

Plantas com efeito na AIDS - SIDA - HIV positivo

Paula Viñas

José de Felipe Junior

Alfavaca

Anti-HIV-1 activity of herbs in Labiatae.

Biol Pharm Bull. 1998 Aug;21(8):829-33.

Yamasaki K, Nakano M, Kawahata T, Mori H, Otake T, Ueba N, Oishi I, Inami R, Yamane M, Nakamura M, Murata H, Nakanishi T.

Osaka Prefectural Institute of Public Health, Japan.

The anti-HIV-1 activity of aromatic herbs in Labiatae was evaluated in vitro. Forty five extract from among 51 samples obtained from 46 herb species showed significant inhibitory effects against HIV-1 induced cytopathogenicity in MT-4 cells. In particular, the aqueous extracts of *Melissa officinalis*, a family of *Mentha x piperita* "grapefruit mint," *Mentha x piperita* var. *crispa*, *Ocimum basilicum* cv "cinnamon," *Perilla frutescens* var. *crispa* f. *viridis*, *Prunella vulgaris* subsp. *asiatica* and *Satureja montana* showed potent anti-HIV-1 activity (with an ED of 16 microg/ml). The active components in the extract samples were found to be water-soluble polar substances, not nonpolar compounds such as essential oils. In addition, these aqueous extracts inhibited giant cell formation in co-culture of Molt-4 cells with and without HIV-1 infection and showed inhibitory activity against HIV-1 reverse transcriptase.

Plant substances as anti-HIV agents selected according to their putative mechanism of action .

J Nat Prod;67(2):284-93, 2004 Feb. Cos P; Maes L; Vanden Berghe D; Hermans N; Pieters L; Vlietinck A

Resumo: Despite the continuous advances made in antiretroviral combination therapy, AIDS has become the leading cause of death in Africa and the fourth worldwide. Today, many research groups are exploring the biodiversity of the plant kingdom to find new and better anti-HIV drugs with novel mechanisms of action. In this review, plant substances showing a promising anti-HIV activity are discussed according to the viral targets with which they interact. Most of these compounds, however, interfere with early steps in the HIV replication, such as the virus entry steps and the viral enzymes reverse transcriptase and integrase, whereas until now almost no plant compounds have been found to interact with the many other viral targets. Since some plant substances are known to modulate several cellular factors, such as NF-kappa B and TNF-alpha, which are also involved in the replication of HIV, their role as potential anti-HIV products is also discussed. In conclusion, several plant-derived antiviral agents are good candidates to be further studied for their potential in the systemic therapy and/or prophylaxis of HIV infections, most probably in combination with other anti-HIV drugs.

Using herbs.

AIDS Action;(46):5, 1999 Oct-Dec.

Mcmillen H; Scheinman D

Antiviral and antiphlogistic activities of Hamamelis virginiana bark.

Planta Med;62(3):241-5, 1996 Jun. Erdelmeier CA; Cinatl J; Rabenau H; Doerr HW; Biber A; Koch E

Resumo: A crude hydroalcoholic extract from *Hamamelis virginiana* bark was subjected to ultrafiltration (UF) with a cut-off limit of 3 kDa to obtain a higher and a lower molecular weight fraction. Characterisation of the fractions was attempted with TLC, HPLC, acidic hydrolysis, and chromatography over Sephadex LH-20. The UF-concentrate was shown to consist mainly of oligomeric to polymeric proanthocyanidins (PA). This fraction was found to exhibit significant antiviral activity against Herpes simplex virus type 1 (HSV-1). In addition, the UV-concentrate displayed radical scavenging properties, inhibited alpha-glucosidase as well as human leukocyte elastase (HLE), and exhibited strong antiphlogistic effects in the croton oil ear edema test in the mouse. With the exception of the antioxidant potential and the inhibition of HLE-action the lower molecular fraction possessed weaker activities and contained mainly hamamelitannin, catechin, and further, unidentified constituents.

The role of traditional healers in HIV / AIDS counselling in Kampala, Uganda. Key issues and debates: traditional healers.

Soc Afr SIDA;(13):2-3, 1996 Jul. Homsy J; King R

País de publicação: FRANCE

Viscum album

Toxicity of a standardized mistletoe extract in immunocompromised and healthy individuals.

Am J Ther;6(1):37-43, 1999 Jan. van Wely M; Stoss M; Gorter RW

Resumo: Iscador is being used by many patients as unconventional anticancer and immunomodulating therapy. To determine the toxicity profile and biochemical effects of Iscador Qu Spezial (Weleda AG Schwäbisch Gmünd, Germany) in human immunodeficiency virus (HIV)-positive patients and healthy controls, we performed a phase I/II study. Escalating doses of Iscador Qu Spezial, standardized for its lectin and viscotoxin content, were administered to 16 HIV-positive patients and 8 healthy subjects during a period of 6 to 8 months. Iscador Qu Spezial preparations were administered twice per week subcutaneously in increasing doses (ie, 0.01 mg, 0.1 mg, 1.0 mg, 2.0 mg, 5.0 mg, and 0.1 mg/kg for 2-6 weeks per dose). Drug-related adverse effects were flulike symptoms, gingivitis, fever, local erythema, and eosinophilia. These side effects were never severe. The incidence of systemic adverse events was highest in HIV-positive patients. Furthermore, increased urea levels and slightly decreased total protein caused by a minor decrease in albumin were observed. None of the HIV-positive patients progressed in disease stage. Iscador Qu Spezial can be administered safely to immunocompromised patients.

Study on local inflammatory reactions and other parameters during subcutaneous mistletoe application in HIV-positive

patients and HIV-negative subjects over a period of 18 weeks.

