Evaluation of selected South African medicinal plants for inhibitory properties against human immunodeficiency virus type 1 reverse transcriptase and integrase

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Abstract

Seventeen aqueous and methanol extracts from nine South African medicinal plants, ethnobotanically selected, were screened for inhibitory properties against HIV-1 reverse transcriptase (RT). Isolated compounds were additionally evaluated on HIV-1 integrase (IN). The strongest inhibition against the RNA-dependent-DNA polymerase (RDDP) activity of RT was observed with the methanol extract of the stem-bark of *Peltophorum africanum* Sond. (Fabaceae) (IC$_{50}$ 3.5 μg/ml), while the methanol extract of the roots of *Combretum molle* R.Br. ex G. Don (Combretaceae) was the most inhibitory on the ribonuclease H (RNase H) activity (IC$_{50}$ 9.7 μg/ml). The known compounds bergenin and catechin, and a red coloured gallotannin composed of meta-depside chains of gallic and protocatechuic acids esterified to a 1-O-isobutyro-D-glucopyranose core, were isolated from the methanol extract of the roots and stem-bark of *Peltophorum africanum*. The gallotannin inhibited the RDDP and RNase H functions of RT with IC$_{50}$ values of 6.0 and 5.0 μM, respectively, and abolished the 3′-end processing activity of IN at 100 μM. Catechin showed no effect on RT but had a moderate activity on HIV-1 IN. Bergenin was inactive on both enzymes.

The aqueous and methanol extracts were non-toxic in a HeLaP4 cell line at a concentration of 400 μg/ml.

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Keywords: South African medicinal plants; HIV-1; Reverse transcriptase; Integrase; Plant phenols; Gallotannins

1. Introduction

Currently available therapeutics against HIV infection include the reverse transcriptase, protease and fusion inhibitors. Despite the beneficial effects of these drugs in improving the quality of life of HIV/AIDS patients, the development of virus resistance, appreciable levels of toxicity, high cost, unavailability and above all the lack of a curative effect are
their major short-comings (Pomerantz and Horn, 2003). As a result, the search for better anti-HIV agents continues, and much attention has been focused on natural sources, particularly plant species. Promising results have been achieved through the evaluation of plant derived compounds against several essential points in the life-cycle of HIV (De Clercq, 2000).

The prevalence of HIV in South Africa at the end of 2002 was estimated at 26.5%, with about 4 million people infected (Department of Health, 2003). The use of medicinal plants is widespread in South Africa and a good proportion of HIV/AIDS patients, for traditional and financial reasons, seek relief from traditional healers who administer preparations from a variety of plants (Morris, 2002). AIDS is a syndrome comprising a dysfunction of the immune system, compounded by opportunistic infections of bacterial, fungal, protozoan or viral aetiology. The beneficial effect of an herbal extract in the HIV/AIDS condition could be due to a direct inhibition of HIV replication, boosting of the immune system, or having inhibitory properties against one or several opportunistic infections. There is paucity of data on the potential therapeutic effects of South African medicinal plants on HIV infection.

As a component of our on-going antimicrobial screening of medicinal plants, we are screening selected plants for biological activity against HIV-1 reverse transcriptase (RT) and integrase (IN). In this report we present results on the evaluation of 17 aqueous and methanol extracts of nine plants, used by traditional healers in the Limpopo Province of South Africa in the treatment of HIV/AIDS patients and other suspected viral conditions, for activity against HIV-1 RT. The extracts were evaluated for activity against (1) the ability of the DNA polymerase domain of HIV-1 RT to transcribe viral RNA to a complementary DNA, otherwise referred to as the RNA-dependent-DNA polymerase (RDDP) activity, (2) the ability of the RNase H domain to degrade the RNA component in the RNA:DNA hybrid in the course of reverse transcription (RNase H activity). In addition, the effect of compounds isolated from the roots and stem-bark of Peltophorum africanum on the RDDP and RNase H functions of HIV-1 RT were studied. Their ability to block the 3′ end processing reaction catalyzed by HIV-1 IN, an essential step in the integration of viral DNA in the host cell genome, was also investigated.

