of t			· · · · · · · · · · · · · · · · · · ·	13.6	4.0	
RSV, influenza virus         68.5 influenza virus         I         S           11         Epigallocatechin 3- gallate         HSV, EBV, ADV, HBV, BV, BV, BV, BV, BV, BV, BV, BV, BV,	10	Theattavin				[33]
influenza virus         io i6.2         influenza i6.2         i6.2           11         Epigallocatechin 3- gallate         HSV, EBV, ADV, SV, Enterovirus         38.6         5.7         [54]           11         Epigallocatechin 3- gallate         HSV, EBV, ADV, SV, Enterovirus         38.6         5.7         [54]           12         Luteolin         EBV HEV HEV ADV, VCVB3 JEV         57.6         [57- 60]         [55,56]           13         Baicalein         H3N2 DENV CVB3 JEV         49.6 13.5 VCVB3 42.9 JEV         [57- 60]           14         Hesperetin         CHIKV HEV         8.5         [61-2]           15         Naringenin         CHIKV CVB3 JEV         58.79         [63,64]           11.1         Apigenin         HSV-2 HEV         58.79         [63,64]           10         Apigenin         HSV-3 HBV HCV         10.4 15.7         [63]           18         Nordihydroguaiaretic acid         HIV HCV         20         [65]           19         Salidroside         RSV HSV-1         10.3±1.5 20         [66]           19         Salidroside         RSV HSV-1         33 14.02 ± 0.97         [60,62, 68, 69, 71]           20         Genistein         BV HSV-1         10.50         1.69						
virus         10.2 <t< th=""><th></th><th></th><th></th><th></th><th></th><th></th></t<>						
11         Epigallocatechin 3- gallate         HSV, EBV, ADV, HBV, HRV, BSV, Enterovirus HCV         38.6 5.7         [54]           12         Luteolin         EBV Enterovirus HCV         57.6 10.0 2.5         5.7         [55,56]           13         Baicalein         H3N2 PUV HIV, N2V         6-8 4.56 7.15         [57- 60]         [57- 60]           14         Hesperetin         CHIKV         8.5         [61]           15         Naringenin         CHIKV HCV         8.5         [61]           16         Apigenin         HSV-4 MCV         6.18 8.79         [63,64]           17         Geraniin         HSV-2 MCV         9.7 11.1 7.1         [63,64]           18         Nordihydroguaiaretic acid         HIV HCV         22±3         [65]           18         Nordihydroguaiaretic Acid         HIV HCV         20         [65]           19         Salidroside         RSV CVB3         33+1.2         [66]           19         Quercetin         HIN1 HSV-1         7.75±1 28.9 2.30 ± 1.69         [66, 67]           21         Quercetin         H1N1 DENV 2.30 ± NGV         7.5±1 2.30 ± 1.69         [66]           22         Myricetin         ZIKV         5.8 ± 0.17         [62]				10.2		
ADV, HBV, HV, RSV, Enterovirus HCV         57.6 39.4 9.9 57.6 10.0 2.5         III HV FRV FRV 57.6 10.0 2.5           12         Luteolin         EBV JEV HRV FR         6-8 4.56 7.15         JEV FR         6.8 57.6           13         Baicalein         H3N2 FRV FR         49.6 7.15         JEV FR         60]           14         Hesperetin         CHIKV CVB3 JEV         8.5         I         [61]           15         Naringenin         CHIKV CVB3 JEV         8.5         JE         [63.64]           16         Apigenin         HSV-2 ADV-3 HCV         9.7 FR         [63.64]         [65]           16         Apigenin         HSV-2 ADV-3 FR         10 HSV         18.4±2 