Arzneimittelforschung;49(4):366-73, 1999 Apr. Stoss M; van Wely M; Musielsky H; Gorter RW

Resumo: Subcutaneous injections of fermented and unfermented aqueous extracts of *Viscum album L.* result in a local inflammatory reaction at the injection site. In this trial, the symptoms associated with this local reaction were investigated. Furthermore the occurrence of local reactions was tried to correlate with an increase in CD3/25- and CD8/38-positive lymphocyte counts, with eosinophilic granulocyte numbers, and with the formation of mistletoe lectin antibodies. Included in the trial were 30 HIV-antibody-positive patients and 17 healthy non-smokers, aged 24-51 years. The CD4 cell count in the HIV-negative subjects was > 800/microliter, compared with 200-600/microliter in the HIV-positive patients. All study participants had a Karnofsky score > or = 70. The trial subjects were observed over a period of 18 weeks. With escalation of the dose of a fermented and unfermented extract of *Viscum album L.* (Iscador Qu Spezial and *Viscum album QuFrF*), there was an increase in local reactions. Erythema at the injection site was the most frequently reported symptom. Between the doses and the symptoms induration, swelling and pruritus were marked correlations. Effects of the application of mistletoe extracts on the immune system were demonstrated by an increase in CD3/25-positive lymphocyte counts and antibodies against mistletoe-lectins. There were no changes in eosinophilic granulocytes or CD8/38-positive lymphocyte populations. For evaluation of the therapeutic applications of mistletoe extracts in HIV-positive patients it is advisable to assess primarily activation of CD3-positive lymphocytes and the patient response on the basis of the local reaction. The local inflammatory reaction at the injection site is desirable and well tolerated if the reaction is smaller than 5 cm in diameter.

Tolerability of an extract of European mistletoe among immunocompromised and healthy individuals.

Altern Ther Health Med;5(6):37-44, 47-8, 1999 Nov. Gorter RW; van Wely M; Reif M; Stoss M

Resumo: CONTEXT: European mistletoe (*Viscum album L.*) has been used parenterally for more than 80 years as an anticancer medication with significant immunomodulating action. Since 1984, clinical experience with a *Viscum album* extract (*Viscum album Quercus Frischsaft [Qu FrF]*) among HIV-positive patients has suggested that it inhibits HIV disease progression. OBJECTIVE: To determine the toxicity profile and biochemical effects of a *Viscum album* extract. DESIGN: A dose-escalating phase I/II study. PATIENTS: 32 HIV-positive and 9 healthy participants. INTERVENTION: Standardized for its lectin and viscotoxin content, the extract was administered subcutaneously twice weekly in gradually increasing doses for 2 to 17 weeks per dose increase. Doses of 0.01 mg to 10.0 mg were administered. MAIN OUTCOME MEASURES: Adverse events, hematology, and biochemistry. RESULTS: No severe side effects were found. During gradual dose escalation, more adverse events occurred at the lower dose range. The hazard rate of systemic adverse events was highest among HIV-positive patients. Drug-related adverse events were flu-like symptoms and transient exacerbations of gingivitis, fever, and eosinophilia. An increase of serum urea nitrogen and serum creatinine levels occurred, as did a slight decrease in total protein caused by a minor fall in albumin concentrations. Dose dependence was apparent for inflammation and fever, which may or may not have been side effects of the preparation. CONCLUSIONS: *Viscum album Qu FrF* can be administered safely to HIV-positive patients. It induces immunomodulation in HIV-positive and healthy individuals and may inhibit the progression of HIV disease.

No evidence of IFN-gamma increase in the serum of HIV-positive and healthy subjects after subcutaneous injection of a non-fermented viscum album L. extract.

Nat Immun;16(4):157-64, 1998. Stoss M; Gorter RW

Resumo: Iscador, an aqueous extract of *Viscum album L.*, has been used for more than 80 years as an anticancer drug. Due to its immunomodulatory potential, since the onset of the AIDS epidemic it has also been applied in the treatment of HIV-positive and AIDS patients in the form of the preparation *V. album QuFrF (VaQuFrF; Labor Hiscia, Arlesheim, Switzerland)*. In vitro investigations, incubation of peripheral blood mononuclear cells with *V. album L.* extracts resulted in stimulation of lymphocyte activity with increased gene expression and release of various cytokines and also of interferon gamma (IFN-gamma). In the latent phase, HIV positives exhibit only slightly elevated IFN-gamma concentrations in serum in comparison with HIV negatives, but in the acute phase of AIDS, there is an increase in levels of IFN-gamma. As the assay of cytokine levels in serum is a simple method of measuring immune system reactions, the aim of this trial was to determine whether increases in serum IFN-gamma levels in HIV positives and HIV negatives can be detected using this method after repeated injections of VaQuFrF. Five healthy subjects and 13 HIV-positive patients were investigated. IFN-gamma concentrations in serum were assayed using an ELISA test kit (ELISA test; ENDOGEN, Cambridge, Mass., USA). No drug-related elevation of serum IFN-gamma was observed at any time point during the trial. It can thus be concluded that this method is not suitable for direct investigation of the immunomodulatory effects of VaQuFrF in vivo.

Miscelânea

The mannose-specific plant lectins from *Cymbidium hybrid* and *Epipactis helleborine* and the (N-acetylglucosamine)-n-specific plant lectin from *Urtica dioica* are potent and selective inhibitors of human immunodeficiency virus and cytomegalovirus replication in vitro.

