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Can plantation crops be a remedy for this current pandemic?: A review on reported potential plants as anti-viral agents

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Abstract
Synthetic antiviral medicines expounded for treating viral diseases posed a range of undesirable consequences on human beings necessitating the contribution of natural drugs and medicines of plant origin. Horticultural crops implementing the intent of protective foods have the competence to contend bacterial, fungal and viral diseases debilitating human health. Plantation crops have been well-utilized by our ancestors for formulating medicines to cure several health ailments thus assuring its ability to fight the frightful viral diseases. This manuscript exclusively congregates the phyo-pharmaceuticals acquired in plantation crops imparting protection against retrovirus, enterovirus, influenza, dengue, chikungunya, zika, etc which can be exposed to further analysis in medical milieu to confront the latest life-threatening COVID-19 as well as impending frailties down to budding viruses.

Keywords: Antiviral activity, COVID-19, natural drugs, viral diseases.

Introduction
Human body is a multifaceted ecosystem comprising approximately 10^{13} human cells and 10^{14} bacterial, fungal and protozoan cells which sets up the natural flora eliciting tribulation only when the immune system is weakened. At the same time as, the pathogens are typically definite from these microbiota and are capable of triggering malady even without the immune system being compromised or injured. Human pathogens are customarily supposed to be invaders that assail human bodies but, they are austerely striving to thrive and multiply at the cost of a human-host organism alike other creatures on Earth. As human beings could provide the conducible consistent temperature, moist environment and nutrients for their survival, micro-organisms have been astonishingly advanced to dwell and proliferate in this advantageous niche. Many types of pathogens, say bacteria, fungi, protozoans and dreadful viruses instigates infirmity in human beings. Of these, viruses are basically the nucleic acids draped in a defending shield of proteins and in membranes utilizing the host's central dogma for their replication (Alberts *et al*., 2002) [1]. The most familiar viral diseases range from dengue, influenza, HIV, smallpox, common cold to recent panicking COVID-19.
Corona viruses are a huge faction of viruses recognized to beget ailments that fluctuate amid common cold and rigorous diseases including Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS). They are specified as indicated by their crown appearance in which the viruses are surrounded with spike-like glycoprotein configurations on their envelope (El-Aziz and Stockand, 2020) [8]. An unusual corona virus was documented in December 2019 in Wuhan, China which is at present branded as SARS-CoV-2 with consequent disease being COVID-19. This disease was stated as worldwide pandemic by the World Health Organization in March 2020. According to WHO report, 12.49 million confirmed cases and 5.61 lakh death tolls globally with 8.49 lakh confirmed cases and 22,674 death tolls in India have been recorded as on 12th July, 2020. Presently, no exclusive remedy is endorsed to alleviate COVID-19. Though the antiviral drugs so far developed against Ebola, influenza, HIV and malaria such as remdesivir (Wang, 2020) [37], favilavir (Elfiky, 2020) [9], lopinavir/ritonavir (Lim, 2020) [24] and hydroxychloroquine (Dong *et al*., 2020) [7], correspondingly were demonstrated effectual to an extent to encounter SARS-CoV-2 virus, they are propounding some unusual consequences and even casualties. Other than this, convalescent plasma therapy (CP) can also be harnessed to thwart this virus (Cheng, 2005) [3] but the risk of other blood-abode pathogen transmission as reported by MacLennan and Barbara (2006) [25] may arise. Usually, viruses imperil human health by rerouting body's metabolism to reproduce its viral genome and proteins in several replicas thus making it difficult to control viral infections with currently available drugs. Natural drugs, obtained from plants can serve as a better alternative for treating these infectious viral diseases as synthetic

drugs have their own limitations due to the development of virus's resistance by frequent mutations, low efficiencies, undesirable side effects and high cost involved. So, steps can be taken to develop natural drugs which guarantee zero side effects and reliable cure from the destructive viruses.

