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Phytochemicals and antiviral properties of five dominant medicinal plant species in Bankura district, West Bengal: An overview

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Abstract
In current years, the pandemic of viral diseases have been spreading worldwide, which causes death in humans globally. It leads to the scientific community to investigate on the antiviral phytochemicals against viral diseases. Medicinal herbs possess a variety of phytochemicals that harbour antiviral properties, which are advantages over conventional drug therapy due to their broad therapeutic potency and minimum or no adverse effects. Medicinal plants synthesize and possess a variety of biochemical products useful for therapeutic use, helps in inhibition of viruses. Based on this basis, literature search, discussion with local authority and online search were performed, which helped to identify five most dominant plant species in Bankura District, West Bengal, having bioactive compound and antiviral properties. This mini-review provides information of those five dominant Ayurvedic medicinal plants for their broad spectrum medicinal values in general and effect on viral infections in particular.

Keywords: Medicinal plants, phytochemicals, antiviral activity

Introduction
India have great wealth and rich knowledge of medicinal plants. Plants have various primary and secondary metabolites including carbohydrates, lipids, proteins, phenolics, flavonoids, tannins, alkaloids, essential oils etc. Marine based polysaccharides and other low molecular weight oligosaccharide have been found to be effective against various viral diseases [1-3]. Upon infection with various pathogens like oomycetes, fungi, bacteria, viruses, or insect, plants produce several pathogenesis-related proteins (PRs) through the action of the signaling compounds namely salicylic acid, jasmonic acid, or ethylene. These pathogenesis-related proteins play a significant role in plant defense mechanism [4]. The extensive studies on medicinal plant reveals that natural source secondary metabolites are generally low-toxic small molecules with high potentialities for their novelty in chemical structure which would provide opportunities for new drug development.

Though there is tremendous progress in human medicines, yet a major threat to public health is still observed in infectious human diseases caused by bacteria, fungi, viruses and parasites. Often medicaments are used from the crude extract of medicinal plants. On the other hand it is a great importance of drugs produced by method of isolation, identification of the active principal and to know about the clarification of the mechanism of action. The active molecules that cannot be synthesized economically can be obtained from the cultivation of plant species.

It have been reported that the recent outbreaks of many virus-related new diseases suggest that bioactive compounds from natural products against infectious viruses should be developed for the protection of human health [5]. The recent outbreak in 2019, the first reports of an unknown respiratory infection—in some cases fatal—emerged from Wuhan, China. The source of that infection was quickly recognized as a novel coronavirus, related to those that had caused outbreaks of Severe Acute Respiratory Syndrome (SARS) from 2002-2004 and Middle East Respiratory Syndrome (MERS) in 2012. According to World Health Organization affirmed the illness resulting from the new virus, COVID-19, a Public Health Emergency of International Concern. The novel coronavirus—now named SARS-CoV-2—by early March 2020 had infected more than 90,000 people worldwide and killed at least 3,100. This virus have SARS-CoV-2 particles are spherical and have proteins called spikes protruding from their surface which is similar with other coronavirus. A structural change undergoes after spike (SARS-CoV-2 particles protein) attach onto human cells allows the viral membrane to fuse with the cell membrane. For this reason the viral genes can then enter the host cell to be copied, producing more viruses [6].

The presence of therapeutic metabolites in medicinal plant that helps in inhibit viral replication by regulating viral adsorption, which have helps to binding to cell receptors, inhibition of virus penetration into the host cell and by competing for pathways of activation of intracellular signals [7-9]. To collect traditional information from local or indigenous people or using ethnomedicinally important plant(s) to extract phytochemicals for curing various diseases are quite challenging approach. From the extract of plants, different methods for isolation, purification of bioactive molecules/phytochemicals should carry out to establish the antiviral activity. The development of new herbal drugs from plant phyto-constituents is a fascinating approach from eco-friendly, cost effective and therapeutic perspectives [10].

The forest of South Bengal is rich source of many medicinal plants. Medicinal plants are collected and traded from the forest area. In this review article, a detail description of five mostly traded medicinal plants from the South Bengal forest has been made and emphasis has been given to their antiviral properties.