HV FR         9.7 FR         [65]           18         Nordihydroguaiaretic acid         HIV HCV         20 Salidroside         [65]         [65]           18         Nordihydroguaiaretic acid         HIV HCV         33 FR         10 FR         [65]           19         Salidroside         RSV FR         33 FR         1.69         [66, FR           200         Genistein         BV HCV         33 FR         1.69         [66, FR           200         Genistein         HIV FR         7.5±1 FR         1.69         [66, FR	11		HSV,	38.6		[54]
HBV, HIV, RSV, Enterovirus HCV       39.4 (9.9) 57.6 (10.0) 2.5       (5)         12       Luteolin       EBV JEV H3N2       6-8 (		gallate			5.7	
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13       Baicalein       H3N2 DENV CVB3       49.6 13.5 42.9 7.27       [57- 60]         14       Hesperetin       CHIKV       8.5       [61]         15       Naringenin       CHIKV ZIKV HCV       6.18 58.79       [61,62]         16       Apigenin       HSV-2 ADV-3 HBV HCW       9.7 200       [63,64]         17       Geraniin       EV71 HCV       10 18.891       [65]         18       Nordihydroguaiaretic acid       HIV HCV       20 30       [65]         19       Salidroside       RSV CVB3       10.3±1.5 39±1.2       [65]         20       Genistein       BV HSV-1       33 14.02 ± 0.97       [66, 67]         21       Quercetin       H1N1 DENV ZIKV       7.75±1 0.50       [60,62, 68, 69, 2.30 ± 0.50       [62]         22       Myricetin       ZIKV       J.58 ± 0.17       [62]			H3N2			
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JEV         7.27 7.27            14         Hesperetin         CHIKV         8.5         [61]           15         Naringenin         CHIKV ZIKV         6.18 58.79         [61,62]           16         Apigenin         HSV-2 ADV-3 HBV         9.7 200         [63,64]           16         Apigenin         HSV-2 ADV-3 HBV         9.7 200         [63,64]           17         Geraniin         EV71 HV EBV         10 15.7 8.91         [65]           18         Nordihydroguaiaretic acid         HIV HCV         20 30         [65]           19         Salidroside         RSV CVB3         10.3±1.5 39±1.2         [65]           20         Genistein         BV HSV-1         33 14.02 ± 0.97         [66, 67]           21         Quercetin         HIN1 DENV ZIKV         7.75±1 28.9 2.30 ± 0.30 ± 1.69         [60,62, 68, 69, 71]           22         Myricetin         ZIKV         J.58 ± 0.17         [62]						00]
14       Hesperetin       CHIKV       8.5       [61]         15       Naringenin       CHIKV ZIKV HCV       6.18 58.79       [61,62]         16       Apigenin       HSV-2 ADV-3 HBV HCW       9.7 200       [63,64]         16       Apigenin       HSV-2 ADV-3 HBV HCW       9.7 22±3       [63,64]         17       Geraniin       EV71 HSV HCV       10 18,4±2 6.3 EBV HCV       [65]         18       Nordihydroguaiaretic acid       HIV HCV       20 30       [65]         19       Salidroside       RSV CVB3       10.3±1.5 39±1.2       [65]         20       Genistein       BV HSV-1       33 14.02 ± 0.97       [66, 67]         21       Quercetin       H1N1 DENV ZIKV       7.75±1 0.50       [60,62, 68, 69, 7.1]       68, 69, 7.1]         22       Myricetin       ZIKV       J.58 ± 0.17       1.69       [62]						
