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# EGCG AGAINST ZIKA VIRUS INFECTIONS

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## Commentary

Zika virus (ZIKV) has emerged as a global threat in past 2-3 years that has affected millions of people in more than 40 countries with multiple outbreaks in the Americas, the Pacific, and south-east Asia. ZIKV was first isolated from Uganda in 1947, but the epidemic history of virus started in 2007 from Yap island outbreak, which was further observed in French Polynesia (2014) and Americas in 2015-16 covering larger population and greater consequences. ZIKV infection has also raised alarms among participants of 2016 Summer Olympics games in Rio de Janeiro, Brazil. Due to this preoccupation, a number of athletes had withdrawn their names from the event. Major concerns of ZIKV involves its association with sexual transmission and birth defects [1, 2]. A report of ZIKV infection in pregnant women in Rio de Janeiro during September 2015 to February 2016 described 82% positive cases (72 out of 88) [3]. The US Centers for Disease Control (CDC) have advised pregnant women to consult the doctors and strictly follow preventive measures to avoid the risk of ZIKV infection during travel [4]. Moreover in 2016, World Health Organization (WHO) had declared the situation as a matter of global health concern [5]. At present, there are no licensed therapeutic drugs available in the market for the prevention of ZIKV infection. The situation demands the development of safe and effective therapeutics. Therefore, it is important to explore natural drug like source such as nutraceuticals that could be utilized as preventive measures till the FDA approved drugs are discovered. Since this virus belongs to *Flaviviridae* family, therefore based on repurposing drug discovery, all the drugs that have been previously screened and approved against other flaviviruses may benefit against ZIKV [6, 7].

In May 2017, WHO has confirmed three cases of ZIKV in Ahmedabad District of Gujarat, India (http://www.who.int/). Further, in September 2018, the Ministry of Health and Family Welfare-Government of India (MoHFW) reported a confirmed case of Zika virus infection in Jaipur, Rajasthan State, India. As of 2 November 2018, WHO has confirmed 157 cases of ZIKV infection, including 63 pregnant women (http://www.who.int/). Needless to mention, India is further at high risk of developing ZIKV infection due to suitable geographical conditions required for the growth of vector, Aedes mosquitoes. Despite removing health emergency status by WHO in

November 2016, Centers of Disease Control has still reported cases of Zika virus infection in America in 2018 (www.cdc.gov). However, it has been emphasized to continue the search for Zika specific therapeutics to combat future outbreaks.

A recent report of epigallocatechin gallate (EGCG), one of the major constituent of green tea has shown antiviral activity against two strains of ZIKV infection in Vero E6 cell lines [8]. At higher concentration of EGCG (100μM), more than 90% ZIKV entry inhibition was observed [8] into host cells. The probable mechanism of ZIKV entry inhibition by EGCG has been observed using computational molecular docking and dynamic simulation techniques, where it was found to bind the envelope protein specifically between domain I and domain III [9]. This seems to be promising and encouraging at the current state of emergency and proved that EGCG could be used as a possible therapy to prevent or reduce the ZIKV infection[8]. However, it is important to note that the therapeutic dose of EGCG for ZIKV is at least three times higher than this drug plasma concentration after consumption of green tea.

Several studies have supported the use of green tea as one of the best nutraceuticals without any adverse effects. Apart from that, drinking green tea is marked to have several other physiological and pharmacological health benefits that include cancer prevention, anti-infective, antiviral, cardioprotective, antioxidative, neuroprotective and cholesterol-lowering effects [10]. More importantly, several studies have reported antiviral activities of EGCG against diverse virus families such as *Flaviviridae, Orthomyxoviridae* and *Retroviridae* [10]. EGCG directly interacts with the viral membrane proteins and interferes with the viral entry and membrane fusion steps in hepatitis C virus (HCV) and HIV-1.

EGCG and green tea is safe to use for mammalian systems. EGCG didn't show any adverse effects during the organogenesis period in rats [11], but further safety studies are required to further implement its use for pregnant women. However, initial evidence suggested the use of Green Tea as a nutraceutical for preventive control measure against Zika Virus. Most importantly Green tea is a nutraceutical with several health benefits and provided the discussions mentioned above, why not to increase its consumption in the current situation of ZIKV infectiontransduction, various transporters, ion channels and stabilization of DNA conformation etc.

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