2. Methodology

2.1. Selection and procurement of plants

Two traditional healers in the Limpopo province who receive AIDS patients were interviewed on the type of plants they employ in treating these individuals. These individuals have either disclosed their condition confirmed by a medical report or the healers suspected AIDS when the patients presented with a combination of two or more of the following conditions: chronic diarrhoea, persistent cough, progressive weight loss, skin infections. Based on responses, the following plants were identified namely Bridelia micrantha Baill. (Fabaceae), Combretum molle R.Br. ex G. Don (Combretaceae), Mucuna coriacea Baker (Fabaceae), Elaeodendron transvaalensis Jacq. (Celastraceae), Peltophorum africanum Sond. (Fabaceae), Ricinus communis L. (Euphorbiaceae), Vernonia stipulacea Klatt. (Asteraceae) and Ziziphus mucronata Willd. (Rhamnaceae). Sutherlandia frutescens sub-species microphylla L. R.Br. ex W.T. Aiton (Fabaceae) widely used in South Africa for its reported ability to increase CD4 counts and lower viral load in AIDS patients was also included in the study. Eight of these plants were identified by Mr. Peter Thosikawie of the Botany Unit, Department of Biological Sciences, University of Venda, South Africa, where voucher specimens have been deposited. Leaves and twigs of Sutherlandia frutescens sub-species microphylla were a kind gift of Dr. Carl Albrecht, University of the Western Cape, Stellenbosch, South Africa and botanically identified by Prof. Van Wyk, Rand Afrikaans University, Johannesburg, South Africa. Plants were at different times collected from their natural habitats between July 2002 and April 2003. Bridelia micrantha, Elaeodendron transvaalensis, Peltophorum africanum, Ricinus communis, Ziziphus mucronata were collected within the precincts of Nzhelele, Combretum molle from Lwamondo and Mucuna coriacea from the compound of the University of Venda, Thohoyandou. Vernonia stipulacea was obtained from Bushbuckridge. Table 1 presents ethnobotanical information on the nine selected plants.

2.2. Preparation of aqueous and methanol extracts

Plant parts, roots or leaves, were washed with distilled water and dried at room temperature for 2–3 weeks. Dried plant material was chopped and ground into powder. Two hundred grams of powdered material were soaked in 1 l of either distilled water or methanol overnight on a rotatory platform. The resulting mixture was subsequently strained through a cheesecloth and then vacuum-aided filtered through Whatman filter paper No. 3 (W&R, England, UK). The residue was further extracted twice with 250 ml of the extractant. Filtrates were evaporated to dryness on a rotatory evaporator (Rotavapor R-144 Buchi, Switzerland) at 60 and 40 °C to obtain the aqueous and methanol extracts, respectively. Extracts were stored in the dark at 4 °C until used.

2.3. Expression and purification of HIV-1 RT and IN

Recombinant HIV-1 RT consisting of the p66 and p51 subunits was expressed and purified as earlier reported (Sallafranque-Andreola et al., 1989). HIV-1 IN was prepared as described by Caumont et al. (1996) and Parisiet al. (2000).

2.3.1. HIV-1 RT RDDP activity

The inhibition of HIV-1 reverse transcriptase activity was evaluated by measuring the incorporation of methyl-3H
Identification of plants used to treat HIV/AIDS and related conditions in the Limpopo Province of South Africa