Antiviral Res;18(2):191-207, 1992 Jun. Balzarini J; Neyts J; Schols D; Hosoya M; Van Damme E; Peumans W; De Clercq E

Resumo: A series of four mannose(Man)-, three N-acetylglucosamine (GlcNAc)n-, ten N-acetylgalactosamine/galactose (GalNAc/Gal)-, one 5-acetylneuraminic acid (alpha-2,3-Gal/GalNAc)- and one 5-acetylneuraminic acid(alpha-2,6-Gal/GalNAc)-specific plant agglutinins were evaluated for their antiviral activity in vitro. The mannose-specific lectins from the orchid species *Cymbidium hybrid* (CA), *Epipactis helleborine* (EHA) and *Listera ovata* (LOA) were highly inhibitory to human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2) in MT-4, and showed a marked anti-human cytomegalovirus (CMV), respiratory syncytial virus (RSV) and influenza A virus activity in HEL, HeLa and MDCK cells, respectively. The 50% effective concentration (EC50) of CA and EHA for HIV ranged from 0.04 to 0.08 micrograms/ml, that is about 3 orders of magnitude below their toxicity threshold (50% inhibitory concentration for MT-4 cell growth: 54 to 60 micrograms/ml). Also, the (GlcNAc)n-specific lectin from *Urtica dioica* (UDA) was inhibitory to HIV-1-, HIV-2-, CMV-, RSV- and influenza A virus-induced cytopathicity at an EC50 ranging from 0.3 to 9 micrograms/ml. The GalNAc/Gal-, alpha-2,3-Gal/GalNAc- or alpha-2,6-Gal/GalNAc-specific lectins were not inhibitory to HIV or CMV at non-toxic concentrations. CA, EHA and UDA proved to be potent inhibitors of syncytium formation between persistently HIV-1- and HIV-2-infected HUT-78 cells and CD4+ Molt/4 (clone 8) cells (EC50: 0.2-2 micrograms/ml). Unlike dextran sulfate, the plant lectins CA, EHA and UDA did not interfere with HIV-1 adsorption to MT-4 cells and RSV- and influenza A virus adsorption to HeLa and MDCK cells, respectively. They presumably interact at the level of virion fusion with the target cell.

Proteins with abortifacient, ribosome inactivating, immunomodulatory, antitumor and anti-AIDS activities from Cucurbitaceae plants.

Gen Pharmacol;23(4):579-90, 1992 Jul. Ng TB; Chan WY; Yeung HW

Department of Biochemistry, Faculty of Medicine, Chinese University of Hong Kong

Resumo: 1. The biochemical characteristics and biological activities of eight Cucurbitaceae plant proteins designated trichosanthin

(isolated from tubers of *Trichosanthes kirilowii*), beta-trichosanthin (isolated from tubers of *Trichosanthes cucumeroides*), alpha- and beta-momorcharins (isolated from seeds of *Momordica charantia*), momorchochin (isolated from tubers of *Momordica cochinchinensis*), luffaculin (isolated from seeds of *Luffa acutangula*) and luffin-a and luffin-b (isolated from seeds of *Luffa cylindrica*), were reviewed. 2. The isolation procedures for all eight proteins are based on aqueous extraction, acetone fractionation and ion exchange chromatography. Ammonium sulfate precipitation and gel filtration are steps which may be included to improve purification. 3. The proteins are basic in nature and possess a molecular weight of approx. 30,000. All except trichosanthin are glycoproteins. The content of Asx and Glx residues is high. The N-terminal amino acid residue is Asp. Their amino acid compositions and N-terminal amino acid sequences are similar. 4. Circular dichroism spectroscopic studies revealed that trichosanthin, alpha- and beta-momorcharins possess similar secondary but different tertiary structures. 5. Most of the proteins are immunologically distinct. 6. The proteins exhibit abortifacient, antitumor, ribosome inactivating and immunomodulatory activities. Trichosanthin manifests anti-human immunodeficiency virus activity.

Can ethnopharmacology contribute to the development of antiviral drugs?

J Ethnopharmacol;32(1-3):141-53, 1991 Apr. Vlietinck AJ; Vanden Berghe DA

Faculty of Medicine, University of Antwerp (UIA), Belgium.

Resumo: In recent years, many compounds having potent antiviral activity in cell cultures and in experimental animals have been detected, but only a few have been approved by Western health authorities for clinical use. Nevertheless, some of these compounds are currently undergoing either preclinical or clinical evaluation, and perspectives for finding new interesting antiviral drugs are promising. Among these antiviral substances are several natural compounds isolated from plants used in traditional medicine including polysaccharides, flavonoids, terpenes, alkaloids, phenolics and amino acids. Some of these plant compounds exhibit a unique antiviral mechanism of action and are good candidates for further clinical research. What follows is a brief summary of the selection methods of plants for antiviral screening and in vitro and in vivo assays, which are currently used for detecting this activity in plant extracts. The importance of the plant kingdom as a source of new antiviral substances will be illustrated by presenting a survey on plant-derived antirhinovirus and anti-HIV agents.

TAP 29: an anti-human immunodeficiency virus protein from *Trichosanthes kirilowii* that is nontoxic to intact cells.

Proc Natl Acad Sci U S A;88(15):6570-4, 1991 Aug 1. Lee-Huang S; Huang PL; Kung HF; Li BQ; Huang PL; Huang P; Huang HI; Chen HC

Resumo: An anti-human immunodeficiency virus (anti-HIV) protein capable of inhibiting HIV-1 infection and replication has been isolated and purified to homogeneity from *Trichosanthes kirilowii*. This protein, TAP 29 (*Trichosanthes* anti-HIV protein, 29 kDa), is distinct from trichosanthin [also known as GLQ 223 (26 kDa)] in size, N-terminal amino acid sequence, and cytotoxicity. In addition to three conservative substitutions--namely, Arg-29 to Lys, Ile-37 to Val, and Pro-42 to Ser--a total difference of residues 12-16 was found. TAP 29 yielded -Lys-Lys-Lys-Val-Tyr-, whereas trichosanthin has -Ser-Ser-Tyr-Gly-Val-. Although the two proteins exhibit similar anti-HIV activity, as measured by syncytium formation, p24 expression, and HIV reverse transcriptase activity, they differ significantly in cytotoxicity, as measured by their effects on cellular DNA and protein syntheses. At the dose level of the bioassays, 0.34-340 nM, trichosanthin demonstrates a dose-dependent toxic effect on host cells. TAP 29 displays no toxic effect, even at 100 X ID50, whereas trichosanthin demonstrates 38% and 44% inhibition on cellular DNA and protein synthesis, respectively. These results indicate that the therapeutic index of TAP 29 is at least two orders of magnitude higher than that of trichosanthin. Thus TAP 29 may offer a broader safe dose range in the treatment of AIDS.

