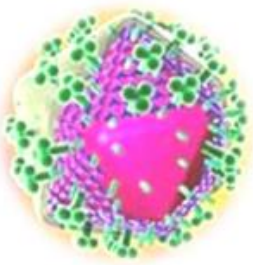
HIV SCIENCE 2014

& Infectious Diseases



Symposium Proceedings

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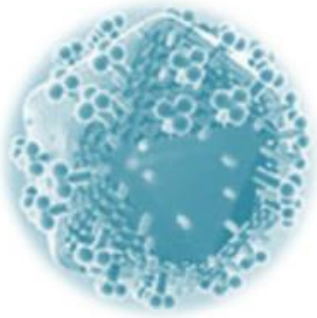

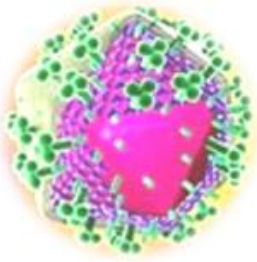

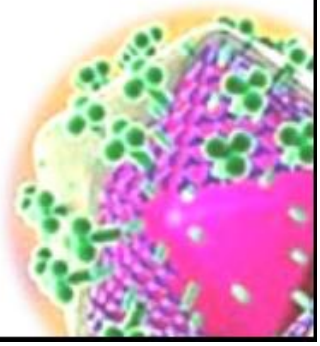

Oral Abstracts

ISSHID - 025-O

Investigation of anti-HIV activity, Cytotoxicity and HIV Integrase inhibitory activity of Polyherbal formulation BH extracts

S. Paul Raj[1], P. Selvam[2], Yves Pommier[3], Mathieu Metifiot[3], Marchand Christophe [3], Christophe Pannecouque[4], E De Clercq[4].

[1]Hans Rover Herbal Clinic, Perambalur, Tamil Nadu, India
[2]Nova College of Pharmaceutical Education and Research, Jupudi, Krishna Dt,
[3]Laboratory of Molecular Pharmacology, National Cancer Institute Mary Land, USA,
[4]Rega Institute for Medical Research, Leuven, Belgium

Background: The development of antiviral drugs has provided crucial new means to mitigate or relieve the debilitating effects of many viral pathogens. A rich source for the discovery of new HIV infection inhibitors has been and continues to be, the 'mining' of the large diversity of compounds from natural products. HIV integrase (IN) plays important roles at several steps, including reverse transcription, viral DNA nuclear import, targeting viral DNA to host chromatin and integration. Identification of novel inhibitors of HIV Integrase has emerged as promising new class of antiviral agents for the treatment of HIV/AIDS. Present work is to investigation of anti-HIV activity, cytotoxicity and HIV integrase inhibitory activity of various extracts of polyherbal formulation BH.

Method: Polyherbal extracts (BH) were tested for anti-HIV activity against HIV-1 and -2 in MT-4 cells and cytotoxicity also tested against uninfected MT-4 cells. BH extracts were investigated for inhibition of HIV integrase enzymatic activity to understand the mechanism of antiviral action. All the extracts were investigated for both 3'processing and strand transfer process of HIV-1 integrase enzymatic activity.

Results: All the extracts exhibited inhibitory activity against HIV-1 integrase enzyme (3'P IC50: 8.8-63 µg/ml and ST IC50: 4.9-65 µg/ml). The ethanolic extract (BH-H-ET) displayed significant inhibitory activity against both step of HIV in enzymatic activity (3'P IC50: 8.8µg/ml and ST IC50: 7.5 µg/ml). The ethanolic extract (BH-H-ET) also inhibits the HIV 1 replication at the concentration of 59.30 µg/ml and Cytotoxicity was found to be more than >125 µg/ml

Conclusion: All the extracts inhibit the HIV integrase enzymatic activity and ethanolic extract inhibit of HIV Virus and Integrase enzyme.