Methodology

From literature survey of South Bengal, we found five most dominant medicinal plants with antiviral potential commonly traded from the Bankura District, West Bengal. Those are Amlaki (*Phyllanthus emblica*), Haritaki (*Terminalia chebula*), Vibhitaki (*Terminalia bellirica*), Kalmegha (*Andrographis paniculata*) and Bilva (*Aegle marmelos*). Beside literature findings, a detail discussion was made with the district forest officer (DFO), Bankura district, Government of West Bengal and with the collectorsof the medicinal plant species in this area for confirmation of the five dominant traded medicinal plants as mentioned above. Based on the information being gathered, effort has been made to depict the outcome of the discussion in this following review.

Outcome of review

Plants mainly medicinal herbs possess a wide array of chemical compounds such as flavones, alkaloids and polyphenols, which play an important role against viruses.Five traded dominant plant species and their phytochemicals and antiviral properties are as follows:

1. Amlaki (*Phyllanthus emblica*)

Phytoconstituents

a. **Leaves**: *P. emblica* leaves were found to contain steroids, flavonoids, carbohydrates, saponins alkaloids, tannins [11]. It contains gallic acid, chebulic acid, ellagic acid, chebulinic acid, chebulagic acid, amlic acid, alkaloids phyllantine and phyllantidine [12].

b. **Seeds:** The seeds yield a brownish-yellow colour fixed oil (16%) along with phosphatides and a small quantity of essential oil [13]. The fixed oil (acid value 12.7; saponification value 185; iodine value 139.5; acetyl value 2.03) have non-saponifiable matter 3.81%; sterol 2.70%; saturated fatty acid 7%. It: contains fatty acids like linolenic acid (8.78%), linoleic (44%). oleic (28.40%), steric (2.15%), palmitic (2.99%) and miristic acid (1.0%) [14-15].

c. **Barks:** Contain leukodelphinidin, tannin and proanthocy-anidin [16].

d. **Roots:** Contain ellagic acid, gallic acid, quercetin, kaempferol, corilagin, geraniin, furosin, gallotanins emblicanins, flavonoids, glycosides, proanthocyanidins and lupeol. Shoot Chebulagic acid, β-sitosterol, chibulinic acid, corilagin, ellagic acid, gallic acid, glucogallin, lupeol [17]. Two new triterpenes, the seco-friedelane type secofriedelanophyllemblicine and the ursane-derived saponinursophyllemblicoside were isolated from the roots of *Phyllanthus emblica* [18].

e. **Fruits:** About 28% of the tannins are present in the fruits as in the whole plant. The fruits are rich in ascorbic acid i.e. Vitamin C and likewise involves quite a lot of polyphenolic compounds. The fruit contains two hydrolysable tannins Emblicanin A and B. The fruit also contains phyllemblin. Amla is one of the most extensively studied plants [19]. Reports suggest that it contains tannins, lignans, alkaloids and phenols.It also contain amino acids L- proline, glutamic acid, cystine, lysine,alanine and organic acid (citric acid). Flavonoids like quercetin and Kaempferol, alkaloids like phyllantine, Phyllembein, and phyllantidine,in phenolic acids tetraphenols,tannin like Pedunculagin, Chebulinic acid (Ellagitannin), Chebulagic acid (Benzopyran tannin), Corilagin (Ellagitannin), Geraniin (Dehydroellagitannin), Ellagotannin are found [20-21].

Antiviral properties

The fruits are known to possess antibacterial, antifungal and antiviral properties [22-24]. Roots of *Phyllanthus emblica* contain 14 highly oxygenated norbisabolane sesquiterpenoids, phyllaemblicins H1-H14 along with phyllaemblicins B and C and glochicoccinoside D which have potent activity against influenza A virus strain H3N2 and hand, foot and mouth virus EV7 [25]. Three new norsesquiterpenoid glycosides, 4'-hydroxyphyllaemblicin B (1) and phyllaemblicins E (2) and F (3), were isolated from the roots of *Phyllanthus emblica*, exhibited strong anti-CVB3 activity [26].

Phyllanthus emblica also contain 1,2,4,6-tetra-O-galloyl-β-D-glucose (1246TGG), a polyphenolic compound, which was found to inhibit herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) infection at different magnitudes of activity *in vitro* [27].