Horticultural crops provide the source of protective foods. Apart from being the sources of health benefits, these crops also serve as a source for various types of phytochemicals which can be exploited to produce supplemented foods to confer resistance against viral diseases in human. Out of the bountiful horticultural crops, plantation crops could be potentially exploited for their innumerable prophylactic and antiviral properties for which they have been employed in home-made preparations to cure cold, cough and other ailments in our day-to-day life from ancient times. To realize the important therapeutic properties of these crops, different types of phyto-compounds have been extracted by using different solvents such as water, methanol, butanol, ethyl acetate from various plant parts and their potential medicinal properties against virus diseases have been identified. Considering the pandemic spread of corona virus throughout the world at present, this review converges on the types of phytochemical compounds especially in different plantation crops and their antiviral properties studied so far to promote the development of preventive and therapeutic natural drugs for treating human viral diseases.

Plantation crops

Among the plantation crops, tea, coffee, coconut, arecanut, cashew and cocoa have been explored for the identification of antiviral compounds. Anti-viral compounds have been isolated from coffee beans, husk from cocoa and oil from coconut and leaves from tea. Chlorogenic acid, caffeic acid and mixture of these from coffee (Sinisi *et al*., 2017; Shen *et al*., 2018) [33, 32], polyphenols and theaflavins (Chowdhury *et al*., 2018) [4], Epigallocatechin-3-gallate (Xu *et al*., 2016) [38] from tea and monolaurin, lauric acid, catechin, epicatechin, condensed tannins (B- type procyanidins) from coconut (Esquenazi *et al.*, 2002) [10] possessed antiviral property against different types of pathogenic human viruses. Table 1 & Fig. 1 shows the antiviral properties imparted by different plantation crops.

Arecanut

The extracts of arecanut at 0.2 mg/ml exemplified antiviral effect against HIV-IPR with more than 70% growth inhibition activity and the procyanidine compound, areca tannin B1 responsible for this activity had also been isolated (Kusumoto *et al*., 1995) [22]. Plant tannins and alkaloids present in arecanut demonstrated strong repression against viral pathogens responsible for HIV and HSV-1 (Kurukawa *et al*., 2010) [21].

Cocoa

Cocoa extract (CE) exhibited anti-influenza activity by inhibiting the viral adsorption to host cells in a dose-dependent manner. In human-involved experiments, a set of people were supplemented with cocoa for 3 weeks both prior and subsequent to vaccination against A (H1N1) pdm 2009 influenza virus and another set without cocoa intake as control. However, the degree of escalation in neutralizing antibody titres produced in response to virus was usual amid the study groups. Even if, the natural killer cell activity perked up in both groups with more ample upsurge in cocoa augmented group (Kamei *et al*., 2015) [20].

Table 1: Antiviral properties present in plantation crops

Plantation crops	Plant parts	Anti- viral compounds	Against Virus	References
Areca nut	Nut	-	HIV	Kusumoto *et al*. (1995) [22]
Cashew	Fruit	Agathisflavone	INV	de Freitas *et al.* (2020) [6]
Cocoa	Defatted powder	-	INV	Kamei *et al.* (2015) [20]
Coconut	Husk fibre	Catechin, epicatechin, condensed tannins (B- type procyanidins)	HSV-1	Esquenazi *et al.* (2002) [10]
	Oil	-	Retro virus	Ogedengbe *et al*. (2018) [29]
Coffee	Coffee beans	Chlorogenic acid	HRSV	Sinisi *et al.* (2017) [33]
		Caffeic acid	HCV	Shen *et al.* (2018) [32]
			Thrombocytopenia syndrome virus	Ogawa *et al.* (2018) [28]
			HSV-1	Ikeda *et al.* (2011) [18]; Utsunomiya *et al.* (2008) [36]
			INV (H1N1)	Kaihatsu *et al.* (2014) [19]
Tea	Leaves	Epigallocatechin-3- gallate	HBV	Xu *et al*. (2016) [38]
		-	HAV, human noro virus	Falco *et al.* (2018) [11]
		Catechins	INV	Furushima *et al.* (2018) [12]
		Polyphenols and theaflavins	HCV	Chowdhury *et al.* (2018) [4]

