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Herbal Formulations: A Periodontal Perspective in AIDS Patients

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Abstract: ***AIDS is characterized by profound infection of the immune system. HIV is a retrovirus, detected in body fluids. AIDS presents certain complications. Intra-oral features include linear gingival erythema, oral hairy leukoplakia, Kaposi's sarcoma, candidiasis in brief. Although HAART cannot cure HIV infections & anteretrovirals have an impact of reducing morbidity, morbifity, mortality, prolonging lives. Many people cannot afford the high costs of treatment of HAART. Herbal medicines, among the most popular complementary therapeutic modalities are derived from plants used for treatment of symptoms. In some countries it is used as primary treatment protocols. It is imperative that the patients maintain meticulous oral hygiene as part of maintenance therapy. Strict infection control is required during treatment. Some herbal contain as many as 31 herbs. This paper presents an overview of periodontal implications of AIDS, the herbal formulations used for treatment for such clinical symptoms. The acquired immunodeficiency syndrome (AIDS) is a result of human immunodeficiency virus (HIV) infection which subsequently leads to significant suppression of immune functions. AIDS is a significant threat to the health of mankind and the search for effective therapies to treat AIDS is of paramount importance. Several chemical anti-HIV agents have been developed. However, besides the high cost, there are adverse effects and limitations associated with using chemotherapy for the treatment of HIV infection. Thus, herbal medicines have frequently been used as an alternative medical therapy by HIV positive individuals and AIDS patients. The aim of this review is to summarize research findings for herbal medicines, which are endowed with the ability to inhibit HIV***

Keywords: herbal formulations, periodontitis, AIDS, HIV, Hiraea reclinata

1. Introduction

Viruses are small obligate intracellular parasites, which by definition contain either a RNA or DNA genome surrounded by a protective, virus-coded protein coat. HIV assembly and replication proceed through the formation of morphologically distinct immature and mature viral capsids that are organized by the Gag polyprotein (immature) and by the fully processed CA protein (mature). The Gag polyprotein is composed of three folded polypeptides (MA, CA, and NC) and three smaller peptides (SP1, SP2, and p6) that function together to coordinate membrane binding and Gag-Gag lattice interactions in immature virions. Following budding, HIV maturation is initiated by proteolytic processing of Gag, which induces conformational changes in the CA domain and results in the assembly of the distinctive conical capsid. Retroviral capsids are organized following the principles of fullerene cones, and the hexagonal CA lattice is stabilized by three distinct interfaces. Recently identified inhibitors of viral maturation act by disrupting the final stage of Gag processing, or by inhibiting the formation of a critical intermolecular CA-CA interface in the mature capsid. Following release into a new host cell, the capsid disassembles and host cell factors can potently restrict this stage of retroviral replication (Pornillos G B K et al). HIV infection remains a significant health care problem. Since Barre-Sonoussi and Gallo's initial description of the human immunodeficiency virus type I (HIV-1) in 1983 and Clavel et al. first described HIV-2 in 1986, these two viruses have been recognized for almost 20 years as the primary cause of the acquired immunodeficiency syndrome (AIDS). Oral manifestations are among the earliest and most important indicators of HIV infection. Few people with HIV infection fail to experience oral opportunistic lesions during the course of their disease. These are several oral mucosa and salivary gland manifestations that were not seen before the AIDS epidemic, while others are more severe in this population. Oral lesions reflect HIV status and the stage of immunosuppression are important clinical elements in HIV staging and classification schemes: these elements raise pertinent questions about mucosal aspects of immunosuppression and provide therapeutic challenges. Their pervasive nature and biological significance emphasize the importance of a careful oral examination as part of the general clinical evaluation. Prevention and treatment of oral diseases are required to maintain and improve the lifestyle of the patients infected with HIV. Odontoiatric and stomatologic managements require a team approach and a close collaboration with the appropriate responsible physicians and other health care workers are necessary (Spardari F et al).