2. Kalmegh (*Andrographis paniculata*)

Phytoconstituent

A. Paniculata enclosed with andrographolide is a most important bioactive phytoconstituent is a colourless or light yellow crystal with a very bitter taste found in various parts, but mainly in the leaves. The plant also possess bitter flavonoids, glucosides, panicalin, panaculoside, andrographonin, neoandrographolide, apigenin7-4-dimethylether.The plant contains other phytochemicals diterpenoids, 12-didehydroandrographolide, 14-deoxy-11-oxoandrographolide; neoandrogra-pholide, 14-deoxy-11, 14-deoxyandrographolide and andrographolide [28-29].

a. **Whole plant:** It consists of andrographolide, furonoidditerpine, 3β-hydroxy-5- stigmasta, 9(11), 22(23)-diene,panicolin,2',5-dihydroxy-7,8 dimethoxyflavone 2'o-β-(D)- Glucoside, diterpeneglucoside neoandrographolide, flavones-5-hydroxy- 7,8,2',3'tetramethoxy flavone, andrographin, 5-hydroxy-7,8-flavanone, apigenin, 7,4- dioxymethylether, mono-oxymethylwigthin, deoxyandro-grapholide -19β-D-glucoside, flavone glucoside A, B, C. Flavonoids, including 5,7,2',3'-tetramethoxyflavanone, as well as several other flavonoids, andrographolidediterpenoids, and polyphenols were found from the whole plant of *A. paniculata* [30- 32].

b. Root: The roots have andrographonin, panicolin, flavonesapigeni7,4'-di-O-methyl ether and α sitosterol, apigenin-7, 4'- di-O-methyl ether, andrographolide and a flavone, 5- hydroxy 7,8,2',3'- tetramethoxy flavone (C19H18O7, mp 150-151°C; yield, 0.006%). They also comprise a monohydroxytrimethyl flavone, a dihydroxy-di-methoxyflavone and andrographin (C18H16O6, mp 190-191°C), panicolin (C17H4O6, mp 263-264°C). The occurrence of Z-sitosterol is also reported [33-34].

c. Leaves: Leaves contain andrographosterol, homoandrographolide and andrographone [35].

Antiviral properties

The extracts of *A. paniculata* have the ability to inhibit the replication of human immunodeficiency virus (HIV) and also interfere with its viability [36]. So, the phytoconstituents of A. *paniculata* could combine with modern medicines for getting better results against Acquired Immuno Deficiency Syndrome (AIDS). Another study was carried out for phase I dose-escalating clinical trial among 13 HIV patients and 5 HIV uninfected, healthy volunteers. The course of treatment was scheduled as follows: a) 5 mg/kg body weight for 3 weeks, subsequently rising to b) 10 mg/kg bodyweight for 3 weeks, and lastly to c) 20 mg/kg body weight for a final 3 weeks. It appeared from the study a major rise in the mean CD4(+) lymphocyte level of HIV even though with no considerable changes in mean plasma HIV-1 RNA levels throughout the trial. These findings demonstrated that due to andrographolide which causes a rise in CD4 (+) lymphocyte levels may be the reason of inhibition of HIV-induced cell cycle dysregulation in HIV-1 infected individuals [37]. The outcome of recent study summarized that the derivatives of andrographolide may have the capability towards preventing HIV infection [38]. This inherent characteristics of Andrographolide come into play perhaps due to restraining enzymes that facilitate the transfer of phosphates. The significant aspect of the fact that andrographolide repressed the gp120-mediated cell fusion of HL2/3 cells with TZM-bl .The other experiment being conducted on antiviral activity of *A. paniculata* explains the cycle threshold (Ct) value which is correspond to the amplification product in a particular cycle on PCR analysis. It was noted that larger final Ct values means fewer targets are amplified, whereas smaller initial Ct value stated that more targets are amplified. The observation on third day after the treatment of sample that *A. paniculata* ethanol extract retarded the virus titer, which is analogous to the positive control Lamivudine. It appears that both of the ethanol extract and positive control have a greater value of Ct as compared with the negative control. This is the obvious indication, that the *A. paniculata* have the similar properties as Lamivudine possess which has the antiviral activity like restraining the replication of virus. It has been observed that the status of treatment after 5 days revealed that the activity of ethanol extract in restraining the virus titer was decreased, but increased the activity of positive control Lamivudine. In spite of this A. *paniculata* ethanol extract still showed significant antiviral activity than negative control [39].