Image: Naringenin         CHIKV ZIKV HCV         6.18 58.79 HCV         [61,62]           16         Apigenin         HSV-2 HCV         9.7 11.1 7.1         [63,64]           16         Apigenin         HSV-2 ADV-3 HBV HCMV         9.7 21         [63,64]           17         Geraniin         EV71 HV ESV HCV         10 18. 20         [65]           18         Nordihydroguaiaretic acid         HIV HCV         20 30         [65]           19         Salidroside         RSV CVB3         10.3±1.5 39±1.2         [65]           20         Genistein         BV HSV-1         33 14.02 ± 0.97         [66, 67]           21         Quercetin         H1N1 DENV ZIKV         7.75±1 28.9 2.30 ± 0.97         [60,62, 68, 69, 71]           22         Myricetin         ZIKV         J.58 ± 0.17         [62]	14	** .*	CURRENT			5613
ZIKV HCV       58.79       200         16       Apigenin       HSV-2 ADV-3 HBV HCMV       9.7 2±3       [63,64]         17       Geraniin       EV71 HSV HCV       10 18.4±2 6.3 15.7 HCV       [65]         18       Nordihydroguaiaretic acid       HIV HCV       20 30       [65]         19       Salidroside       RSV CVB3       10.3±1.5 39±1.2       [65]         20       Genistein       BV HCV       33 14.02 ± 0.97       [66, 67]         21       Quercetin       H1N1 DENV 28.9 2.30 ±       7.75±1 0.97       [60,62, 68, 69, 2.30 ±         22       Myricetin       ZIKV       .58 ± 0.17       1.69	14	Hesperetin	CHIKV	8.5		[61]
ZIKV HCV       58.79       200         16       Apigenin       HSV-2 ADV-3 HBV HCMV       9.7 2±3       [63,64]         17       Geraniin       EV71 HSV HCV       10 18.4±2 6.3 15.7 HCV       [65]         18       Nordihydroguaiaretic acid       HIV HCV       20 30       [65]         19       Salidroside       RSV CVB3       10.3±1.5 39±1.2       [65]         20       Genistein       BV HCV       33 14.02 ± 0.97       [66, 67]         21       Quercetin       H1N1 DENV 28.9 2.30 ±       7.75±1 0.97       [60,62, 68, 69, 2.30 ±         22       Myricetin       ZIKV       .58 ± 0.17       1.69	17		CURRENT	6.10		1(1(0)
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16         Apigenin         HSV-2 ADV-3 HBV HCMV         9.7 11.1 22±3         [63,64]           17         Geraniin         EV71 HSV HCV         10 8.91         [65]           18         Nordihydroguaiaretic acid         HIV HCV         20 8.91         [65]           19         Salidroside         RSV HCV         10.3±1.5 39±1.2         [65]           20         Genistein         BV HCV         33 9±1.2         [65]           19         Salidroside         RSV CVB3         10.3±1.5 39±1.2         [66, 67]           20         Genistein         BV HSV-1         33 14.02 ± 0.97         [66, 67]           21         Quercetin         H1N1 DENV ZIKV         7.75±1 2.30 ± 0.97         [60,62, 68, 69, 2.30 ± 0.169           22         Myricetin         ZIKV         J.58 ± 0.17         [62]				58.79		
ADV-3 HBV HCMV       ADV-3 HBV 22±3       11.1 7.1       11.1 7.1         17       Geraniin       EV71 HSV HCV       10 18.4±2 6.3 EBV HCV       10.4±2 8.91       [65]         18       Nordihydroguaiaretic acid       HIV HCV       20 30       [65]         19       Salidroside       RSV HCV       10.3±1.5 39±1.2       [65]         20       Genistein       BV HSV-1       33 14.02 ± 0.97       [66, 67]         21       Quercetin       H1N1 DENV 28.9 ZIKV       7.75±1 28.9 2.30 ± HSV-1       [60,62, 68, 69, 71]         22       Myricetin       ZIKV       .58 ± 0.17       [62]						