Inhibition of HIV replication by *Hyssop officinalis* extracts.

Antiviral Res;14(6):323-37, 1990 Dec. Kreis W; Kaplan MH; Freeman J; Sun DK; Sarin PS

Resumo: Crude extracts of dried leaves of *Hyssop officinalis* showed strong anti-HIV activity as measured by inhibition of syncytia formation, HIV reverse transcriptase (RT), and p17 and p24 antigen expression, but were non-toxic to the uninfected Molt-3 cells. Ether extracts from direct extraction (Procedure I), after removal of tannins (Procedure II), or from the residue after dialysis of the crude extract (Procedure III), showed good antiviral activity. Methanol extracts, subsequent to ether, chloroform and chloroform ethanol extractions, derived from procedure I or II, but not III, also showed very strong anti-HIV activity. In addition, the residual material after methanol extractions still showed strong activity. Caffeic acid was identified in the ether extract of procedure I by HPLC and UV spectroscopy. Commercial caffeic acid showed good antiviral activity in the RT assay and high to moderate activity in the syncytia assay and the p17 and p24 antigen expression. Tannic acid and gallic acid, common to other teas, could not be identified in our extracts. When commercial products of these two acids were tested in our assay systems, they showed high to moderate activity against HIV-1. *Hyssop officinalis* extracts contain caffeic acid, unidentified tannins, and possibly a third class of unidentified higher molecular weight compounds that exhibit strong anti-HIV activity, and may be useful in the treatment of patients with AIDS.

Ethnobotany and the identification of therapeutic agents from the rainforest.

Ciba Found Symp;154:22-31; discussion 32-9, 1990. Balick MJ

Resumo: Many rainforest plant species, including trees and herbaceous plants, are employed as medicines by indigenous people. In much of the American tropics, locally harvested herbal medicines are used for a significant portion of the primary health care, in both rural and urban areas. An experienced curandero or herbal healer is familiar with those species with marked biological activity, which are often classified as 'powerful plants'. Examples are given from studies in progress since 1987 in Belize, Central America. The Institute of Economic Botany of The New York Botanical Garden is collaborating with the National Cancer Institute in Bethesda, Maryland (USA) in the search for higher plants with anti-AIDS and anticancer activity. Several strategies are cited for identification of promising leads from among the circa 110,000 species of higher plants that are present in the neotropics, the focus of this search. Recommendations are offered for the design of future efforts to identify plant leads for pharmaceutical testing.

***Castanospermum* and anti-AIDS activity.**

J Ethnopharmacol;25(2):227-8, 1989 Apr.

Duke JA

País de publicação: SWITZERLAND

Anti-human immunodeficiency virus phenolics from licorice.

Chem Pharm Bull (Tokyo);36(6):2286-8, 1988 Jun.

Hatano T; Yasuhara T; Miyamoto K; Okuda T

País de publicação: JAPAN

Castanospermine and other plant alkaloid inhibitors of glucosidase activity block the growth of HIV. Lancet;2(8566):1025-6, 1987 Oct 31.

Tyms AS; Berrie EM; Ryder TA; Nash RJ; Hegarty MP; Taylor DL; Mobberley MA; Davis JM; Bell EA; Jeffries DJ

Antiviral saponins from Tieghemella heckelii.

J Nat Prod;65(12):1942-4, 2002 Dec. Gosse B; Gnabre J; Bates RB; Dicus CW; Nakkiew P; Huang RC

Resumo: Arganine C (1) and a new saponin, tieghemelin (2), were isolated from Tieghemella heckelii fruits. Arganine C (1) strongly inhibited HIV entry into cells in a cell fusion assay. The less potent tieghemelin (2) was converted into arganine C (1) by reduction of its ethyl ester with sodium borohydride. The removal of the four-sugar chains from arganine C (1) and tieghemelin (2) to give 16alpha-hydroxyprotobassic acid 3-O-beta-D-glucopyranoside (3) and 16alpha-hydroxyprotobassic acid 3-O-beta-D-glucuronopyranoside (4), respectively, caused total loss of activity in both cases. Arganine C (1) was not significantly cytotoxic to HeLa-CD4(+) cells at the level required to reduce the syncytium count to zero, suggesting it to be a promising candidate for further study as an antiviral drug.

Screening of South American plants against human immunodeficiency virus: preliminary fractionation of aqueous extract from Baccharis trinervis.

Biol Pharm Bull;25(9):1147-50, 2002 Sep. Sanchez Palomino S; Abad MJ; Bedoya LM; García J; Gonzales E; Chiriboga X; Bermejo P; Alcami J

Resumo: Ethanolic and aqueous extracts of 14 South American medicinal plants were tested for inhibitory activity on human immunodeficiency virus (HIV). Both extracts were relatively non-toxic to human lymphocytic MT-2 cells, but only the aqueous extract of Baccharis trinervis exhibited potent anti-HIV activity in an in vitro MTT assay. To delineate the extract-sensitive phase, some studies of the antiviral properties of the active extract are described in this paper. Based on the results presented here, a separation scheme was devised, which permitted the preliminary fractionation of the extract, with the aim of finding an inhibitor of this virus.