The phytochemicals of *A.paniculata* like andrographolide, neoandrographolide and 14-deoxy11, 12-didehydroandrographolide are reported to be viricidal against herpes simplex virus 1 (HSV-1) without having any significant cytotoxicity at viricidal concentrations [40].

3. Bael (*Aegel marmelos*, L.)

Phytoconstituent

Various chemical constituents like alkaloids, flavanoids, tannin, polysaccharide, phenols, coumarins and steroids have been isolated and identified from different parts of the tree.

a. Leaves: The leaves contain four new alkaloids viz, O-halfordinol, N-2-ethoxy-2- ethylcinnamid, N-2-methoxy--2-ethylcinnamid, besides aegelenine and aegeline. Condensedtannins, pholobatannins, flavan-3-oIs, leucoanthocyanins, anthocyanins, flavanoid glycosides, skimmianine and y-sitosterol. Rutin, γ-sitosterole, β-sitosterol, Lupeol, Cineol, Citral, Glycoside, O-isopentenyl, Hallordiol, Mameline, Citronellal, Cuuminaldehydephenylethylecinnamamides, Euginol and Marmesinin, are also present [41- 44].

b. Roots: Contain coumarins such as scoparone, scopoletin, umbellliferone, marmesin and skimming. Fruits in addition contain xanthotoxol, imperatorin and alloimperatorin and alkaloids like aegeline and marmelline.Dibutyl phthalate is the major compound found in root.Other important compounds such as coumarin (2H-1-Benzopyran-2-one, 7-[(3,7- dimethyl-2,6-octadienyl)oxy]-, (E)-), skimmianine (Furo[2,3-b] quinoline, 4,7,8-trimethoxy-), terpenes and cyclobarbital were found in plant root [45-48].

c. Fruits: Fruits contains moisture 61.5%; protein 1.8%; fat 0.3%; Carbohydrate 31.8%; and fibre 2.9% (Chaubey, &Dubey, 2020;).. Besides the following are present in small amounts (mg/l00 gm); Calcium, 85.0; phosphorous, 50.0; iron 0.6; thiamina, 0.13; riboflavin 1.2; niacin, 1.1; oxalic acid 18.7; and Vit C, 8.0 and ; Carotene, 55 microgram/l00 gm. The fruit contains allo-imperatorin, marmelosin which are identical with imperatorin and Bsitosterol. Phenol only found in the fruit of the plant with more percentage in fruit peel (4.38%) than in fruit pulp (0.58%) [49-52].

d. Bark: Bark contains Fagarine, Marmin, Furoquinoline, Alkaloids [53].

e. Seeds: The seeds yield an oil (34.4% on dry weight basis). The fatty acid composition of the oil is as follows: palmitic 16.6; stearic 8.8%; Oleic 30.5%; linoleic 36.0%; and linolenic 8.1%. It is noted that the fruit pulp, although, is not a good source of vitamin C (920 mg per 100 g of pulp) while fruit is a very good source of protein which is 5.12 per cent of the edible portion. The total mineral content of the edible portion, as represented by ash, is 2.663 per cent. The percentage content of some of the minerals, viz. phosphorus, potassium, calcium, magnesium and iron is 0.137, 0.746, 0.188, 0.127 and 0.007 respectively [54-56].

Other chemical constituent

A. marmelos also contains coumarin, marmelosin, marmesin, imperatorin, marmin, alloimperatorin, methylether, xanthotoxol, scoparone, scopoletin, umbelliferone, psoralen and marmelide. Polysaccharide: Galactose, arabinose, uronic acid and L-rhamnose was obtained on hydrolysis. Tannin: Tannin was also present in leaves and fruit as skimmianine. Carotenoids such as marmelosin, skimmianine and umbelliferone were also reported in the *A. marmelos*, which is responsible for pale colour to fruit and known as therapeutically active principale of bael plant. Presence of minor constituents are like sitosterol ascorbic acid, crude fibers, α- amyrin, tannins, carotenoids, and crude proteins are also resent. Several organic acids including tartaric, oxalic, malic and ascorbic acids are also found.

