INTRODUCTION

HIV/AIDS is now the leading cause of death in Sub-Saharan Africa and has moved up to fourth place among all causes of death worldwide. According to estimates from the UNAIDS 2009 report (UNAIDS 2009), on the global AIDS epidemic, around 33.4 million people were living with HIV and 2 million people died of AIDS related causes in 2008. Current prevention strategies are inadequate to stop the rapid spread of the epidemic. The search for safe, affordable treatments for HIV thus remains a major challenge and a key towards controlling the disease.

A collaborative research programme was initiated between the Council for Scientific and Industrial Research (CSIR) in South Africa and Esperanza Medicines Foundation (EMF), InPheno in Switzerland to evaluate South African medicinal plants for the identification of potentially new anti-HIV drug leads.

METHOD

Procedure for plant selection

Potential plant-based candidates were selected after undertaking an extensive literature study to identify plants reportedly used for the treatment of HIV or related illnesses including “soothing the immune system”. The various databases of the CSIR were searched including publications, books in the public domain and information received from indigenous knowledge holders.

Bioassay screening

EMF and InPheno provide a state-of-the-art cellular-based HIV infection system “decipher, deCIPh” (Figure 1) to measure HIV replication (including various subtypes with particular relevance for Africa such as subtypes D, D/C, A/E, B and HIV variants using either of the dominant cellular co-receptor types for HIV: CCR5 and CXCR4, or dual-tropic). These, combined with assays for cellular cytotoxicity are used to define a potential candidate for further development.

An accelerated compound identification approach

In an effort to speed up the process of identifying HIV drug leads or active compounds, an accelerated approach was adopted (Figure 2). This approach is based on 96-well fractionation using semi-preparative HPLC and LC-MS de-replication technology targeted at the identification of a significant proportion of compounds within botanical extracts.

RESULTS AND DISCUSSION

Twenty-nine plants were selected, collected and extracted resulting into 48 plant extracts which were screened using the HIV assay. The screening results are shown in Figures 3, 4 and 5. Inhibition of 50% viral replication is reported as IC_{50} while concentration of extract providing 50% of cell death after a 4-day time-window is reported by CD_{50} (cytotoxicity). The cytotherapeutic window (CW) being the ratio between CD_{50}/IC_{50} was determined. The results showed that most of the plant extracts demonstrated specific anti-viral activity in a concentration range that would also significantly affect cell viability that is, a low CW. However, three extracts, Alseudea anthelmintica (Figure 5 no. 38), Terminalia sericea (Figure 5 no. 39) and Schefflera umbellata (Figure 5 no. 40) were identified as potential hits for further development as these had CW values that were sufficiently large to warrant their further development.

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REFERENCE