Anti-HIV and HIV integrase inhibitory activity of Herbal Formulation (BH)

Extracts	HIV Integrase activity		Anti-HIV activity	
	IC_{50} 3'P [a], (µg/ml)	IC_{50} ST[b], (µg/ml)	IC_{50} [c](µg/ml)	CC_{50} [d] (µg/ml)
BH-H-ET	8.8 ± 1.5	7.3 ± 1.9	59.30±12.73	>125
BH-H-CH-S1	63 ± 15	75 ± 30	>147	147±6.56
BH-H-CH-S2	58 ± 8	39 ± 18	>145	145±4.24
BH-H-Me	42 ± 7	47 ± 13	>121	121±9.47
BH-H-P.E	>100	65± 23	>20.71	20.71±10.80
PH-H-HEX Ext	9.5 ± 3.2	4.9 ± 1.2	>87.08	87.08 ±19.81

The results are IC50 ±S.D, n = 3 for HIV-1 IN inhibitory activity

[a]Concentration required to inhibits 3' processing reaction (3'P),
[b]Concentration required to inhibits 3' processing reaction (ST).
[c]Effective concentration of compound, achieving 50% protection of MT-4 cells against the cytopathic effect of HIV. d50% Cytotoxic concentration of compound, required to reduce the viability of mock infected MT-4 cells by 50%.

HIV I (HTLV IIIB) USED FOR ANTI-HIV ACTIVITY IN MT-4 CELLS

ISSHID - 026-O

A study of cardiac complications in HIV infected children

Pushpalatha S, Anitha K

Centre of Excellence in HIV care, Bowring and Lady Curzon Hospital, Department of Pediatrics, Bangalore Medical College and Research Institute, Bangalore, India

Background: Cardiac involvement in HIV infected children is sub-clinical and progressive resulting in an increase in the morbidity and mortality. Studies have demonstrated the presence of abnormality on echocardiography in HIV infected adults but there is a paucity of similar data regarding children in the Indian subcontinent. The objectives of this study were to evaluate the cardiac abnormalities in HIV infected children and to know the metabolic and nutritional risk factors for cardiac disease.

Methods: 100 consecutive HIV infected children were subjected to history, examination, nutritional assessment, complete hemogram, lipid profile,CD4 count, chest Xray,12 lead ECG and M mode transthoracic 2DECHO.Statistical analysis was done using univariate and multivariate regression analysis.

Results: Out of 100 HIV infected children,42% [25 males,17 females] had cardiac abnormalities of which only 6[14%]were symptomatic. Majority belonged to WHO clinical stage IV, with 13[28%] having low CD4 count. The most common cardiac abnormality was left ventricular systolic dysfunction(LVSD) in 19% ($p<0.05$),LVSD on ECHO was defined as fractional shortening % of < 28 %.Other abnormalities were mild tricuspid regurgitation in 14%,pericardial effusion in 6%,pulmonary artery hypertension in 6%,dilated right ventricle, right atrium in 3%,pulmonary regurgitation in 3% and mitral regurgitation in 1%.ECG showed sinus tachycardia in 14%,right ventricular hypertrophy in 6%,irregular rhythm in 3%. Among children with cardiac abnormalities, dyslipidemia was seen in 32[77%] ($p<0.05$), anemia in 29[69%]($p<0.05$),and malnutrition in 19[45%]($p>0.05$).

Conclusion: Though majority of children were asymptomatic, investigations revealed 42% of the children with subclinical cardiac abnormalities, they had significant dyslipidemia and anemia as compared to children without cardiac abnormalities. The study thus emphasizes the need for routine echocardiographic screening.