The effects of long-term herbal treatment for pediatric AIDS.

Am J Chin Med;30(1):51-64, 2002. Tani M; Nagase M; Nishiyama T; Yamamoto T; Matusa R

Resumo: This paper presents our long-term (1992-2000) treatment of pediatric Acquired Immune Deficiency Syndrome (AIDS) patients (maximum 100 children, last three years 65) using native herbal remedies in a voluntary medical assistance program in Constanta, Romania. We primarily report the progress of 10 children at a facility called the [quot]House of Tomorrow[quot] and three other facilities. The long-term (8 years and 8 months) treatment contributed to a drop of the amount of Human Immunodeficiency Virus Ribonucleic Acids (HIV-RNA) below the measurable level for 9 out of 10 patients at the [quot]House of Tomorrow.[quot] Furthermore, the treatment led to preservation and increase of the cluster of differentiation (CD4) count, a remarkable decrease in mortality rate, as well as the maintenance of a good quality of life. It took one to three years for the beneficial effects of the treatment to emerge. No side-effects were recognized either clinically or biochemically, nor was there any emergence of drug-resistant strains of HIV as seen with anti-HIV chemical treatments. This paper also refers to which herbal remedies were used and their general mechanism of action.

Anti-HIV-1 activity and structure-activity relationship of cepharanoline derivatives in chronically infected cells.

Antivir Chem Chemother;12(5):307-12, 2001 Sep. Baba M; Okamoto M; Kashiwaba N; Ono M

Resumo: Cepharanthine (12-O-methyl cepharanoline) is a plant alkaloid and has been shown to inhibit tumour necrosis factor-alpha- or phorbol 12-myristate 13-acetate-induced HIV-1 replication in the chronically infected promonocytic cell line, U1. Its mechanism of action is considered to be the inhibition of nuclear replication kappaB, a potent inducer of HIV-1 gene expression. In this study, we have synthesized 96 derivatives of cepharanoline, including cepharanthine, and examined their inhibitory effects on HIV-1 replication in U1 cells. Among the 12-O-alkyl derivatives, cepharanthine proved to be the most active, and the activity decreased as the length of the alkyl chain increased. All of the 12-O-acyl derivatives were totally inactive, while a few 12-O-carbamoyl derivatives displayed modest activity. Since 12-O-ethyl derivatives were found to be as active as cepharanthine against HIV-1 replication, we further synthesized various 12-O-ethyl derivatives of cepharanoline. Among the derivatives, five proved to be more active inhibitors than cepharanthine, and the most active compound was 12-O-ethylpiperazinyl cepharanoline. The 50% effective concentrations of this compound and cepharanthine were 0.0041 and 0.028 microg/ml (0.0060 and 0.046 microM), respectively.

Isolation of an anti-HIV diprenylated bibenzyl from Glycyrrhiza lepidota.

Phytochemistry;58(1):153-7, 2001 Sep. Manfredi KP; Vallurupalli V; Demidova M; Kindscher K; Pannell LK

Resumo: The organic soluble extract from the leaves of Glycyrrhiza lepidota showed moderate activity in the US National Cancer Institute in vitro anti-HIV-1 bioassay. Chromatographic separation of this extract resulted in the identification of a new diprenylated bibenzyl as the compound responsible for the observed anti-viral activity. Extensive spectroscopic experiments provide the complete 1H NMR and 13C NMR spectral assignments to support the proposed structure. Known compounds glepidotin B and glepidotin A were also isolated from the extract and shown to be inactive in the anti-viral assay.

Antiviral, haemolytic and molluscicidal activities of triterpenoid saponins from Maesa lanceolata: establishment of structure-activity relationships.

Planta Med;67(6):528-32, 2001 Aug. Apers S; Baronikova S; Sindambiwe JB; Witvrouw M; De Clercq E; Vanden Berghe D; Van Marck E; Vlietinck A; Pieters L

Resumo: Ten saponins isolated from the leaves of Maesa lanceolata were tested for their antiviral, haemolytic and molluscicidal activities. The influence of the substitution pattern of these acylated triterpenoid saponins on their biological activities was investigated and structure-activity relationships were established. Maesasaponin VI(2) (3 beta-O-[[alpha-L-rhamnopyranosyl-(1 --> 2)-beta-D-galactopyranosyl-(1 --> 3)]]-[beta-D-galactopyranosyl-(1 --> 2)]]-beta-D-glucopyranuronyl]-21 beta,22 alpha-diangeloyloxy-13 beta,28-epoxyolean-16 alpha,28 alpha-diol), the most potent molluscicidal compound (LC(50) 0.5 ppm), also showed virucidal and haemolytic activity. In general, 21,22-diacylation appeared to be associated with a virucidal (reduction factor of the viral titer > or = 10(3) at 50 microg/ml) and haemolytic activity (HC(50) < or = 1 microg/ml).

HIV-Inhibitory prenylated xanthenes and flavones from Maclura tinctoria.

J Nat Prod;63(11):1537-9, 2000 Nov. Groweiss A; Cardellina JH; Boyd MR

Resumo: The organic extract of the plant *Maclura tinctoria* exhibited moderate anti-HIV activity. Seven prenylated phenolic derivatives were isolated from the active fractions and characterized by spectroanalytical methods. New compounds macluraxanthone B (1), macluraxanthone C (2), and dihydrocudraflavone B (8) were identified.

Coumarins and bicoumarin from *Ferula sumbul*: anti-HIV activity and inhibition of cytokine release.