Antiviral properties

A. marmelos shows better virucidal potential and may be exploited as apotent antiviral agent in the near future. Recent

studies showed that seselin (8,8-dimethylpyridooxazine-2-one) from *A. marmelos* could be used as a natural medicine for the management of NPV infection in the silk
worm larvae under commercial conditions after suitable field evaluations [57]. The experiments from the ethanolic fruit extracts have shown antiviral activity against virus of Ranikhet disease. Bael fruit have marmilide which is the most useful viricidal agent which interferes with early events of replicating cycle. The *in vitro* viral activity of various parts of *A. marmelos* tree has been assessed towards their effectiveness against human coxsackie viruses B1-B6 [58]. The IC50 of leaves, stem and stem bark, fruit, root and root bark and purified compound marmelide are 1000, 500 to 1000, 250 to 500 and 62.5 µg/ml, respectively, whereas, the IC50 of Ribavirin, a standard antiviral agent, is 2000 µg/ml for the same viruses and at the same time period. Fruits also contain interferon–like activity against the same virus. *A. marmelos* has a showed that extracts against white spot syndrome virus in shrimp at the concentration of 150 mg/kg of animal body weight. Another study demonstrated that the bael extracts act upon towards viral replication at the early stages with minimum host cytotoxicity. In contrast ribavirin (a modern virucidal chemotherapeutic agent), that act in the later stages of viral replication with a lot of side effects [59-60].

4. Haritaki (*Terminalia chebula*)

Phytoconstituent

T. chebula is rich sources of tannins and maximum amount was found in fruits. Besides this, it also contain good amount of other phytochemicals like *flavonoids*, tannins, sterols, fructose, amino acids, resin, fixed oils etc.

a. **Fruit:** High amount of tannins (about 32%-34%) are present in the fruits of *T. chebula* and its content varies with geographical distribution [61]. There are about 14 hydrolysable tannins (namely gallic acid, chebulagic acid,punicalagin, chebulanin, corilagin, neochebulinic acid, ellagic acid, chebulinic acid, 1,2,3,4,6-penta-O-galloyl- β-D-glucose, 1,6-di-o-galloyl-D-glucose, casuarinin, 3,4,6-tri-o-glloyl-D-glucose, terchebulin) were isolated from the fruits of *T. chebula* [62]. Besides that, chebulinic acid, ellagic acid, anthraquinones, corilagin, galloyl glucose, punicalagin, terflavin A, maslinic acid, fructose, amino acids, succinic acid, betasitosterol, resin and purgative principle of anthraquinone are also present. Fatty acids namely palmitic, stearic, oleic, linoleic were isolated from oil extracted from seed kernels [63, 64].
b. **Stem bark:** Contains high amount of triterpenoids and glycosides. Recent studies shows that presence of abundant phenols (chebulinic acid, ellagic acid and polyphenols includes punicalagin, terflavin A corilagin, galloyl glucose, and triterpenemaslinic acid.) as compared with other plants [65, 66].

Antiviral properties

The extract of fruits of *T.chebula* showed inhibitory effects on human immune deficiency virus-1 reversetranscriptase from extract of fruit. In a study the hot water extract showed anti-herps simplex virus (HSV) activity *in vivo* and anti-cytomegalovirus (CMV) activity both *in vitro* and *in vivo* [67, 68]. It was found in early studies that the *T. chebula* is active in protective activity against cytotoxic [69]. In view of this it is expected that it should shows protecting epithelial cells against damage caused by influenza A virus in the event of 23 components when applied to the epithelial cells individually. But Ledretan-96 and each of its 23 individual components were tested the outcome of the test observed that the only one component showed a significant protective effect out of 23 components. A work was proved that *fruits of T. chebula*contain four human HIV-type 1 integrase inhibitors such as gallic acid and three galloyl glucoses, and suggested that galloyl moiety had a major role for inhibition of the 3′-processing of HIV-1 integrase by these compounds [70, 71]. *T. chebula* can also be used in sexually transmitted diseases and AID [72]. Herpes simplex virus 1 (HSV-1) is the cause of lifelong latent infection of sensory neurons. From the dried fruit of *T. chebula* two hydrolyzable tannins, chebulagic acid and punicalagin, were isolated inhibited HSV-1 entry at non-cytotoxic doses in A549 human lung cells by preventing binding, penetration, and cell- to-cell spread, as well as secondary infection [73]. *T. chebula* fruits were famous home-based therapy forcough and cold. *T. chebula* extract, chebulagic and chebulinic acids have higher direct antiviral activity against HSV-2. It was also useful to fight against acute pulmonary infections which defended upper respiratory cells from influenza A virus [74]. It is noted that healing activity against herpes simplex virus was recognized in different studies. Antiviral action reported on *T. chebula* by a group of Japaneseinvestigators. They found that *T. chebula* was active in preventing the CMV replication in immune compromised mice and determined that it could be useful to inhibit CMV infections in immune compromised patients [75]. *T. chebula* were repressed HSV-1 pass at non cytotoxic concentrations in human lung A549 cells due to punicalagin and chebulagic acid found in fruits. Another from dried fruits that chebumeinin A, chebumeinin B and two new hydrolysable tannins together with 8 identified and displayed activity against Hepatitis C virus [76]. Its extracts *T. chebula* extracts have been displayed important antiviral activity on influenza A virus H3N8 viral assays when used at higher doses. On cytomegalovirus, *T. chebula* was shown to have significant antiviral action. Aqueous extract of *T. chebula* plant suppressed the plaque development of HCMV independent of dose. Recently acetone extract of *T. chebula* also play a potent inhibitor of pandemic swine influenza A infection due to its low cost, easy preparation and potential effect on virus [77].

