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# MINI REVIEW ON MORINGA PLANT'S ROLE AGAINST HIV AND POTENTIAL MECHANISM OF FLAVONOID'S HYDROXYL GROUP IN INHIBITION OF HIV

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## ABSTRACT

Biological activity of Moringa oleifera.Lam, having potential applications in medicines, attributed to the presence of Phenolics compounds, such as phenolic acids, flavonoids. Previous study showed the role of moringa powder as nutritional as value by providing reduced mortality rates and enhancement health for HIV-positive and Aids patients. Following the highest rate of flavonoids in Moringa, we argued a potential mechanism of flavonoids against Reverse transcriptase of HIV-1. And the evidence that flavonoids structure are best promising anti-HIV compounds.

**KEYWORDS:** Moringa oleifera.Lam, Flavonoids, Anti-HIV, Hydroxyl group.

## INTRODUCTION

The proceedings of the 14th International AIDS Conference held in Barcelona, Spain in 2002 included a recommendation that moringa powder be considered as an alternative treatment to boost the immune systems of HIV-positive patients in Africa who would otherwise not receive antiretroviral drugs or, in fact, any treatments at all. Because moringa also provides superior nutritional value for patients it can also prove useful in preventing immune system breakdown due to malnutrition, thus offering even more help for poorer areas in Africa and around the globe.[32]

Moringa has a good safety profile consistent with its long history of use as food and medicine[31] in Africa, the leaf powder of *Moringa oleifera* Lam. is commonly used as a medicinal herb, rather than food as is the case in Asian populations. It is often taken as a supplement by HIV-infected people to enhance immunity and manage opportunistic infections.[32-33] In-vitro data suggest that moringa inhibits cytochrome P450 (CYP) 3A4, 1A2 and 2D6 activity which could potentially lead to metabolic interactions with antiretroviral drugs metabolized via the same pathways.[34-35-36]

Flavonoids consist of a large group of polyphenolic compounds with over 5000 flavonoids[22] and are ubiquitously present in plants are the result of metabolism of phenylpropanoides which is an exclusive secondary metabolism in the plant kingdom. it is made by the shikimate pathway, from phenylalanine.[27] Flavonoids are hydroxylated phenolic substances and are known to be synthesized by plants in response to microbial infection.[17] Recently there has been an upsurge of interest in the therapeutic potential of medicinal plants which might be due to their phenolic compounds, specifically to flavonoids.[18,19]

In higher plants, flavonoids are involved in UV filtration, symbiotic nitrogen fixation and floral pigmentation. They may also act as chemical messengers, physiological regulators, and cell cycle inhibitors. Flavonoids secreted by the root of their host plant help *Rhizobia* in the infection stage of their symbiotic relationship with legumes.[26]

They are a major coloring component of flowering plants. Flavonoids are an integral part of human and animal diet. Being phytochemicals, flavonoids cannot be synthesized by humans and animals[28] Thus flavonoids found in animals are of plant origin rather than being biosynthesized in situ.[17]

**Flavonoids are polyphenols universally found in plants except algae. They have been historically determinant for the discovery of fundamental biological phenomena such as the laws of heredity by Mendel, the presence of transposable elements and co-suppression RNAi[25]:** Some studies have showed Moringa leaves that an interesting level of flavonoids, due to their important antioxidant property, are involved in anti-carcinogenic, anti-viral, anti-estrogenic and immune-stimulating activities.[13,14,15,16,17]