HBV HCMV         10 12±3         7.1           I7         Geraniin         EV71 HSV HCV         10 18.4±2 6.3 15.7 8.91         [65]           I8         Nordihydroguaiaretic acid         HIV HCV         20 30         [65]           I9         Salidroside         RSV CVB3         10.3±1.5 39±1.2         [65]           20         Genistein         BV HSV-1         33 14.02 ± 0.97         [66, 67]           21         Quercetin         H1N1 HSV-1         7.75±1 28.9 ZIKV         [60,62, 28.9 2.30 ± 1.69         [60,62, 68, 69, 71]           22         Myricetin         ZIKV         .58 ± 0.17         1.62	16	Apigenin				[63,64]
HCMV $22\pm3$ $7.1$ IT         Geraniin         EV71 HSV HIV EBV HIV eBV HCV         10 18.4±2 6.3 15.7 8.91         [65]           IB         Nordihydroguaiaretic acid         HIV HCV         20 30         [65]           IB         Salidroside         RSV CVB3 $10.3\pm1.5$ 39±1.2         [65]           20         Genistein         BV HSV-1 $33$ 14.02 ± 0.97         [66, 67]           21         Quercetin         H1N1 DENV 28.9 ZIKV $7.5\pm1$ 28.9 2.30 ± 0.97         [60,62, 68, 69, 71]           22         Myricetin         ZIKV $.58 \pm$ 0.17         [62]						
17         Geraniin         EV71 HSV HIV BSV HIV C         10 18.4±2 6.3 15.7 8.91         [65]           18         Nordihydroguaiaretic acid         HIV HCV         20 30         [65]           19         Salidroside         RSV CVB3         10.3±1.5 39±1.2         [65]           20         Genistein         BV HSV-1         33 14.02 ± 0.97         [66, 67]           21         Quercetin         H1N1 HSV-1         7.75±1 0.97         [60,62, 68, 69, 2.30 ± 1.69           22         Myricetin         ZIKV         .58 ± 0.17         [62]					7.1	
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$				22±3		
$\begin{array}{ c c c c c c c c } & HiV & B.5 \\ & HiV & B.8 \\ & BV & 15.7 \\ & B.91 \\ \hline \begin{tabular}{ c c c c c } & HiV \\ & HCV & & & & & & & & & & & & \\ \hline \begin{tabular}{ c c c c c c c } & HiV & B.8 \\ & acid & & & & & & & & & & & & & \\ \hline \begin{tabular}{ c c c c c c c } & HiV & HiV & & & & & & & & & & & \\ \hline \begin{tabular}{ c c c c c c c c c c c c c c c c c c c$	17	Geraniin				[65]
EBV HCV     15.7 15.7 8.91     [65] 30       18     Nordihydroguaiaretic acid     HIV HCV     20 30     [65] 39±1.2       19     Salidroside     RSV CVB3     10.3±1.5 39±1.2     [65] 67]       20     Genistein     BV HSV-1     33 14.02 ± 0.97     [66, 67]       21     Quercetin     H1N1 DENV 28.9 ZIKV     7.75±1 28.9 2.30 ± 0.97     [60,62, 68, 69, 2.30 ± 1.69       22     Myricetin     ZIKV     .58 ± 0.17     [62]						
HCV         15.7 8,91         Image: Second system         Image: Second system <th< th=""><th></th><th></th><th></th><th></th><th></th><th></th></th<>						
18         Nordihydroguaiaretic acid         HIV HCV         20         30         [65]           19         Salidroside         RSV CVB3         10.3±1.5 39±1.2         [65]           20         Genistein         BV HSV-1         33         [66, 67]           21         Quercetin         H1N1 DENV 28.9         7.75±1 28.9         [60,62, 68, 69, 2.30 ±           22         Myricetin         ZIKV         .58± 0.17         [62]				15.7		
acid         HCV         30         HCV           19         Salidroside         RSV CVB3 $10.3\pm 1.5$ $39\pm 1.2$ [65]           20         Genistein         BV HSV-1 $33$ $14.02 \pm$ 0.97         [66, 67]           21         Quercetin         H1N1 $ZIKV$ $7.5\pm 1$ $2.30 \pm$ 1.69         [60,62, 68, 69, 2.30 \pm $1.69$ 22         Myricetin         ZIKV $1.58 \pm$ 0.17         [62]				8.91		