Oral Lesions:[1,2]

Oral manifestations are among the earliest and most important indicators of HIV infection. At present, three groups of oral manifestations of AIDS are defined based on their intensity and features. Group 1 is composed of seven cardinal lesions (oral candidosis, hairy leukoplakia, Kaposi sarcoma, linear gingival erythema, necrotizing ulcerative gingivitis, necrotizing ulcerative periodontitis, and non-Hodgkin lymphoma) that are strongly associated with HIV infection. The second group includes atypical ulcers, salivary glands diseases, viral infection such as cytomegalovírus (CMV), herpes simplex virus (HSV), papillomavirus (HPV), and herpes zoster virus (HZV). On group 3 are lesion rarer than those on groups 1 and 2, such as diffuse osteomyelitis and squamous cell carcinoma

Plaque control in AIDS patients with intra-oral lesions[3]

The presence of oral lesions can have a significant impact on health-related quality of life. Oral health is strongly associated with physical and mental health, and there are significant increases in oral health needs in people with HIV infection, especially in children, and in adults particularly in

relation to periodontal diseases. Monitor the incidence of tooth loss, caries and attachment loss during a 30-year period in a group of adults who maintained a carefully managed plaque control program. The present study reported on the 30-year outcome of preventive dental treatment in a group of carefully monitored subjects who on a regular basis were encouraged, but also enjoyed and recognized the benefit of, maintaining a high standard of oral hygiene. The incidence of caries and periodontal disease as well as tooth mortality in this subject sample was very small. Since all preventive and treatment efforts during the 30 years were delivered in one private dental office, caution must be exercised when comparisons are made with longitudinal studies that present oral disease data from randomly selected subject samples

Role of herbal mouthwashes:[4]

Some natural products are shown to have activity against HIV. These have variety of chemical structure & modes of action.

Target	Compound	Class	Plant
Reverse transcriptase	Elagtannin	Tannin	-----
	Hydroxymapruonic acid, hydroxybenzoate	Terpenoids	Maprounea africana
	Betulinic acid, platanic acid	Terpenoids	Syzigium claviforum
	Catechin	Polyphenol	----
	Faicalein, quercetin, myricetin, baicalin	Flavonoids	Querus rubra others
	Nigranoic acid	Terpenoids	Schisandre sphaerandra
	Amentoflavone acutelarein	Flavonoids Flavones	-----

Algae:[5]

The acquired immune deficiency illness syndrome is caused by the human immunodeficiency virus (HIV) (AIDS). This article reviews the anti-HIV activity of extracts and compounds isolated from freshwater and marine algae, as well as cyanobacteria (formerly called "blue-green algae"). Compounds and extracts with anti-HIV activity are also active against other retroviruses such as herpes simplex virus (HSV), but the antiviral activity varies depending on the compound and the virus. Sulfated homopolysaccharides and heteropolysaccharides have dominated the majority of research. Other classes of anti-HIV compounds isolated from algae, including sulfoglycolipids, carrageenans, fucoidan, and sesquiterpene hydroquinones, have received less attention. A few in vivo studies using compounds isolated from algae or analogues produced synthetically or isolated from other natural sources have been conducted. Compared to sulfated heteropolysaccharides, sulfated homopolysaccharides are more potent. Anti-HIV activity requires the presence of a sulphate group, and the degree of sulfation increases potency. Studies utilising nonsulfated and sulfated homo- and heteropolysaccharides isolated from algae or other natural sources, or synthesised, have elucidated the mechanisms of drug binding to the virion and the mechanisms of viral binding to host cells. Hiraea reclinata:6 The genus Hiraea (Malpighiaceae) consists of about 40 species in the American tropics, primarily found in rain forests.