Phytochemistry;53(6):689-97, 2000 Mar. Zhou P; Takaishi Y; Duan H; Chen B; Honda G; Itoh M; Takeda Y; Kodzhimatov OK; Lee KH

Resumo: The methanol extract of the dried roots of *Ferula sumbul* afforded two furanocoumarin esters, fesumtuorin A, B, one bicoumarin, fesumtuorin C, five spirobicoumarins, fesumtuorin D, E, F, G and H, along with nineteen known coumarins. Their structures were established on the basis of spectroscopic studies. Some of the isolated compounds showed anti-HIV activity and very weak inhibition of cytokine release.

Plant products as antimicrobial agents.

Clin Microbiol Rev;12(4):564-82, 1999 Oct. Cowan MM

Resumo: The use of and search for drugs and dietary supplements derived from plants have accelerated in recent years. Ethnopharmacologists, botanists, microbiologists, and natural-products chemists are combing the Earth for phytochemicals and [quot]leads[quot] which could be developed for treatment of infectious diseases. While 25 to 50% of current pharmaceuticals are derived from plants, none are used as antimicrobials. Traditional healers have long used plants to prevent or cure infectious conditions; Western medicine is trying to duplicate their successes. Plants are rich in a wide variety of secondary metabolites, such as tannins, terpenoids, alkaloids, and flavonoids, which have been found in vitro to have antimicrobial properties. This review attempts to summarize the current status of botanical screening efforts, as well as in vivo studies of their effectiveness and toxicity. The structure and antimicrobial properties of phytochemicals are also addressed. Since many of these compounds are currently available as unregulated botanical preparations and their use by the public is increasing rapidly, clinicians need to consider the consequences of patients self-medicating with these preparations.

Antimicrobial activity of extracts from the cell cultures of some Turkish medicinal plants.

Phytother Res;13(4):355-7, 1999 Jun. Sokmen A; Jones BM; Erturk M

Department of Biology, Faculty of Science, University of Cumhuriyet, Sivas, Turkey.

Resumo: Twenty-four callus, and eleven cell suspension, cultures were established from Turkish medicinal plants, and crude extracts prepared from them tested against microorganisms to assess their antimicrobial activities in vitro. Of the extracts tested, those belonging to the cell cultures of five of the plant species showed antibacterial activity against mainly three bacteria and a yeast. No activity was observed against herpes simplex viruses, HSV-I and II, but an extract from *Hypericum capitatum* showed a slight anti-retroviral activity against HIV-I.

Bioactive kaurane diterpenoids from *Annona glabra*.

J Nat Prod;61(4):437-9, 1998 Apr. Chang FR; Yang PY; Lin JY; Lee KH; Wu YC

Graduate Institute of Natural Products, Kaosiung Medical College, Taiwan, Republic of China.

Resumo: Phytochemical analysis of the fruits of *Annona glabra* yielded two new kaurane diterpenoids, annoglabasin A (methyl-16 beta-acetoxy-19- α -ent-kauran-17-oate)(1) and annoglabasin B (16 α -hydro-19-acetoxy-ent-kauran-17-oic acid)(2), along with 11 known kaurane derivatives (3-13). The structures of the new compounds were established by spectral and chemical evidence. Among these, methyl-16 α -hydro-19- α -ent-kauran-17-oate (11) exhibited mild activity against HIV replication in H9 lymphocyte cells, and 16 α -17-dihydroxy-ent-kauran-19-oic acid (4) showed significant inhibition of HIV-reverse transcriptase.

HIV-inhibitory and cytotoxic oligostilbenes from the leaves of *Hopea malibato*.

J Nat Prod;61(3):351-3, 1998 Mar. Dai JR; Hallock YF; Cardellina JH; Boyd MR

Resumo: Three new oligostilbenes, malibatols A (1) and B (2) and dibalanocarpol (3), together with one known oligostilbene balanocarpol (4), were isolated from the organic extract of the leaves of *Hopea malibato*. The structure elucidation of these compounds was based on the interpretation of their chemical and spectral data. Compounds 3 and 4 exhibited very modest HIV-inhibitory activity, while compounds 1 and 2 were cytotoxic to the host cells (CEM SS) in the antiviral assay.

Plant-derived leading compounds for chemotherapy of human immunodeficiency virus (HIV) infection.

Planta Med;64(2):97-109, 1998 Mar. Vlietinck AJ; De Bruyne T; Apers S; Pieters LA

Department of Pharmaceutical Sciences, University of Antwerp (UA), Belgium. vlietink@uta.ua.ac.be

Resumo: Many compounds of plant origin have been identified that inhibit different stages in the replication cycle of human immunodeficiency virus (HIV): 1) virus adsorption: chromone alkaloids (schumannifine), isoquinoline alkaloids (michellamines), sulphated polysaccharides and polyphenolics, flavonoids, coumarins (glycycoumarin, licopyranocoumarin) phenolics (caffeic acid derivatives, galloyl acid derivatives, catechinic acid derivatives), tannins and triterpenes (glycyrrhizin and analogues, soyasaponin and analogues); 2) virus-cell fusion: lectins (mannose- and N-acetylglucosamine-specific) and triterpenes (betulinic acid and analogues); 3) reverse transcription; alkaloids (benzophenanthridines, protoberberines, isoquinolines, quinolines), coumarins (calanolides and analogues), flavonoids, phloroglucinols, lactones (protolichesterinic acid), tannins, iridoids (fulvoplumierin) and triterpenes; 4) integration: coumarins (3-substituted-4-hydroxycoumarins), depsidones, O-caffeoyl derivatives, lignans (arctigenin and analogues) and phenolics (curcumin); 5) translation: single chain ribosome inactivating proteins (SCRIP's); 6) proteolytic cleavage (protease inhibition): saponins (ursolic and maslinic acids), xanthenes (mangostin and analogues) and coumarins; 7) glycosylation: alkaloids including indolizidines (castanospermine and analogues), piperidines (1-deoxynojirimicin and analogues) and pyrrolizidines (australine and analogues); 8) assembly/release: naphthodianthrones (hypericin and pseudohypericin), photosensitisers (terthiophenes and furoisocoumarins) and phospholipids. The target of action of several anti-HIV substances including alkaloids (O-demethyl-buchenavianine, papaverine), polysaccharides (acemannan), lignans (intheriotherins, schisantherin), phenolics (gossypol, lignins, catechol dimers such as peltatols, naphthoquinones such as conocurvone) and saponins (celasdin B, *Gleditsia* and *Gymnocladus* saponins), has not been elucidated or does not fit in the proposed scheme. Only a very few of these plant-derived anti-HIV products have been used in a limited number of patients suffering from AIDS viz. glycyrrhizin, papaverine, trichosanthin, castanospermine, N-butyl-1-deoxynojirimicin and acemannan.