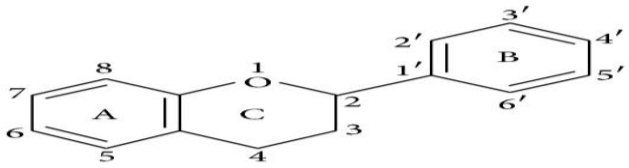


**Figure. 1: Basic flavonoid structure.**

**Table 2: Antiretroviral activity of flavonoids, by Reverse Transcriptase against HIV-1**

| Flavonoids | Mechanisms | References |
|---|---|---|
| 1. | Quercetin, | (Ono et al., 1990) |
| 2. | **Kaempferol,** | (Mohan K et al. 2012) |
| 3. | Apigenin, | (Critchfield JW et al .,1996) |
| 4. | Rutin | (Tao J et al.,2007) |
| 5. | 3-O-glucosides - kaempherol, | (Schinazi et al.1997), |
| 6. | 3-O-glucosides – quercetin | (Schinazi et al. (1997), |

**Antiviral Activity**

Natural compounds are an important source for the discovery and the development of novel antiviral drugs because of their availability and expected low side effects. Naturally occurring flavonoids with antiviral activity have been recognized since the 1940s and many reports on the antiviral activity of various flavonoids are available. Search of effective drug against human immunodeficiency virus (HIV) is the need of hour. Most of the work related with antiviral compounds revolves around inhibition of various enzymes associated with the life cycle of viruses. Structure function relationship between flavonoids and their enzyme inhibitory activity has been observed.[38]

Cushine et al 1983 demonstrated that flavan-3-o1 was more effective than flavones and flavonones in selective inhibition of HIV-1, HIV2, and similar immunodeficiency virus infections. Baicalin, a flavonoid isolated from Scutellaria baicalensis (Lamieaceae), inhibits HIV-1 infection and replication. Baicalein and other flavonoids such as robustaflavone and hinokiflavone have also been shown to inhibit HIV-1 reverse transcriptase.[39]

Fu et al. 2002 revealed inhibition of HIV-1 entry into cells expressing CD4 and chemokine coreceptors and antagonism of HIV-1 reverse transcriptase by the flavone O-glycoside. Catechins are also known to inhibit DNA polymerases of HIV-1. Flavonoid such as demethylated gardenin A and robinetin are known to inhibit HIV-1 proteinase.[39] J. W. Critchfield et al. 1996[40], reported that the flavonoids chrysin, acacetin, and apigenin prevent HIV-1 activation via a novel mechanism that probably involves inhibition of viral transcription.

Fu et al. 2010[39] reported that combinations of flavones and flavonols have been shown to exhibit synergism. Kaempferol and luteolin show synergistic effect against herpes simplex virus (HSV). Synergism has also been reported between flavonoids and other antiviral agents. Quercetin is reported to potentiate the effects of 5-ethyl-2-dioxyuridine and acyclovir against HSV and pseudorabies infection. Studies have displayed that flavonols are more active than flavones against herpes simplex virus type 1 and the activity order was found to be galangin, kaempferol, and quercetin.[39]

Zandi et al.[42] confirmed the antidengue virus properties of quercetin, hesperetin, naringin, and daidzein at different stages of DENV-2 (dengue virus type-2) infection and replication cycle. Quercetin was found to be most effective against DENV-2 in Vero cells. Many flavonoids, namely, dihydroquercetin, dihydrofisetin, leucocyanidin, pelargonidin chloride, and catechin, show activity against several types of virus including HSV, respiratory syncytial virus, polio virus and Sindbis virus 938). Inhibition of viral polymerase and binding of viral nucleic acid or viral capsid proteins have been proposed as antiviral mechanisms of action.[42] List of some flavonoids and their efficacy against viruses is given.

## DISCUSSION

According Chen et al.[29] found the chelate complexes of isoflavonoids with metal ions, demonstrate the antiviral, anti-cancer and antioxidant activity; following that, **the chelation of metals from flavonoids could be crucial in the prevention of radical generation which damage target biomolecules.[17]**

According Korkinat[44] reported by Nijveldt 2001 et.al 2001[43] Flavonoids can prevent injury caused by free radicals in various ways. One way is the direct scavenging of free radicals. Flavonoids are oxidized by radicals, resulting in a more stable, less-reactive radical. In other words, flavonoids stabilize the reactive oxygen species by reacting with the reactive compound of the radical. Because of the high reactivity of the hydroxyl group of the flavonoids, radicals are made inactive, according to the following equation: Flavonoid(OH) + R· > flavonoid(O·) + RH

where $R^{\cdot}$ is a free radical and $O^{\cdot}$ is an oxygen free radical. Selected flavonoids can directly scavenge superoxides, whereas other flavonoids can scavenge the highly reactive oxygen-derived radical called peroxynitrite.