19         Salidroside         RSV CVB3         10.3±1.5 39±1.2         [65]           20         Genistein         BV HSV-1         33 14.02 ± 0.97         [66, 67]           21         Quercetin         H1N1 LEV         7.75±1 28.9 2.30 ± 0.50         [60,62, 68, 69, 2.30 ± 1.69           22         Myricetin         ZIKV         1.58 ± 0.17         [62]	18	Nordihydroguaiaretic	HIV	20		[65]
CVB3         39±1.2         Image: CVB3           20         Genistein         BV         33         [66, 67]           HSV-1         14.02 ±         67]           0.97         0.97         [60,62, 0.97           21         Quercetin         H1N1         7.75±1         [60,62, 28.9           ZIKV         2.30 ±         71]           HSV-1         1.69         [62]           22         Myricetin         ZIKV         .58 ±         [62]		acid	HCV		30	
CVB3         39±1.2         Image: CVB3           20         Genistein         BV         33         [66, 67]           HSV-1         14.02 ±         67]           0.97         0.97         [60,62, 0.97           21         Quercetin         H1N1         7.75±1         [60,62, 28.9           ZIKV         2.30 ±         71]           HSV-1         1.69         [62]           22         Myricetin         ZIKV         .58 ±         [62]	19	Salidroside	RSV	10.3±1.5		[65]
$\begin{array}{ c c c c c c c c c c c c c c c c c c c$			CVB3			
HSV-1         14.02 ± 0.97         67]           21         Quercetin         H1N1 DENV 28.9 ZIKV         7.75±1 28.9 2.30 ± 0.50         [60,62, 68, 69, 71]           22         Myricetin         ZIKV         1.69	20	Genistein	BV	33		[66,
0.97         0.97           21         Quercetin         H1N1 DENV ZIKV         7.75±1 28.9 2.30 ± 0.50         [60,62, 68, 69, 71]           21         Myricetin         ZIKV         28.9 2.30 ± 0.50         71]           169         1.69         1.69			HSV-1	14.02 ±		
21         Quercetin         H1N1 DENV ZIKV         7.75±1 28.9 2.30 ± 0.50         [60,62, 68, 69, 71]           22         Myricetin         ZIKV $0.58 \pm 0.17$ [62]						
DENV ZIKV         28.9 2.30 ± 0.50         68, 69, 71]           HSV-1         1.69           22         Myricetin         ZIKV         0.58 ± 0.17         [62]	21	Ouercetin	H1N1			[60,62.
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		~				
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$						
HSV-1         1.69           22         Myricetin         ZIKV         1.58 ±         [62]           0.17         0.17         1.69         1.69						
22         Myricetin         ZIKV         1.58 ± 0.17         [62]			HSV-1	0.50	1.60	
0.17	22	Myricetin	ZIKV	) 58 +	1.09	[62]
	44	wiyileeun				[02]
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Abbreviations: ND virulent Newcastle disease, VSV Vesicular Stomatitis Virus, IAV Influenza A virus, HAV Hepatitis A virus, CDV Canine Distemper Virus, HCMV Human Cytomegalovirus, VZV Varicella-Zoster Virus, HRV Human Rhinoviruses, VACV Vaccinia Virus, MPXV monkeypox virus, RABV Rabies virus, JEV Japanese encephalitis virus, CVB Coxsackievirus B, CHIKV chikungunya virus, ZIKV Zika virus, EV Enterovirus.. HN type of influenza viruses the half maximal inhibitory concentration (IC50) is a measure of the potency of a substance in inhibiting a specific