Hiraea reclinata[6]

The (Malpighiaceae) family is found in Mexico, Panama, Colombia, Venezuela, and Brazil. For this genus, neither phytochemical research nor ethnomedicinal claims have been reported. The anti-HIV activity of the total methanolic extract of the mature leaves of H. reclinata, prompted us to conduct a phytochemical investigation in order to isolate the anti-HIV active component(s) of this plant. Only 1,3,4,5-tetragalloyl quinic acid possessed anti-HIV activity in the Methanolic extract of Hiraea reclinata. Various water-soluble polysulphonated and polycarboxylated porphyrins and some of their metallated derivatives have been prepared, and their antiviral properties against human immunodeficiency virus (HIV-1, HIV-2) and other viruses have been reported (Hussein A A et al). In addition to these polyanionic compounds, two new series of porphyrins were included and studied from the standpoint of bioavailability modulation: I acefylsulphonamido derivatives with weak acidity properties (deprotonation gives the corresponding anionic derivatives in a pH range of 4.5-8.5) and (ii) compounds with the anionic charge transiently masked by esterification (acetoxymethyl- and pivaloyloxymethylesters). The sulphonated and carboxylated porphyrin complexes were discovered to interact directly with the HIV protein gp 120 but not with the CD4 cellular receptor, making them among the most potent compounds for inhibiting HIV-induced cytopathic effects.

Scutellaria baicalensis Georgi: [7]

Scutellaria baicalensis Georgi has been included in the Chinese Pharmacopoeia, the Japanese Pharmacopoeia, the Korean Pharmacopoeia, and the European Pharmacopoeia due to its long history of use in traditional medicine for the treatment of a wide range of diseases. Flavonoids, particularly wogonin, wogonoside, baicalin, and baicalein, are its primary active ingredients with diverse pharmacological effects. Although pharmacological studies on these flavonoid components have been conducted effectively, the molecular mechanism underlying their biosynthesis in S. lycopersicum is still unknown. baicalensis. In this study, Illumina/Solexa deep sequencing was used to generate over 91 million paired-end reads and 49,507 unigenes from S. baicalensis stems, roots, leaves, and flowers. Scutellaria baicalensis Georgi (Baikal skullcap or Huang-Qin in Chinese), a member of the Lamiaceae family, has been included in the Chinese Pharmacopoeia [1], the Japanese Pharmacopoeia [2], the Korean Pharmacopoeia [3], and the European Pharmacopoeia [4]. Numerous diseases, including cancer, hepatitis, allergies, inflammation, skin conditions, and epilepsy, have been successfully treated with its flavone-rich dry root [5]. Baicalin, baicalein, wogonoside, and wogonin are the principal flavonoid constituents of S. baicalensis, and have various pharmacological activities, including antitumor effects, antioxidative action, anti-inflammatory, antibacterial and antiviral activities [6–8]Scutellaria baicalensis Georgi and its identified components (i.e., baicalein and baicalin), which have been shown to inhibit HIV infection and replication.

Sho-Saiko-To[8]

is a Japanese herbal supplement that contains baicalin, baicalein, and wogonin as its primary active ingredients. Baicalin is the glucuronide of baicalein, and wogonoside is

the glucuronide of wogonin. Baicalin and wogonoside are hydrolyzable directly into baicalein and wogonin. The total amount of baicalein in the roots of S. baicalensis is considerably taller, including stems, leaves, and flowers, in the aboveground portion of the plant. With the exponentially increasing use of S. baicalensis for medicinal purposes in recent years, the plant's wild resource is insufficient to meet demand.

O. sanctum, T. cordifolia, A. both R. officinalis and R. mucronata: (Rege A A et al)

O. sanctum, T. cordifolia, A. the plant species R. By inhibiting the virus via two distinct mechanisms, mucronata demonstrated anti-HIV potential. Interference with the gp120/CD4 interaction and inhibition of viral ReverseTranscriptase (RT) contributed to the total in vitro antiviral activity.

