NOTES ON NATURAL HISTORY

HIV Treatment: Towards Bioactive Compounds of plant origin

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Introduction:

The year 1983 saw the detection of one of the most deadly and malicious viruses, known as the Human Immunodeficiency Virus (HIV). Following the report of World Health Organisation, over 36.9 million people had HIV at the end of 2017, all over the world (Deeks *et al.*, 2015, WHO http://www.who.int/hiv/data/epi_plhiv_2016_regions.png?ua=1) Over 1.8 million people were newly infected in 2017, out of which 59% were adult and 52% were children. In South Africa it was estimated that over 18.9% of adults had HIV in 2016, however, in Botswana there were 21.9% of adults having HIV infection (WHO *et al.*, 2017). In Lesotho there were 25% of adults having HIV infection. Fortunately, in India, there was a reduction in HIV patients. It is recorded that there were 0.274 million HIV patients in 2000 but this number reduced to 0.116 million in the year 2011. According to the data obtained in 2016, there were approximately 2 million new cases of HIV infection recorded globally and approximately one million people died of the infection (WHO *et al.*, 2017).

Scientists have been researching from time immemorial to find suitable medicinal plants that would act as anti-HIV. There are some plants that could be used to cure HIV/AIDS. For example, *Agastache rugosa* / Lamiaceae contain compounds like Arastanol and Agastaquinone. These compounds play an important role as they are protease inhibitors (Min *et al.*, 1999). *Alpinia rugosa* / Zingiberaceae contain 1'S-1' -acetoxychavicol which plays a crucial role against HIV as it has anti-HIV activity. There are many more plants like *Acer okamotoanum*, *Arnebia euchroma*, members of Labiateae, Clusiaceae, Ginkgoaceae, Dipterocarpaceae, *etc.* whose anti- HIV activity has been discovered. These plants contain some compounds which are responsible for these activities.

Pathophysiology:

HIV virus integrates the viral genome DNA, into host cell DNA. The receptors present on monocytes, dendritic cells, T lymphocytes, and macrophages are responsible for the entry of the virus into the cell (Deeks *et al.*, 2015). The

retrovirus, HIV attaches to the chemokine receptor 5 or CXCR4 chemokine receptor 4 presents on monocytes, dendritic cells, macrophages, and T lymphocytes. After entering the cell, RNA through reverse transcription becomes HIV DNA and is then incorporated into the host genome. Then it replicates over and over till the cell is present. This is why it is very tough to get rid of HIV fully. The genome now undergoes transcription and forms viral mRNA which is transferred to the cytoplasm and the mRNA translates into Gag-Pol, viral Gag, and Nucleoproteins and are cleaved during the final step of the cycle i.e. the formation of virus particles, their assembly, maturation and thus release of new virions takes place. The therapies inhibit either of the one stages of this cycle i.e. either inhibit the entry, reverse transcription, integration or transfer, *etc.*

Current treatment for HIV:

Since HIV identified, till there is no medicine or vaccines to cure it completely. In 1996, many antiretroviral therapies had been introduced which led to a significant decrease in the mortality of HIV and AIDS. Protease inhibition therapy is not committed (Auvert *et al.*, 2005; Bailey *et al.*, 2007; Anderson *et al.*, 2014). Due to the introduction of new therapies, HIV became a chronic and manageable disease from a fatal one. The survival rate has been increasing due to the introduction of highly active antiretroviral therapies. Scientists are finding new ways to cure HIV by developing new vaccines, antimicrobial agents, *etc.* (Anderson *et al.*, 2014; Maartens *et al.*, 2014). There are various substitutes available nowadays such as histone deacetylase (HDAC) inhibitors, anti-HIV antibodies, immune modulation and gene therapies which are considered to be a better alternative for antiretroviral therapy (ART) (Bailey *et al.*, 2007, Anderson *et al.*, 2014, Kharsany *et al.*, 2016).

Plant extracts and secondary metabolites:

Since the prehistoric period, several parts of the plants are used as medicine. Plants naturally fight against fungal, bacterial and viral attacks. Many plants produce secondary metabolites like phenolics, glycosides, alkaloids, essential oils and peptides (Sharifi *et al.*, 2016, Lucera *et al.*, 2014).

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These secondary metabolites have many biological activities and some of them also help in increasing antiviral immunity. Since antiretroviral therapies have many side effects such as liver infection, etc so, scientists are focusing on plants to cure HIV (WHO *et al.*, 1989, 1989, Kurapati *et al.*, 2016). During the course of finding a cure for HIV, excess of mind storming was done and this led to many new significant and beneficial discoveries. One such discovery is the identification of the anti-HIV activity of *Eclipta prostrata*. Although this plant is known to cure blood diseases and has been used for this purpose by the doctors in Thai, its anti-HIV property was first recorded by the bioassay technique. The six compounds identified were 5-hydroxymethyl-(2,2':5',2'')-terthienyltiglate, 5-hydroxymethyl-(2,2':5',2'')-terthienylagelate, 5-hydroxymethyl-(2,2':5',2'')-terthienyl acetate, ecliptal, orobol and wedelolactone. Out of all of them, wedelolactone showed highest activity against HIV-1 Integrase (IN) and had 4.0+0.2UM IC₅₀ value and orobol had IC₅₀ value of 8.1+0.5 UM whereas the other four compounds were inactive and had IC₅₀>100 UM. In terms of HIV-1 protease inhibitory activity, 5-hydroxymethyl-(2,2':5',2'')-terthienyltiglate had highest activity. HIV-1 PR with IC₅₀ of 58.3+0.8UM followed by ecliptal with IC₅₀ of 83.3+1.6UM and IC₅₀ of 93.7+0.8UM of 5-hydroxymethyl-(2,2':5',2'')-terthienyl acetate meanwhile 5-hydroxymethyl-(2,2':5',2'')-terthienylagelate, orobol and wedelolactone were inactive and had IC₅₀>100 UM. (Tewtrakul *et al.*, 2007).

So, there is a need to develop plant-based medicines or vaccines in order to reduce the side effects. The use of secondary metabolites to fight with HIV is one of the important steps (Guay *et al.*, 1999). The extracts of medicinal plants have been reviewed, which have shown to possess anti-HIV activities and some of these medicinal plants are - *Artemisia annua*, *Astragalus membranaceus*, *Calendula officinalis*, *Chelidonium majus*, *Combretum molle*, *Diospyros lotus*, *Dittrichia viscosa*, *Galanthus nivalis*, *Garcinia edulis*, *Hoodia gordonii*, *Hypericum perforatum*, *Hyssopus officinalis*, *Justicia gendarussa*, *Momordica charantia*, *Pachyma hoelen*, *Phyllanthus pulcher*, *Rhus chinensis*, *Sceletium tortuosum*, *Smilax corbularia*, *Terminalia paniculata* and *Tuberaria lignosa*.

Conclusion:

With the advancement in the techniques developed for curing HIV, there is an important need for natural methods. Several medicinal plants have been identified which are proven to have anti-HIV properties and can be seen as a potential cure for HIV. Thus, medicinal plants can be switched over the other antiretroviral therapies. Natural alternatives have less side effects as compared to ART.

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