concentration (EC50) is a toxic unit, which measures the concentration of a drug, antibody or toxicant which induces a response halfway between the baseline and maximum after a specified exposure time.

Table 4: Phenolics with anti-COVID-19 activity

No	Compund	IC 50	Ref
8	Curcumin,	20	[70]
14	Herbacetin,	33.17	[71]
21	Quercetin	23.8	[73]
22	Myricetin	43	[72]
23	Rhoifolin,	27.45	[71]
24	Pectolinarin	37.78	[71]
25	Tannic acid	13.4	[74]
26	Puerarin	42	[72]
27	Diadzein	56	[72]
28	Xanthoangelol E	11.4	[75]
29	Amentoflavone,	8.3	[76]
30	Kaempferol	16.3	[77]
31	Papyriflavonol A	3.7	[77]

biological or biochemical function. Half maximal effective

Viral infection is one of the main hazards for public health, and caused considerable damage to human population. A number of medicinal plants rich in phenolics have been used against viral infection. Recently, the role of phenolics in the prevention and treatment of many diseases has been investigated [78]. So far, antiviral activity of these compounds has been reported using both in vitro and in vivo model of the investigations.

Viruses are infectious microbes made up of nucleic-acid genome (RNA or DNA) surrounded by a protective protein envelope. They can't propagate alone. The obligate intracellular parasites aim to deliver their genetic material to the host cell to permit the transcription by the host cell and continue to survive. Phenolic compounds have promising antiviral properties through various mechanisms. They could act as a treatment or prevention strategy during virus life cycle stages [79-81].

Phenolics can attach themselves to the viruses' surface proteins prohibiting their penetration into the host cells. They act as a transcription blocker to hamper viral DNA replication. They hinder protein translation and poly-protein processing. They can also inhibit virion release to invade other healthy host cells. Indirectly, they reduce the ubiquitin molecule level that the virus uses for its replication in the host cell. Moreover, phenolics can also modify the immune system and decrease the viral load [82].

Gallic acid (1), one of the most widely distributed phenolics of tea, exhibited great anti-HIV potency (IC<sub>50</sub>=23.9  $\mu$ M), while its methylgallate derivatives (2) was more active (1C<sub>50</sub>=0.2  $\mu$ M) [35,36].

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Chlorogenic (**3**) and caffeic acids (**4**) isolated from coffee showed inhibition to HSV ( $EC_{50}$ =47.6; 15.3  $\mu$ M), adenovirus ( $EC_{50}$ =13.3; 14.20  $\mu$ M), HBV ( $IC_{50}$ =1.30;0.70  $\mu$ M) and influenza virus ( $IC_{50}$ =84.0; 24.3  $\mu$ M) [37-40]. Also, from coffee, Ferulic acid (4-hydroxy-3-methoxy cinnamic acid (**5**) exhibited antiviral activity against HSV ( $EC_{50}$ > 100mM) and canine distemper virus (CDV,  $IC_{50}$ =3.6  $\mu$ M) [41,42]. Resveratrol (3, 5, 4-trihydroxystilbene, (**6**), showed activities against EBV, HCMV, VZV and HIV viruses ( $EC_{50}$ =52.20  $\mu$ M,  $IC_{50}$ =1.7  $\mu$ M,  $EC_{50}$ = 19.0 Mm,  $EC50>2.5 \ \mu$ M). Also, it showed antiviral activity against vaccinia virus (VACV), monkeypox virus (MPXV) with  $IC_{50}$ = 3.5 and 15.23 $\mu$ M [43-48].

Epicatechin (7), isolated from green tea, demonstrated relatively more potent activity against HSV (EC<sub>50</sub> = 2.5  $\mu$ M), rabies virus (EC<sub>50</sub> = 85.4  $\mu$ M) and influenza virus (IC<sub>50</sub> > 145.1  $\mu$ M, EC50 > 600.0  $\mu$ M) [50]. Curcumin (8), isolated from turmeric, showed great and diverse antiviral potencies against HSV (IC50= 33.0  $\mu$ M), HBV (IC<sub>50</sub>=150), HIV (IC<sub>50</sub>= 40.0  $\mu$ M) [49-52].