Phytochemical analysis of *Geigeria alata* and *Francoeuria crispa* essential oils.

Planta Med;63(5):479-82, 1997 Oct. Ross SA; el Sayed KA; el Sohly MA; Hamann MT; Abdel-Halim OB; Ahmed AF; Ahmed MM

Resumo: Phytochemical analyses of *Geigeria alata* (Benth. & Hook.) and *Francoeuria crispa* (Forssk., Cas.) (Asteraceae) essential oils were performed. *G. alata* oil showed moderate in vitro cytotoxicity (IC₅₀, micrograms/ml against tumor cells; P388: 2.0, A-549: 2.5 and HT-29: 5.0), and also showed weak anti-HIV activity. S-Carvotanacetone, the major component of *F. crispa* oil (93.0%), was isolated and its structure was elucidated by 2D-NMR analysis.

Compounds with anti-HIV activity from plants.

Trans R Soc Trop Med Hyg;90(6):601-4, 1996 Nov-Dec. Houghton PJ

Resumo: Natural products are described which have shown activity against human immunodeficiency virus in vitro. These compounds have a variety of chemical structures and modes of action. The discovery of these compounds and features of their development are used to illustrate aspects of the wider use of natural products as novel pharmaceutical agents. Several compounds detailed are being tested clinically and may provide new leads for viral chemotherapy. The use of extracts with isolated constituents is also discussed.

Analysis of the disulfide linkage pattern in circulin A and B, HIV-inhibitory macrocyclic peptides.

Biochem Biophys Res Commun;228(2):632-8, 1996 Nov 12. Derua R; Gustafson KR; Pannell LK

Resumo: Circulin A and B are members of a family of macrocyclic peptides, originally isolated from the tropical tree *Chassalia parvifolia*, that have been shown to display anti-HIV activity. Complete structural elucidation of these highly constrained peptides was difficult due to their cyclic amide backbone and the presence of six disulfide-linked cysteines. In the present study, the disulfide pairing motif of circulin A and circulin B was determined. Since the circulins were resistant to enzymatic proteolysis, cysteine residue pairings were identified by analysis of the complex mixture of cleavage products that resulted from partial acid hydrolysis of the native peptides. Combined utilization of HPLC, fast atom bombardment mass spectrometry and peptide recognition software ([quot]F-MASS[quot] and [quot]F-LINK[quot] programs) were employed to identify the cleavage products. Thus, we were able to unambiguously identify the disulfide linkage pattern in circulin A and circulin B as Cys1-Cys4, Cys2-Cys5 and Cys3-Cys6, where the numbers on the cysteine residues refer to their respective order in the peptides.

Three new naphthyldihydroisoquinoline alkaloids from *Ancistrocladus tectorius*.

J Nat Prod;59(9):854-9, 1996 Sep. Manfredi KP; Britton M; Vissieche V; Pannell LK

Resumo: Three new 5--1'-linked naphthyldihydroisoquinoline alkaloids (1-3) have been isolated from the organic extract of *Ancistrocladus tectorius*. The gross structures of the compounds have been established using 1D and 2D NMR spectroscopy and difference NOE experiments. The absolute stereochemistry of 1, 2, and 3 was determined from CD spectral comparison and chemical degradation. Evidence is presented to show that two of the compounds exist exclusively in the keto form at C-8 of the isoquinoline system (2b, 3b).

Constituents of *Ardisia japonica* and their in vitro anti-HIV activity.

J Nat Prod;59(6):565-9, 1996 Jun. Piacente S; Pizza C; De Tommasi N; Mahmood N

Dipartimento di Chimica delle Sostanze Naturali, Università degli Studi di Napoli Federico II, Italy.

Resumo: As part of our screening of anti-AIDS agents from medicinal plants, the MeOH extract of the aerial parts of *Ardisia japonica* was tested, and it showed moderate in vitro anti-HIV activity. Reexamination to identify the compounds responsible for the anti-HIV activity revealed several known compounds and a new triterpenoid saponin (4) whose structure elucidation was accomplished by 1H-1H correlation spectroscopy (COSY, HOHAHA, ROESY) and 1H-13C heteronuclear correlation (HETCOR) NMR experiments. All of the isolated compounds were tested and, although none of the triterpenoid saponins was active, bergenin and norbergenin showed weak anti-HIV activity.

Drug leads from the Kallaway herbalists of Bolivia. 1. Background, rationale, protocol and anti-HIV activity.