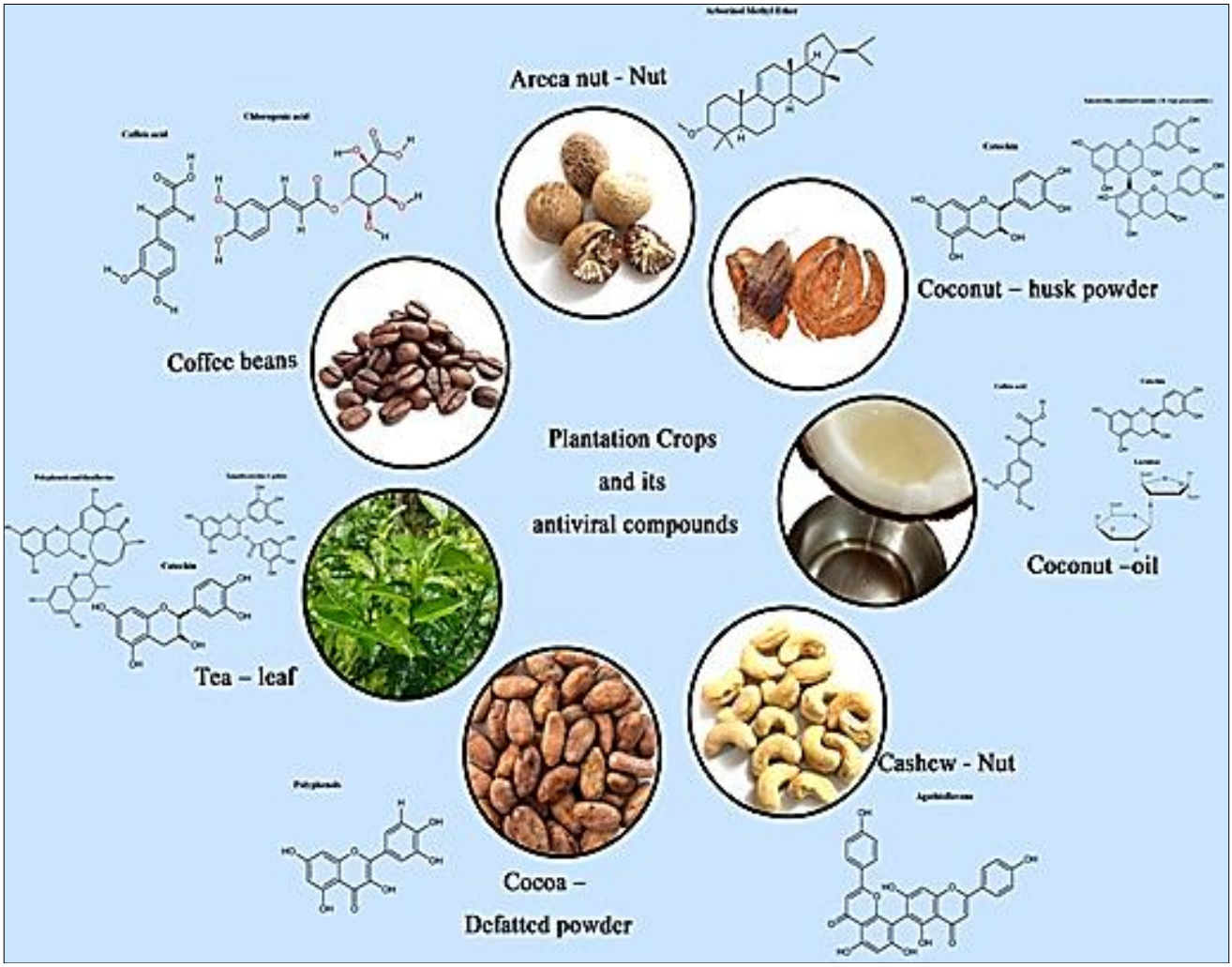

Fig 1: Plantation Crops and its antiviral compounds

Coconut

Monolaurin (product of esterification in human body which combines lauric acid and glycerol) which is obtainable from coconut could lessen infectivity of RNA and DNA enclosed viruses by >99.9% by disintegrating the virus envelope *in vitro* (Hierholzer and Kabara, 1982) [14]. Thormar *et al.* (1987) [35] validated the capability of lauric acid and monolaurin to inactivate viruses by collapsing the cell membrane. Lauric acid obstructed the production of infectious vesicular stomatitis virus in a dosage-reliant and reversible way due to triacylglycerol (TAG) dependent reduction in the amount of glycoprotein (G) and matrix protein M which subsequently prevented attachment to host cell membrane (Hornung *et al*., 1994) [17].

A medical assessment was performed with 15 HIV infected patients in which 3 treatment groups were provided with 7.2 g monolaurin (ML), 2.4 g ML and 50 ml of coconut oil daily for 6 months, respectively. By 3rd month, 7 patients (50%) expressed viral load diminution and by 6th month, 8 patients (2 in 7.2 g ML group, 4 in 2.4 g ML group and 3 in coconut oil group) displayed meager viral count. The CD4/ CD8 counts fortunately amplified in 5 patients. Whereas, three people built up AIDS on 3rd month when their CD count declined < 200. Out of them, the one in coconut oil group passed away 2 weeks post-study. Rest 2 persons were in 2.4 g ML group in which one recuperated fully by 6th month and the other evidenced quick gain to the regular CD 4 and CD 8 estimates (Dayrit 2000) [5].