<table>
<thead>
<tr>
<th>Plant identity and family</th>
<th>Common name</th>
<th>Voucher number</th>
<th>Part used</th>
<th>Ethno-medical information</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Brodiaea microstria Baill. (Ephorbiaceae)</td>
<td>Manzeze (T)</td>
<td>BP03</td>
<td>Roots</td>
<td>Diarrhoea, sore eyes, stomach ache, abortifacient (Lin et al., 2002)</td>
</tr>
<tr>
<td>2 Combretum natans R. Br. ex G. Don (Combretaceae)</td>
<td>Majowi (T), scepter bushwillow (E)</td>
<td>BP07</td>
<td>Roots</td>
<td>Abdominal pains, snake bites, leprosy, fever, convulsions, hookworm infection (Malogo, 1990)</td>
</tr>
<tr>
<td>3 Elaeodendron transsudatorium Jacq. (Celastraceae)</td>
<td>Mukhavhuzu (T), bushwillow</td>
<td>BP05</td>
<td>Roots</td>
<td>Colds, skin rashes, fever, candidiasis, dysmenorrhoea (Steenkamp, 2003)</td>
</tr>
<tr>
<td>4 Musanga cecropia Baker (Fabaceae)</td>
<td>Vulafula (T), buffalo-bean (E)</td>
<td>BP02</td>
<td>Roots</td>
<td>Fever, diarrhoea</td>
</tr>
<tr>
<td>5 Peltophorum africanum (L.) Bridelia micrantha (Fabaceae)</td>
<td>Mpuuze (T), weeping/African wattle (E)</td>
<td>BP01</td>
<td>Roots/stem-bark</td>
<td>Wounds, toothache, sore throat, cough, tuberculosis, abdominal disorders, diarrhoea, dysentery, menstruation, infertility (Arnold and Galumian, 1994; Obi et al., 2003)</td>
</tr>
<tr>
<td>6 Ricinus communis (L.), (Euphorbiaceae)</td>
<td>Mupfare (T), castor-bean (E)</td>
<td>BP06</td>
<td>Leaves</td>
<td>Wounds and sores, abscesses, asthma, arthritis, dermatitis, flu, fever, tuberculous, toothache, antihelmentic, diarrohea, abortifacient (Cretien and Afolayan, 2000)</td>
</tr>
<tr>
<td>7 Sutherlandia frutescens subsp. microphylla (L.), R. Br. ex W.T. Aiton (Fabaceae)</td>
<td>Cancer bush (E)</td>
<td>–</td>
<td>Leaves and twigs</td>
<td>Relieving cold, influenza, chicken pox, diabetes, vanccue venes, piles, backache, rheumatism, physical and mental stress</td>
</tr>
<tr>
<td>8 Vernonia stipulacea Klett (Asteraceae)</td>
<td>Muhuluula (T), blue bitter tea (E)</td>
<td>BP08</td>
<td>Roots</td>
<td>Diarrhoea, fever, flu, contraceptive (Malogo, 1990; Obi et al., 2003)</td>
</tr>
<tr>
<td>9 Ziziphus mucronata Willd. (Rhamnaceae)</td>
<td>Mukhale (T), buffalo thorn (E)</td>
<td>BP04</td>
<td>Leaves</td>
<td>Diarrohea, dysentery, stomach ulcers, fever, antiperistaltic, skin diseases and anti-inflammatory, menorrhagia, infertility (Arnold and Galumian, 1994; Kayser and Arndt, 1999)</td>
</tr>
</tbody>
</table>

* T: Tshivenda (Limpopo Province, South Africa), E: English. 
* Ethno-medical information are based on interviews with traditional healers where the plants were collected and on published literature. Plant parts used for the various disease conditions may be inclusive or different from the parts investigated in this study. 
* Both traditional healers used these plants to treat HIV/AIDS patients.
the reaction was stopped as described in the RDDP assay. The RNase H inhibition was estimated by measuring the degradation of 32P-labelled RNA in the RNA/DNA hybrid in the presence or absence of test substance. Percentage inhibition of RNase H activity was calculated as \[ 1 - \frac{(CPM of hybrid without extract – CPM of hybrid with test substance)}{CPM of hybrid without extract} \times 100 \]. Reactions were carried out in duplicate for each of two independent determinations. A DNA aptamer (ODN 93) as described by Andrèola et al. (2001b) was used as a positive control.

2.3.2.3. Evaluation against the 3′-end processing activity of HIV-1 integrase. Biological activity of isolated molecules against the 3′-end processing activity of HIV-1 IN was performed as described by Parissi et al. (2000). Briefly, the processing substrate was synthesized with 10 nM of a 5′-32P labelled 21 nucleotide long ODN (5′-GTGTGGAAATCTTCTAGCAGT3′) annealed to its complementary strand (5′-ACTGCTAGAGATTTTCCACAC-3′). The reaction mixture contained 20 mM HEPES pH 7.5, 10 mM EDTA, 7.5 mM MnCl2, 10 nM NaCl, 0.05% Nonidet-P 40, 10 nM processing substrate and 600 nM IN in a final volume of 20 μL. After 1 h incubation, the 3′-end processing products were resolved on a 12% polyacrylamide-7 M urea gel in Tris borate EDTA pH 7.6 and autoradiographed. Gels products were resolved on a 12% polyacrylamide-7 M urea gel in Tris borate EDTA pH 7.6 and autoradiographed. Gels were analyzed using an NIH-image apparatus. For inhibition tests, preincubation for 20 min at 37 °C of IN and different concentrations of compounds was performed before adding the processing substrate. Diketo acid L-731,988 (a gift of Merck & Research Laboratories) was used as a positive control (Grobler et al., 2002).