J Ethnopharmacol;50(3):157-66, 1996 Mar. Abdel-Malek S; Bastien JW; Mahler WF; Jia Q; Reinecke MG; Robinson WE; Shu Y; Zalles-Asin J

Resumo: Aqueous, organic and alcoholic extracts of over 100 samples of 60 species of Kallaway medicinal herbs representing 30 plant families were assayed to compare their toxicity and ability to protect MT-2 T-lymphoblastoid cells from the cytopathic effect of human immunodeficiency virus (HIV). The results are reported as a therapeutic index (TI) which was > 25 for eighteen species, including seven > 50 and one > 100. The anti-HIV activity resided primarily in the aqueous rather than in the organic extracts and was concentrated in plants used in ethnomedicine to treat lung and liver diseases.

Antitumor germacranolides from *Anvillea garcinii*.

J Nat Prod;59(4):403-5, 1996 Apr. Abdel Sattar E; Galal AM; Mossa GS

Department of Pharmacognosy, College of Pharmacy, King Saud University, Riyadh Saudi Arabia.

Resumo: The aerial parts of *Anvillea garcinii* yielded two new germacranolides, 9 alpha-hydroxy-1 beta, 10 alpha-epoxyparthenolide (4) and parthenolid-9-one (5), in addition to the known 9 alpha-hydroxyparthenolide (1), 9 beta-hydroxyparthenolide (2), and 9 beta-hydroxy-1 beta, 10 alpha-epoxyparthenolide (3). The structures of the new compounds were elucidated from their spectral data (IR, MS, 1H- and 13C-NMR, 1H-1H COSY, and 1H-13C HETCOR) and by chemical derivatization. The hitherto unreported 13C-NMR data and carbon atom assignments of the previously isolated lactones 1, 2, and 3 were given. The in-vitro antitumor and anti-HIV activities were evaluated for the isolated compounds.

Biologically active flavonoids and terpenoids from *Egletes viscosa*.

Phytochemistry;41(1):217-23, 1996 Jan. Lima MA; Silveira ER; Marques MS; Santos RH; Gambardela MT Curso de Pós-Graduação em Química Orgânica, Departamento de Química Orgânica e Inorgânica, Laboratório de Produtos Naturais, Universidade Federal do Ceará, Fortaleza, Brazil.

Resumo: The steam volatile components from the hexane extract of dried flower buds of *Egletes viscosa* were identified by gas chromatography-mass spectrometry as trans-carvyl acetate, cis-carvyl acetate, sabinyl acetate, verbenyl acetate, cyclopentaethyldiene, geranyl acetate and 5-methylfuranone, and trans-pinocarvyl acetate (major component). From the non-volatile residue, centipeditic acid and a novel clerodane diterpene, 12-acetoxy-hawthraic acid lactone, were isolated. From the ethanol extract,

ternatin (4',5-dihydroxy-3,3',7,8-tetramethoxyflavone), was isolated. Ternatin showed anti-inflammatory, hepatoprotection and gastroprotection properties, and, according to the NCI protocols, it showed moderate activity against HIV. The diterpenes showed antispasmodic activity. Structure determination of these secondary metabolites was accomplished by spectrometric methods, including 2D NMR, chemical interconversion and X-ray crystallographic analysis.

A reinvestigation of Maprounea triterpenes.

J Nat Prod;58(7):1039-46, 1995 Jul. Beutler JA; Kashman Y; Tischler M; Cardellina JH; Gray GN; Currens MJ; Wall ME; Wani MC; Boyd MR

Resumo: Anti-HIV activity and the inhibition of phorbol ester receptor binding activity in two species of Maprounea were traced to small amounts of highly potent phorbol esters of the daphnane type. The triterpenes previously isolated from this genus were found to be devoid of biological activity when scrupulously purified. Four new triterpene esters were elucidated; two [3,4] were found in *M. africana*, while three [4,6,7] were found in *M. membranacea*. Nmr assignments have also been made for two previously known compounds [2,5] in this group.

Suksdorfin: an anti-HIV principle from Lomatium suksdorfii, its structure-activity correlation with related coumarins, and synergistic effects with anti-AIDS nucleosides.

Bioorg Med Chem;2(10):1051-6, 1994 Oct. Lee TT; Kashiwada Y; Huang L; Snider J; Cosentino M; Lee KH

Resumo: Suksdorfin (1), which is isolated from the fruit of *Lomatium suksdorfii*, was found to be able to inhibit HIV-1 replication in the T cell line, H9, with an average EC50 value of 2.6 +/- 2.1 microM. In addition, suksdorfin was also suppressive during acute HIV-1 infections of peripheral blood mononuclear cells, monocyte/macrophages and the promonocytic cell line, U937. Combinations of 1 and the anti-HIV nucleosides ddI and ddC demonstrated statistical synergy in inhibiting HIV-1 replication (ddC > ddI). However, the viral inhibition mediated by combining 1 with AZT was not statistically synergistic. Furthermore, the presence of suksdorfin did not antagonize the suppression mediated by the three nucleoside reverse transcriptase inhibitors. Comparison of the structure and activity of 1 with those of ten related compounds indicated that the dihydroseselin type of pyranocoumarin possessing a 4'-isovaleryl group is important to suksdorfin's enhanced anti-HIV activity.

Astragalosides from Egyptian Astragalus spinosus Vahl.

Pharmazie;48(6):452-4, 1993 Jun. Abdallah RM; Ghazy NM; El-Sebakhy NA; Pirillo A; Verotta L

Resumo: Four cycloartane triterpene oligoglycosides were isolated from the n-butanol extract of the aerial parts of *Astragalus spinosus* Vahl. (Leguminosae). They were identified as astragaloside I (1), isoastragaloside I (2), astragaloside IV (4) and cycloastragenol 6-O-glucoside (5) on the basis of comparing their m.p.'s, 1H NMR and 13C NMR spectra and chromatographic patterns with the data given in the literature. The results of AIDS antiviral and antitumor screening of the major component, astragaloside II (3), are dealt with.