CD Abstracts

ISSHID - 185- C

Seroprevalence of Hepatitis B and Hepatitis C viral infections in HIV seropositive individuals at a tertiary care teaching hospital at Karimnagar, South India

K V Ramana, Anand Kalaskar, B Mohan Rao, Sanjeev D Rao

Department of Microbiology, Prathima Institute of Medical Sciences, Karimangar, Andhrapradesh, India

Background: Human immunodeficiency virus (HIV) infection and the disease course are influenced by many factors. Hepatotrophic viruses including Hepatitis B virus and Hepatitis C viral infections have been attributed to cause non-AIDS related morbidity and mortality among HIV infected patients. We aim to study the prevalence of HBV and HCV among HIV infected patients at a tertiary care teaching hospital at Karimnagar, South India

Methods: This study has been conducted between Jan. 2008 and Dec. 2012 which included 258 HIV seropositive individuals among 16796 patients tested. HIV infection was screened using National Aids Control Organization (NACO) guidelines using three different ELISA methods (conventional ELISA, Immunocomb and tridot). HBV and HCV infections were screened using commercially available enzyme linked immunosobent assays (ELISA).

Results: The total Seroprevalence for HIV, HBV and HCV was found to be 258 (1.5%), 305 (1.8%) and 7 (0.04%) respectively. Of the 258 HIV seropositive individuals screened for antibodies against HBV, 10 (3.8%) were reactive and none of the HIV infected patient was positive for HCV infection.

Conclusion: The results of the current study revealed that the prevalence of HBV among HIV infected population was significantly higher than among the HIV sero-negative individuals. There was no prevalence of HCV infection among HIV infected population. In the era of highly active antiretroviral therapy, though newer infections with HIV show a decline, it is necessary to monitor HIV infected population for hepatotrophic viruses that may influence disease progression and treatment response.

ISSHID - 186- C

Design and Synthesis of Novel Isatine-3-thiosemicarbazone derivatives as novel inhibitors of HIV Integrase/LEDGF protein-protein interaction

Periyasamy selvam[1], K.Nagarajan[2], Nouri Neamati[3], Tino Sanchenz[3].

[1]Nova College of Pharmaceutical Education and Research, Jupudi, Krishna Dt, India
[2]Unichem laboratories, Bangalore,
[3]Department of Pharmacology and Pharmaceutical Sciences, University of Southern California, School of Pharmacy, Los Angele, CA 90089, United States

Background: HIV integrase (IN) plays important roles at several steps, including reverse transcription, viral DNA nuclear import, targeting viral DNA to host chromatin and integration. Previous studies have demonstrated that HIV-1 Integrase interacts with a cellular lens epithelium-derived growth factor (LEDGF/p75) and that this viral/cellular interaction plays an important role for tethering HIV-1 preintegration complexes (PICs) to transcriptionally active units of host chromatin. Small molecule inhibitors of HIV IN/LEDGF have emerged as promising new class of antiviral agents for the treatment of HIV/AIDS. Present work is to Design, Synthesis and investigation of isatin-3-thiosemicarbazone derivatives as potential inhibitors of HIV replication and HIV integrase, HIV Integrase/LEDGF interaction.

Method: Novel isatin-3-thiosemicarbazone derivatives were synthesized and tested for anti-HIV activity against HIV-1 and -2 in MT-4 cells. Synthesized compounds were also investigated for inhibition of HIV integrase enzymatic activity and HIV Integrase/LEDGF interaction to understand the mechanism of antiviral action.

Results: Isatin-3-Semicarbazone derivative (PS 5) inhibits HIV Integrase/Lense Epithelium Derived Growth factor (LEDGF) interaction with inhibitory concentration of 42 ± 1 µM.

Conclusion: Isatin-3-Semicarbazone derivatives are the novel class of inhibitors of HIV IN/LEDGF interaction (protein-protein) and this lead molecule is suitable for further molecular modifications.

HIV Integrase and LEDGF inhibitory activity of Isatine-3-semicarbazone derivatives

Compounds	3' Proc.[a] (µM)	Integration[b] (µM)	LEDGF/p75-IN[c] (µM)
PS 2	>100	>100	>100
PS 3	>100	>100	>100
PS 4	>100	>100	>100
PS 5	>100	>100	>100
PS 6	>100	>100	**42 ± 1**
PS 7	>100	>100	>100
PS 11	>100	>100	>100

[a]Concentration required to inhibits 3' processing reaction, [b]Concentration required to inhibits 3' processing reaction, [c]Concentration required to inhibits HIV IN/LEDGF interaction.