2.4. Cytotoxicity assay

Cytotoxicity of extracts was determined in a HeLaP4 cell line (Andréola et al., 2001a). A 96 flat-bottom well microtiter plate was seeded with 12,000 cells in a total volume of 200 μL Dulbecco’s Minimum Essential Medium containing 10% Foetal Calf Serum and gentamycin (45 μg/mL) was incubated for 24 h at 37 °C in 5% CO2 humidified atmosphere. Culture medium was discarded and a two-fold serial dilution of test substance was done in a total volume of 200 μL for a concentration range of 400–0.295 μg/mL. The plate was incubated for a further 48 h as indicated above. Prior to testing, aqueous extracts were dissolved in distilled water and the methanol extracts were initially dissolved in 50% DMSO. The final DMSO concentration in the assay was 2%. Controls consisted of cells in growth medium without extract for aqueous extracts, and cells in growth medium with 2% DMSO for methanol extracts. Extract concentrations were evaluated in duplicate. Cell viability was determined using the CellTiter 96 AQueous One Solution Cell Proliferation Assay (Promega) according to the manufacturer’s instructions. Incubation was done for 3 h. Absorbance values were measured at 490 nm. The assay was performed twice. Fifty percent cytotoxic concentration (CC50) was determined as the concentration of extract that reduced cell viability by 50% when compared to controls.

2.5. Bioassay guided fractionation and isolation of active principles

The methanol extracts of the roots and stem-bark of Peltophorum africanum were further investigated for active compounds based on their activities in the screening assays. Isolation of pure compounds was done through the combination of thin layer, flash column and vacuum liquid chromatographic techniques. Chemical identification of pure compounds was achieved through the analyses of spectroscopic data derived from 1H and 13C nuclear magnetic resonance, mass spectrometry, infrared, ultraviolet and MALDI-ToF profiles and by comparison with published literature.

### Table 2

<table>
<thead>
<tr>
<th>Plant</th>
<th>RDDP IC50a (μg/mL)</th>
<th>RNase H IC50b (μg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Aqueous</td>
<td>Methanol</td>
</tr>
<tr>
<td>1 Bruxa microsperma</td>
<td>18.5</td>
<td>10.5</td>
</tr>
<tr>
<td>2 Combretum molle</td>
<td>37.5</td>
<td>9.5</td>
</tr>
<tr>
<td>3 Elaeocarpus grandiflorus</td>
<td>80.0</td>
<td>131.0</td>
</tr>
<tr>
<td>4 Mucuna coriacea</td>
<td>ND</td>
<td>10.5</td>
</tr>
<tr>
<td>5 Peltophorum africanum (roots)</td>
<td>58.3</td>
<td>8.0</td>
</tr>
<tr>
<td>6 Peltophorum africanum (bark)</td>
<td>ND</td>
<td>3.5</td>
</tr>
<tr>
<td>7 Ricinus communis</td>
<td>182.0</td>
<td>42.5</td>
</tr>
<tr>
<td>8 Sutherlandia frutescens</td>
<td>425.0</td>
<td>&gt;2000</td>
</tr>
<tr>
<td>9 Vernonia stipulacea</td>
<td>ND</td>
<td>350</td>
</tr>
<tr>
<td>10 Ziziphus mucronata</td>
<td>77.5</td>
<td>81.5</td>
</tr>
</tbody>
</table>

ND: not determined.

a IC50 was the amount of extract required to reduce the reverse transcriptase activity by 50%. The IC50 values were determined from the activity/concentration regression curves with at least seven concentration/activity points.

b The methanol extracts of Sutherlandia frutescens and Vernonia stipulacea were observed to stimulate RT activity at 100 μg/mL.
3. Results

3.1. Effect of crude extracts on RT activities, and cytotoxicity

The effect of the aqueous and methanol extracts was tested on DNA polymerase and RNase H activities of HIV-1 RT. The IC_{50} values of the plant extracts evaluated against HIV-1 RDDP and RNase H activities are shown in Table 2. Generally, the methanol extracts were more inhibitory than the aqueous extracts. No cytotoxicity was observed at the maximum tested concentration of 400 μg/ml for all the extracts (data not shown).

3.2. Isolated compounds

Bioassay-guided fractionation carried out on the roots and stem-bark of *Peltophorum africanum* afforded the known compounds bergenin (Atchuta et al., 1979) and catechin (Foo et al., 1996), and a red coloured gallotannin. Structural information gathered by MALDI-ToF, LC/MS, silylation and acid hydrolysis of the gallotannin indicated that it is composed of meta-depside chains of gallic and protocatechuic acids esterified to a 1-O-isobutyroyl-β-D-glucopyranose core (Haddock et al., 1982; Niemetz et al., 1999; Kandil and Grace, 2001). The red colour is probably due to the occurrence of some of the constituting catecholic units under their oxidized orthoquinone form (Fig. 1).