Catechin (9) was isolated from green tea and displayed antiviral potency against herpes simplex virus [HSV, 50% maximal effective concentration  $(EC_{50}) = 4.0 \ \mu M$ ], HIV  $(IC_{50} = 5.3 \ \mu M)$ , rabies virus  $(EC_{50} = 36.5 \ \mu M)$  and influenza virus  $(IC_{50} > 144.6 \ M)$  $\mu$ M), while Theaflavin (10) showed potent inhibitory activity against adenovirus (ADV), HIV, respiratory syncytial virus (RSV) and influenza virus with a mean 50% inhibitory concentration (IC<sub>50</sub>) of 13.6, 5.3, 68.5 and 16.2 µM, respectively [53]. Also, from green tea, epigallocatechin 3-gallate (11) showed different modes of action in combating important human pathogens like HSV (IC<sub>50</sub> = 38.6  $\mu$ M, EC<sub>50</sub> = 2.5 µM), Epstein-Barr virus (EBV, EC50 = 5.7 µM), adenovirus (IC<sub>50</sub> > 57.6  $\mu$ M), hepatitis B virus (HBV,  $IC_{50} = 39.4 \ \mu M$ ), HIV ( $IC_{50} = 9.9 \ \mu M$ ), RSV ( $IC_{50} =$ 57.6  $\mu$ M), influenza virus (IC<sub>50</sub> = 56.5  $\mu$ M, EC<sub>50</sub> = 28.4  $\mu$ M), enterovirus (IC<sub>50</sub> = 10.0  $\mu$ M) and hepatitis C virus (HCV, IC<sub>50</sub> = 2.5 µM, EC<sub>50</sub> = 17.9 µM) [54]. Luteolin (12) exhibits inhibitory effects on Epstein-Barr Virus, Japanese encephalitis virus and influenza A virus (H3N2) [55,56].

In vitro antiviral experiments, baicalein (13) inhibited Influenza A virus subtype H3N2 virus with  $IC_{50} = 13.5$ . It also exhibited significant effects against DENV (Dengue virus), coxsackievirus B3 (CVB3) and JEV (Japanese encephalitis virus) with

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IC<sub>50</sub>= 13.5, 42.90, 7.27. [57-60]. Hesperetin {14) with  $IC_{50} = 8.500 \ \mu M$  and naringenin (15) with  $IC_{50} =$ 6.818 µM inhibited the post entry stages of CHIKV (Chikungunya virus) replication activity. Also, naringenin showed antiviral activity against ZIKV (Zika virus) and HCV (Hepatitis C virus) with IC<sub>50</sub>=58.7 and EC<sub>50</sub>=200 [61,62]. As a flavone type, apigenin (16) showed high activity against HSV-2 (Herpes simplex virus) (EC<sub>50</sub> = 9.7 mg/L), ADV-3 (adenoviruses type 3) (EC50 = 11.1 mg/L), hepatitis B surface antigen (EC50 = 7.1 mg/L). Its activity against HCMV (Human Cytomegalovirus) was reported (IC<sub>50</sub> =  $22\pm3$ ) [63, 64]. Geraniin (17) have also been reported against enterovirus 71 (EV71) (IC<sub>50</sub>=10 µg/mL), herpes simplex virus type 2 (HSV-2) (IC<sub>50</sub>=18.4  $\pm 2.0 \mu$ M), human immunodeficiency virus (HIV) (IC<sub>50</sub>= 6.28 µg/mL, Epstein-Barr virus (EBV) (IC<sub>50</sub>=15.7  $\mu$ M,), and hepatitis C virus (HCV)  $(IC_{50} = 8.91 \ \mu M)$  [65]. Nordihydroguaiaretic acid (18) can inhibit HIV (IC<sub>50</sub> = 20  $\mu$ M), and lipid metabolic pathways necessary for HCV replication in Huh7.5.1 cells (EC<sub>50</sub>=  $30 \mu$ M) [65].