Lauric acid (C12) diminished virus yields of numerous attenuated and pathogenic strains of Junin virus (JUNV) corresponding to dosage level without disturbing cell viability. Also, a direct correlation between stimulation of TAG cell content and inhibition of JUNV production was noticed. Thus, the increased incorporation of TAG inhibited JUNV maturation and release by affecting the insertion of viral glycoproteins into host plasma membrane (Bartolotta *et al*., 2001) [2].

The crude extract obtained coconut husk fibre exhibited protective effect against HSV-1 virus with viral inhibition index (VII) > 3.0 (PI > 99.9%) in HEp-2 and Vero cells at non-toxic concentrations. Direct treatment of catechin (isolated fraction from extract) showed higher antiviral activity than crude extract showing VII of 5.0 and 4.59 and virucidal index (VI) of 3.0 and 3.25 for HEp-2 and Vero cells, respectively before infection (Esquenazi *et al*., 2002) [10].

Fatty acids, monoglycerides and fatty alcohols present in coconut oil proved their virucidal activities towards HRSV and Human Para-Influenza Virus type 2 (HPIV 2) in a strength, time and pH level-dependent approach. Moreover, the compound monocaprin showed virucidal activity against influenza A virus even at lower concentration of 0.06-0.12% (Hilmarsson *et al*., 2007) [15]. Lauric acid (which constitutes 47.5% of coconut oil) hampered late replication phase of JUNV which is an enveloped virus figuring glycoproteins entrenched in lipid bilayer producing viral spikes alike nCoV-2019 (Grant *et al*., 2012) [13].

Coffee

The compound caffeine isolated from coffee inhibited the multiplication of virus but did not exhibit virucidal activity. Moreover, caffeine induced selective apoptosis in virus infected cells and aborted infection. The extracts additionally

hindered the proliferation of polio virus, a non-enveloped RNA virus. Thus replication of HSV-1 and polio virus is responsive to caffeine, signifying its inhibition against DNA and RNA virus and its potential as antiviral agent (Murayama *et al*., 2008) [26].