Phytochemicals of *T. chebula* mainly chebulagic and chebulinic acids possess potential antiviral activity against HSV-2 by inhibiting the virus towards its attachment and penetration to the host cells as compared to acyclovir. However, acyclovir is more active to render post-infection virus replication. So *T. chebula* can be used as alternative herbal drug for prevention of sexually transmitted HSV-2 infection [78].

Baheda (*Terminalia bellerica*) Phytoconstituent

Fruits of *Terminalia bellirica* contain ellagitannins such as corilagin, chebulagic acid, galloylpunicalagin, and digalloyl-hexahydroxydiphenoyl-hexoside as major components. Arjungenin and its glycosides, belleric acid, bellericosides were found stem bark extract of baheda [79 - 82].

Antiviral properties

Terminalia bellirica fruit pericarp were found to be good antibacterial and antiviral activity [83] against different bacterial strains and two common animal viruses namely newcastle disease virus or NDV (thermostable I-2Strain, its EID50 is 10 9.13/mL) and papillomavirus or PV. Compounds having *in vitro* anti-HIV-1, antimalarial, and antifungal properties have been isolated from the fruit extract of *T. bellerica* [84, 85].

Conclusion and future plan

There exist several reports for exploring antiviral properties of plant extracts and phytochemicals. Herbal preparations enhances the body's immune system which helps to fight against invading infectious viruses. Viruses are the smallest infectious agents (ranging from about 20 to 300 nm in diameter) and vary greatly in structure, genome organization and expression, and strategies of replication and transmission and have the ability to persist within the host for short or long period of time. Herbal antiviral compounds are now gaining much attention as alternatives of synthetic drug due to their broad spectrum activity, low cost and easy availability without any side effects. It has been proof that many promising herbal treatments safety in advanced clinical trials. However, a lot of work still remains to be done to understand and determine optimal treatments, doses, and formulae for those herbal preparations. It has been observed that in several part of the world herbal plant preparation are widely in use. So, the traditional knowledge about herbal medicinal practice should be connected with scientific research facilitating modern drug discovery from bioactive compounds. In this review effort has been made to enlist the possible dominant plants as reported antiviral activity. These plantshave a wide spectrum of medicinal usage and documented in different traditional treatment system such as the Ayurveda, Unani, Siddha, and other conventional medical systems. This review infers that these medicinal plants act against viral diseases but still remain a gap and subsequently opens various avenues for the other researchers to gather the essential ideas and information for further study towards the clinic trials to be carried out which requires extensive research, isolation and mechanistic studies. Tissue culture has emerged as a promising technique would provide a means of rapid propagation and conservation of these plant species and from considering vast range of photochemistry, gives a wide scope for enhancement of the quality and quantity of the bioactive secondary metabolites occurring in the plant. Based on the present pandemic situation, it is urgently needed to explore unknown phyto-constituents from this known as well as unusual plant with potent antiviral activities. So a detail investigation to validate the desired activity of the phyto-constituent in an *in vivo* and/or *in vitro* model will be required in future.

Conflict of interest statement

Authors declare that they have no conflict of interests among them regarding the publication of this paper.

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