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Tea Polyphenol Extracts as a Natural Dietary Supplement to Current Treatments of HIV/AIDS

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Introduction

The human immunodeficiency virus (HIV) belongs to the *Lentivirus* genus, a member of the Retroviridae family of enveloped, single-stranded, positive-sense RNA viruses that replicate characteristically in a host cell through the process of reverse transcription. HIV is the etiological agent of acquired immunodeficiency syndrome (AIDS) which affects the human immune system including $CD4^+$ T lymphocytes, monocytes, macrophages and dendritic cells [1]. Worldwide, more than 35 million people are thought to live with HIV [2], of whom 69% reside in sub-Saharan Africa where one adult in every 20 is HIV-positive [3]. The Centres for Disease Control and Prevention estimate that in the USA approximately 50,000 people contract HIV each year [4]. The latest statistics from China reveal that 501,000 people had HIV/AIDS among whom 205,000 were living with AIDS [5]. Drug injection using contaminated shared needles [6], unprotected sexual contact, percutaneous blood exposure, mucus membrane exposure to contaminated blood or other body fluids, mother-to-child transmission and receipt of contaminated blood products are all identified as major routes of HIV transmission [7].

There are over 25 anti-retroviral (ARV) drugs licensed for HIV therapy [8]. A range of side effects including liver, metabolic and blood disorders, constipation, fever, muscular dystrophy, lipoatrophy, hypersensitivity reactions, peripheral neuropathy, hyperlactemia, pancreatitis and mitochondrial toxicity [1,9,10], as well as multi-drug resistance and toxicity caused by the high genetic variability of HIV, have restricted long term treatment with those currently available ARV drugs [11]. The wealth of botanical-based therapies that are both efficacious and safe has prompted research to screen different known medicinal plants for anti-HIV activity, of which different types of tea – with their broad range of polyphenols as an active ingredient – could be considered as among the most important [12].

Polyphenols have been recognized as extremely important plant-derived dietary compounds due to producing a vast range of effects considered to be beneficial to humans. Of several polyphenol sources in the human diet, tea is one of the most consumed beverages. This is prepared from leaves of the evergreen shrub *Camellia sinensis*. Globally, over 4.52 million tons of tea was produced in 2014 [13]. Depending on the degree of processing and fermentation, tea is divided into green tea, which is consumed mostly in South East Asian countries, black tea, which is commonly consumed in the Indian subcontinent and Western societies, and Pu-erh, white, yellow and oolong teas that are produced and drunk mainly in China [14].

Green, Pu-erh and black teas contain such phenolic compounds as (-)-epicatechin gallate (ECG), (-)-epigallocatechin (EGC), (-)-epigallocatechin gallate (EGCG), (-)-gallocatechin gallate (GCG), theaflavin (TF1), theaflavin-3-gallate (TF2A), theaflavin-3′-gallate (TF2B) and theaflavin-3,3′-digallate (TF3), which have demonstrated anti-HIV activity in several *in vitro* and *in vivo* studies [12,15]. While all are classified as flavonoids, green tea polyphenols consist mostly of EGCG and other catechin gallates, whereas theaflavins are the main constituents of black tea and more fermented varieties of Pu-erh.

Tea polyphenols are involved in subcellular pathways such as JAK/STAT signaling [16], in addition to intercellular and virus-cell interactions [15].These exert anti-viral and immunomodulatory effects on HIV infection via different mechanisms including inhibition of virus replication, of HIV-induced cytopathic activities, and of antigen and reverse transcriptase (RT) expression, prevention of virus attachment and destruction of virus particles. In particular, EGCG inhibits HIV-1 replication in several steps of the virus life cycle by interfering with RT and protease activity, blocking gp120-CD4 interaction via binding to CD4 and destroying virus particles [17-21]. Tea polyphenols also show activities against HIV infection in concentrations that are non-toxic for mammalian cell lines *in vitro* [22]. Pu-erh tea has been studied mostly in the form of crude extracts and isolated compounds were not assessed; however, these preparations were successful in demonstrating anti-HIV properties [15].

A number of beneficial properties have been attributed to tea polyphenols, including anti-viral functions [15,23]. When drank regularly, tea has health-enhancing effects due to its highly active anti-oxidant and anti-inflammatory polyphenolic compounds, especially catechins [24].The European Food Safety Authority reported that each 100 ml of green tea contains about 126 mg of catechin derivatives [25]. As a principal property of polyphenols, anti-oxidant effects are likely to play a key role in their noted anti-retroviral activities. Also, immunomodulation could be one of the mechanisms involved in the anti-HIV function of these molecules [14].

It is proposed that in future tea polyphenols and polyphenol-rich extracts could be utilized as dietary supplements in combination with conventional anti-HIV medicaments. As investigation in humans of the protective effects of tea-derived polyphenolic compounds is very limited to date, there is a pressing requirement to perform detailed clinical trials in order to acquire sufficient and robust data to either

substantiate or refute the putative beneficial role of tea polyphenols in the therapy of HIV/AIDS patients.

Conflict of Interests

The author does not have any conflict of interest to declare.

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