Hot aqueous coffee extracts and instant coffee mixture revealed anti-HSV activity by directly inactivating the infectivity of virus particle and inhibiting the further virus multiplication. The compound caffeic acid present in the extracts inhibited multiplication of HSV-1 *in vitro* without any virucidal effect. Addition of caffeic acid at an initial post infection stage surprisingly impeded the development of progeny contagious virus in the infected cells, but its addition after 6 h of post infection (i.e. after completion of viral genome replication) failed to stop this process (Ikeda *et al*., 2011) [18]. Kaihatsu *et al*. (2014) [19] separated the hydrophobic and hydrophilic fractions of coffee and assessed its antiviral activity against influenza virus. The hydrophobic fraction (mainly caffeine and caffeic acid) precisely repressed seasonal Influenza A/Puertorico/8/24 (H1N1) virus and neuraminidase-defiant influenza A/Yokohama/77/2008 (H1N1) virus in a concentration-dependent mode, whilst the hydrophilic portion failed to inhibit still at doses >100 µg/ ml. Moreover, di-octanoyl ester of caffeic acid demonstrated 38-fold elevated anti-influenza action.

Tea

Nakayama *et al*. (1993) [27] found that Influenza A virus (IAV) and Influenza B virus (IBV) were deterred by Epigallocatechin gallate (EGCG) which exerts fusion effects on virions and checks the virus from captivating onto the host cell surface. EGCG showed destructive effect on virus particles of HIV-1 by suppressing viral infectivity and preventing virus binding to the cellular surfaces (Yamaguchi *et al*., 2002) [40]. EGCG and epicatechin gallate (ECG) from green tea extracts were found as potent inhibitors of influenza virus replication with EC_{50} being 22-28 and 22-40 µM, respectively. These compounds possessed antiviral activity by inhibiting the haemagglutination and neuraminidase activity, suppressing viral RNA synthesis and modifying the physical properties of viral covering (Song *et al*., 2005) [34].

An investigation unit scrutinized the correlation between influenza virus infection and gargling tea catechin extract and confirmed that catechins noticeably dropped infection rate in 124 populace aged more than 65 years (Yamada *et al*., 2006) [39]. A study illustrated that QR-435 (a green tea extract) obstructed the virus spread and imparted immunity against IAV H3N2. More fascinatingly, wearing masks incorporated with QR-435 was competent to preclude H3N2 infection (Oxford *et al*., 2007a and b) [31, 30]. Proliferation of Enterovirus 71 (EV71) was subdued by 95% on post-treatment with EGCG and Gallocatechin gallate (GCG) which was related with diminished reactive oxygen species (ROS) synthesis on EGCG administration (Ho *et al*., 2009) [16].

EGCG from green tea extracts strongly inhibited the HBV antigen expression by behaving as an adversary towards farnesoid X receptor alpha (FXRα) and downgrading transcriptional activities of HBV EnhII/core promoter (Xu *et al*., 2016) [38]. Green tea extract (GTE) exhibited potent antiviral activity against influenza virus (H1N1) still following storage for 56 days at distinctive temperatures. GTE at 0.1% totally attenuated 10^6 plaque forming units (PFU) of virus (6 log reduction) and at 0.01 and 0.05% concentration resulted in 2 log reduction of viral titres. Thus, it can be suggested tht GTE could be formulated as a safe and environmental friendly antiviral agent against virus infections (Lee *et al*., 2018) [23].

Conclusion

Humans and animals are incessantly being exposed to diverse and unusual pathogenic viruses which provokes serious illness and even casualties. Quite a lot of synthetic antiviral drugs have been developed till date, but the resistance of viruses to these drugs and their side effects insists the exigency of plant derived antiviral medicines. Horticultural crops have been conferred with innumerable phyto-pharmaceuticals as secondary metabolites like polyphenols, flavonoids and alkaloids. Of these, plantation crops have much potential to fight viral diseases and are habitually acquired from our day-to-day consumption as well. These crops can be well-exploited for their antiviral properties to develop natural drugs. As these crops have noble anti-oxidant and prophylactic activity, awareness should be created among people for home-made preparations out of these produces which invigorates the intrinsic immunity and render protection from viruses like COVID-19 which is threatening the whole world at present.

Conflict of interest

The authors declare no conflict of interest.

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