Alkaloids

Several alkaloids have HIV-inhibiting properties. Michellamines are atropisomeric naphthylisoquinoline alkaloid dimers isolated from the leaves of Ancistrocladus korupensis (family Anci strocladaceae), a plant native to the southwest Province of Cameroon's Korup National Park. Michellamine B inhibits reverse transcriptase and cellular fusion and syncytium formation during early and late stages of the HIV life cycle, respectively. Castanospermine, a tetrahydroxy indolizidine alkaloid isolated from Castanospermum austral (Fabaceae), a plant native to the rainforests of eastern and northern Australia, inhibited HIV replication and syncytium formation induced by the HIV envelope glycoprotein. Additionally, glycosidase-inhibiting properties have been reported. Buchapine, a quinolinone with two isoprene units, and its structural isomer (3-methyl-2-butenyl), 4[(3-methyl-2-butenyl) oxy]-2(1H)-quinolinone (4) isolated from Eodia roxburghiana, a plant native to Southeast Asia and Australia, protected CEM-SS cells from the cytopathic effects of HIV-1 in vitro. wilfordii exhibited potent anti-HIV activity in vitro, with a therapeutic index greater than 1,000.[9]

FK-3000

A morphine-related compound derived from the methanolic extract of the root tubers of Stephania cepharantha (family Menispermacea), inhibited the cytopathic effects of HIV1 on MT4 cells at 7.8g/ml. Nitidine (isolated from roots of Toddalia asiatica (family Rutaceae) exhibited significant anti-HIV activity in the cell-based assay. Cepharanthine (9) isolated from the same plant has been reported to have antiallergic, anti-inflammatory, and immunomodulatory properties, as well as inhibit HIV-1 replication potently. There is also evidence that it inhibits HIV reverse transcriptase. O-Demethyl-buchenavianine (11), a piperidine-flavone-related alkaloid isolated from Buchenavia capitata (family Combretaceae), exhibited anti-HIV and anti-cancer cell-based activity. Harmine isolated from Symplocos setchuensis was discovered to inhibit HIV replication in H9 lymphocyte cells. Among its 28 derivatives, N-butylharmine (13) was found to be the most potent, with an EC50 of 0.037 M and a therapeutic index of 1. Methoxy canthinone isolated from Leitneria floridana demonstrated significant anti-HIV activity (ECis 0.26g/ml).[10]

Coumarins

including calanolides and inophyllums, have been identified as non-nucleoside-specific inhibitors of HIV reverse transcriptase. These are derived from various species of Callophyllum (family Clusiaceae), a genus found primarily in the Indo-Pacific region, specifically Malaysia. Calanolide A (calanolide B (16) and its dihydro derivative, (7,8-dihydrocalanolideB, inhibited the cytopathic effects of HIV 1 in T-cell lines, including both CEM-SS and MT-2 cells. [11]

Calanolide A is undergoing phase II clinical trials that are assessing its long-term anti-HIV activity in combination with other anti-HIV agents as well as the long-term durability of such drug combinations. Cordatolide A (17) and B (18), structural analogues of calanolides isolated from Callophyllum corditolongum, exhibited potent inhibitory activity against HIV1 replication in a novel reporter cell assay utilising green fluorescent protein.

Other extracts

include Cistus incanus extract, Desmos (Chalones & flavonoids), the aqueous extracts of Melissa officinalis, a member of the Menthapiperita "grapefruit mint" family, and Menthapiperita var. crispa, Ocimum basilicum cv "cinnamon", Perilla frutescens var. crispa f.viridis, Prunella vulgaris subsp. asiatica and Satureja montana exhibited powerful anti-HIV-1 activity (with an ED of 16g/ml). Active components in the extract samples were found to be water-soluble polar substances, as opposed to nonpolar compounds like essential oils. In addition, these aqueous extracts inhibited giant cell formation in co-cultures of Molt-4 cells with and without HIV-1 infection and demonstrated inhibitory activity against HIV-1 reverse transcriptase. Pure Compounds Isolated from Rosa damascene, Anti-HIV Coumarins Extracted from Calophyllum Seed Oil. Hypoxis and Sutherlandia are two African medicinal plants used to treat HIV. Certain Chinese and Mongolian herbal medicines, including Prunella vulgaris and Rhizoma cibotte, have also been investigated for their anti-human immunodeficiency virus type 1 (HIV-1) properties.[12]

2. Summary & Conclusion

Oral hygiene products containing these formulations may play a significant role in reducing the bacterial load in saliva and plaque, as well as in other niches where microbes reside.

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