3.2.1. Bioactivity of isolated compounds against HIV-1 RT

The strongest inhibition against the RDDP activity of HIV-1 RT was shown by the gallotannin with an IC_{50} of 6.0 μM, compared to 0.048 μM for AZT-TP used as a positive control. The gallotannin also inhibited the RNase H activity by the gallotannin was dose dependent (data not shown). Below 2.0 and 1.0 μM, the gallotannin, respectively stimulated the RDDP and RNase H activities, while the RDDP and RNase H activities were completely abolished at 10.0 and 8.0 μM, respectively. Bergenin and catechin did not inhibit the RDDP and RNase activities of HIV-1 RT even at 100 μM.

3.2.2. Bioactivity of isolated compounds against HIV-1 IN

The relative inhibitions of catechin, the gallotannin and bergenin against the 3’-end processing activity of HIV-1 IN resolved on a 12% polyacrylamide-7M urea gel are presented in Fig. 2. Quantification by densitometry showed that the strongest inhibition was obtained with the gallotannin with an IC_{50} of about 6 μM, while IN activity was abolished at 100 μM. Bergenin, at 100 μM inhibited IN activity by almost 65%. Bergenin had no effect on IN at the maximum tested concentration of 100 μM.

4. Discussion and conclusions

In the hunt for novel anti-HIV compounds, there are a good number of country-based reports on the inhibitory properties of medicinal plants on different targets in the life cycle of HIV. Some of these investigations have led to the discovery of molecules, a few of which have entered clinical trials (De Clercq, 2000; Kong et al., 2003). South Africa has a huge variety of plants used in folkloric medicine. Several evaluations of South African plants for activity against bacteria (Eloff et al., 2001; Obi et al., 2003; Lall and Meyer, 2001), fungi (Motsei et al., 2003), protozoans (Van Zyl and Viljoen, 2002), viruses (Meyer et al., 1997) and non-infectious conditions (Eloff et al., 2001) have been documented. However, there is a dearth of information on the anti-HIV properties of plants used in South African traditional medicine, despite the administration of plant based decoctions and concoctions to HIV/AIDS persons in the country.

In this report, 17 extracts from nine plants used in traditional medicine in the Limpopo Province of South Africa were screened for RDDP and RNase H activities of HIV-1 RT. Isolated principles from the roots and stem-bark of *Peltophorum africanum* were additionally evaluated on the 3’-end processing activity of HIV-1 IN. The results showed that the...
methanol extracts of the roots of *Bridelia micrantha*, *Combretum molle*, *Mucuna coriacea*, *Peltophorum africanum* and its stem-bark have strong activity against HIV-1 RT. In general, the methanol extracts were more inhibitory than the aqueous extracts and moreso on the RNase H activity of RT. This observation could be related to the fact that many classes of compounds are obtained when methanol is used as an extractant (Cowan, 1999), in which case the chances of non-specific bioactivity is high. Worthy of note however, is the aqueous extract of *Elaeodendron transvaalensis* which was more inhibitory than the methanol extract against RDDP activity. The methanol residues of *Sutherlandia frutescens* subspecies *microphylla* and *Vernonia stipulacea* stimulated RT activity at 100 μg/ml. Though molecules responsible for this activity were not sought, l-canavanine, asparagines, pinitol and a triterpenoid glucoside (SU1) have been isolated from *Sutherlandia frutescens*, while sesquiterpene lactones with biological activities have been isolated from *Vernonia* species (Laekeman et al., 1983; Kuo et al., 2003). Some non-nucleoside RT inhibitors have also been shown to strongly stimulate RT activity and viral replication at defined concentrations. Huang et al. (2000) observed that drug dependent-stimulation reproducibly enhanced viral replication by as much as 400%. Though the mechanism of drug-induced stimulation is not known, it could be attributed to conformational changes on the enzyme. The implication of the stimulatory activity shown by the plant extracts investigated herein could be undesirable if the same scenario takes place in vivo. A recent report by Harnett et al. (2005) showed that the aqueous extract of the leaves of *S. frutescens* showed inhibition, albeit minimal, against HIV-RT in a non-radioactive colorimetric assay. An observation that we did not find. However, this seemingly contradiction could be due to the different experimental protocols used.