Flavonoids are known to chelate iron thereby removing a causal factor for the development of free radicals. Quercetin is known for its iron-chelating and iron-stabilizing properties. Direct inhibition of lipid peroxidation is another protective measure.[43]

According Schinazi et al. (1997), reported by (9) among the 17 flavonols tested only 3-O-glucosides of kaempferol, quercetin, and myricetin caused significant inhibition of HIV-1 at nontoxic concentrations. At the same time other comparative studies with other flavonoids revealed that the presence of both the double bond between positions 2 and 3 of the flavonoids pyrone ring, and the three hydroxyl groups introduced on positions 5,6 and 7 (ie, baicalein) was a prerequisite for the inhibition of RT-activity.

Overall, the flavonol, Myricetin, with adjacent hydroxyl groups at the 3′, 4′, and 5′ positions, showed superior inhibition of HIV activity compared to the other two flavonoids that presented only modest activity against HIV-1: Quercetin, which lacks a hydroxyl group at the 5′ position, and Pinocembrin that lacks hydroxyl groups at the 3′, 4′, and 5′ positions. Results from previous studies by Mehla et al.[21] have shown that the flavonoid, Luteolin, which lacks hydroxyl groups on 5′ and 3′ positions, presents higher toxicity and activity against HIV-1 than Myricetin, Quercetin or Pinocembrin. These observations suggest that a hydroxyl group at position 3 is required for inhibitory effects, and additionally, the hydroxyl groups at 3′, 4′, and 5′ affect the toxicity.[9]

The prenylflavonoids had positive effects on anti-virus activity. (−)-5,4′-Dihydroxy-7,8-[(3″-hydroxy-4″-one)-2″,2″-dimethylpyrano]-flavone from *Poncirus trifoliata* L. (Rutaceae) showed significant anti-HIV-1 activity with high therapeutic index (TI) of 143.65 (37) ,the anti-virus mechanism of prenylated flavonoids is still waiting to be elucidated.

**Hypothesis**

From the above, it is clear that the hydroxyls group, described by Schinazi would give evidence of the anti-HIV role of flavonoids, by their precise role of enzymatic inhibitors by the mechanism of induced fit, and confer their toxicity through suicide inhibition[13], all because of the ability of this group of polyphenols to constantly change their structures as a result of their interactive state through their sensitivity to PH of the medium[23] and in contact with enzymes[24], as confirmed in the plants or has collected more than 4000 flavonoids.[22]

Reverse Transcriptase from HIV requires the presence of divalent $Mg^{2+}$ for both its activities including. It is the p66 subunit that carries these activities within the heterodimer[30], our hypothesis would be that most flavonoids which have the capacity to create chelation from their hydroxyl groups with the metal ions of the p66 subunit of HIV thereby inhibiting and affecting the whole virus By interference of the normal functioning of the virus, blocking a DNA or RNA dependent DNA polymerase activity and also the R Nase H activity which degrades the RNA strand in an RNA-DNA hybrid.

## CONCLUSION

Prevention and cure of diseases using Moringa phytochemicals especially flavonoids, should be better, following le role of flavonoids as anti-HIV compounds. Our research allowed us to discover over 100 phenolics compounds, mostly flavonoids, through insoluble-phenolic, Free-phenolic and esterified phenolic extractions from moringa. Which were reported should have Medicinal efficacy as antimicrobial, antiviral.

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