The antiviral effect of salidroside (19) has also been reported against RSV (IC<sub>50</sub>= 10.3) and CVB3 in vitro in myocytes and in vivo in BALB/c mice (IC<sub>50</sub>=39.0 1.2 mg/L; 20 and 40 mg/kg at days 7 and 14) [65]. Genistein (20) prevented plaque formation of B virus and reduced virus production with an  $IC_{50} = 33$  and HSV-1 by 10.04±0.97 [66, 67]. Quercetin showed potent anti-ZIKV activity by targeting the replication process of the virus. Quercetin (21) showed strong inhibitory effect on different viral strains of Influenza-A Virus. The IC<sub>50</sub> values of quercetin against (H1N1) was.756  $\pm$  1. [60] with the virus at a concentration of  $IC_{50} = 28.9 \ \mu g/ml$ . Quercetin exhibited inhibitory effect against DENV-2. [62]. Quercetin showed potent anti-ZIKV activity by targeting the replication process of the virus. Quercetin nearly obtained complete inhibition on the process of zika virus viral RNA production. The IC<sub>50</sub> quercetin was 2.30  $\pm$  0.50  $\mu$ M. for quercetin [69] Quercetin tested against the HSV-1 and showed strong inhibitory effects and reduced the CPE (cytopathic effect) in the virus infected cells. quercetin at  $EC_{50} = 1.69 \ \mu g/ml$  [71], Myricetin (22) was analyzed for its anti-ZIKV activity, it showed potent anti-ZIKV activity by targeting the replication process of the virus. The  $IC_{50}$  value for myricetin was 0.58 ± 0.17 µM, [62].

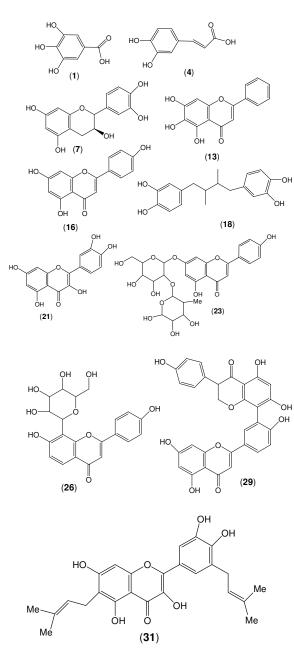


Figure 1: Structure of some phenolic compounds with antiviral activity

Concerning COVID-19, the highly contagious novel disease caused by SARS-CoV-2, has become a major international concern as it has spread quickly all over the globe. Numerous phenolics were found to have antiviral effects against SARS.

Curcumin, (8) being already explored *in vitro* as a potent inhibitor of SARS-CoV Mpro with an  $IC_{50}$  value of 20 M[70]. The flavonoids Herbacetin,

rhoifolin, and pectolinarin (14, 23, 24) were found to be effective inhibitors of Mpro of SARS-CoV. Using FRET-based assay, IC<sub>50</sub> values were determined and were 33.17, 27.45, and 37.78 M, respectively [71]. Isoflavones puerarin and daidzein (26, 27) and flavonol myricetin (22) were found to be potent inhibitors with IC<sub>50</sub> values of 42, 56, and 43 M, respectively [72]. Quercetin (21) was the most promising flavonoids with anti-CoV potential with  $IC_{50} = 23.8$  [73]. Tannic acid (25) was revealed to be another potential natural drug against SARS-CoV-2. The concentration of tannic acid required to inhibit 50% of the proteases activity, IC<sub>50</sub>, was 13.4 M [74]. An chalcone, isolated from Angelica keiskei, named xanthoangelol E (28), was shown to be an effective inhibitor of SARS-CoV with IC50 values of 11.4 M [75]. Amentoflavone, (29) a biflavone isolated from Torreya nucifera, demonstrated a prominent inhibitor of SARS-CoV with  $IC_{50} = 8.3 IM$  [76]. Kaempferol (30) exhibited anti-SARS activity with  $IC_{50}=16.3$ , while the papyriflavonol A (31), a double prenylated flavone derivative, presents one of the most significant inhibitors of SARS with IC<sub>50</sub> value of 3.7 [77].

## **3. CONCLUSION**

Literature search has led to the identification of numerous phenolics exerting antiviral activity. Medicinal plants are a rich source of phenolic compounds with potential antiviral activity. They are found both in underground and above-ground plant organs. The bioactive phenlic compounds in plants and their extracts have antiviral activity and can be used preventively or to fight infections.

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#### 5. Conflicts of Interest:

The author declares no conflict of interest.

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