As a result of the strong inhibitory effect of the methanol extract of the roots and stem-bark of *Peltophorum africanum* on HIV-1 RT, a bioassay-guided fractionation was done to isolate and identify possible active principles. A red-coloured gallotannin, the known catechin and bergenin were isolated and identified. The gallotannin inhibited the RDDP activity of RT (IC50 = 6.0 μM), not as strong as AZT-TP, but as good as the unmodified candidate non-nucleoside RT inhibitor TIBO R82913 (IC50 = 10 μM), and to a few Curie-pyridones, a new class of candidate non-nucleoside RT inhibitors (Andréola
The compound of interest arising from this study is the gallotannin because of its strong in vitro inhibitory effects on the RDDP and RNase H activities of HIV-1 RT. The question is to assess the effect of the gallotannin on the 3′-end processing of HIV-1 IN, the 12% PAGE analysis revealed the abolition of IN 3′-end processing activity at a concentration of 100 μM indicated by the lack of the expected 19 nucleotide product, while at 10 μM the level of inhibition was comparable to that of dikeot acid which was used as a positive control.

Bergenin, a C-galloylglucose, was also isolated from *Peltophorum africanum* in the present investigation. Bergenin has previously been isolated from *Peltophorum africanum* (Mebe and Makuhunga, 1992), and several other plants: for example, the roots of *Astilbe thunbergii* (Han et al., 1998), and the aerial parts of *Astilbe thunbergii* (Han et al., 1998), and the aerial parts of *Flueggea virosa* (Pu et al., 2002). In the present study, bergenin had no activity against the RDDP and RNase H activities of HIV-1 IN, 12% PAGE analysis revealed the abolition of IN 3′-end processing activity at a concentration of 100 μM indicated by the lack of the expected 19 nucleotide product, while at 10 μM the level of inhibition was comparable to that of dikeot acid which was used as a positive control.

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The methanol extracts of the roots of *Bridelia micrantha*, and *Combretum molle* also showed relatively strong inhibitory properties against the RDDP and RNase H activities of HIV-1 RT. The compounds responsible for these activities in these plants were not sought. However, Astes et al. (2001) isolated the ellagitannin, punicalagin as a major compound, and the pentacyclic triterpene glucosides arjangucoside and sercoside from the stem-bark of *Combretum molle*. Ellagatannins and some pentacyclic triterpenes do inhibit HIV-1 RT in the micromolar range (Huang and Chen, 2002).

The compound of interest arising from this study is the gallotannin because of its strong in vitro inhibitory effects on the polymerase and ribonuclease H functions of HIV-1 RT and the 3′-end processing action of HIV-1 IN. The question is to know if this compound has a broad spectrum of activity and if its effects are specific. Gallotannins are examples of plant polyphenols, and some researchers (Tan et al., 1991; Wall et al., 1996) have proposed that polyphenols and tannins are responsible for apparent inhibitory properties in enzyme systems, since polyphenols precipitate proteins from solution, and therefore the activity of such compounds against enzymes may be non-specific. However, Zhu et al. (1997) in an evaluation of 20 phenolic compounds representing proanthocyanidins (condensed tannins) and gallotannins were shown to inhibit the 3′-end processing action of HIV-1 RT and IN activities, as well as its mode of action regarding competitiveness to template-primer and deoxyribonucleotide triphosphate, and cell culture evaluation.

The plants evaluated in this study for anti-HIV activities, are also used by traditional healers in the treatment of various other diseases. Decoctions and concoctions are usually administered as aqueous or alcoholic extracts. Decades of use of a particular plant material may point to its non-toxicity. However, incidents of poisoning have been reported due to the ingestion of plant parts used in medicine (Hamouda et al., 2001). Cytotoxicity experiments performed herein using a human epithelial cervical carcinoma cell line appear to indicated that the 17 aqueous and methanol plants from the nine plants employed in this study could be safe.

In summary, this investigation has evaluated the inhibitory properties of a selection of medicinal plants used in the Limpopo Province of South Africa against HIV-1 reverse transcriptase and integrase. An oxidized gallotannin isolated from the stem-bark of *Peltophorum africanum* was shown to have a strong activity against HIV-1 reverse transcriptase and integrase in an enzyme cell-free system. Further investigations are needed to elucidate the specificity and mode of action of this compound.

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References


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