the different selected clones were performed on BSC-1 cells by viral DNA reduction assay in presence of CDV. The DNA of each clone was extracted and purified for quantification by real time PCR to study the sensitivity of the selected drug resistant clones.

Results: Among the 16 HPMPC-resistant clones selected and genotyped, all bear the mutation V505A localized in the first shell of residues around the ATP binding site of the helicase domain. A212G is present in 14 out of 16 clones, suggesting that this mutation might also be important in the acquisition of drug resistance, or at least in the fitness of the virus. The mutation K697N, present in 6 clones, is localized at the acetylation site of the LTag and interestingly the lysine is mutated into an asparagine which mimics an acetyl-moiety. The presence of this mutation reverses the drug resistance phenotype as measured by quantitative PCR. The other mutations encountered, E92K and R130K described in previous studies and E279G, G649A and C695G which are new mutations as far as we know, may not contribute to the drug resistance phenotype.

Conclusion: The impact of these different characterized mutations has to be investigated in order to understand the mechanism of CDV resistance. Introduction of the mutations A212G, V505A and K697N in SV40 genome by site-directed mutagenesis is ongoing. All these data are consistent with a LTag dependant resistance mechanism.

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Poster Session 1: Retroviruses, Hepatitis Viruses, Respiratory Viruses, Emerging Viruses, and Antiviral Methods

Chairs: 4:00–6:00 pm, Pacific D-O

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Studies of HIV-1 Integrase Inhibitory Activity of *Wrightia tinctoria*

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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-1 infection inhibitors has been and continues to be the 'mining' of the large diversity of compounds already available in nature and exclusively those from botanical extracts. *Wrightia tinctoria* (WT) is used in the Indian system of medicine for the treatment of variety of diseases including HIV/AIDS and enriched with diketo indole derivatives such as indirubin and indigotin, but activity against HIV-1 integrase (IN) not yet been studied. In the present work we studied HIV-1 integrase inhibitory activity of different extracts of *WT*.

Methods: *W. tinctoria* leaf extracts have been studied against inhibition of HIV-1 IN enzymatic activity. All extracts of *WT* were investigated for both 3′-processing (3′-P) and strand transfer (ST) process of HIV-1 IN enzymatic activity.

Results: All extracts exhibited significant inhibitory activity against HIV-1 integrase enzyme (3′-P: 1.9–12 μg/ml and ST: 2.2–12 μg/ml). The aqueous extract (AWT) displayed potent inhibitory activity against both step of HIV-1 IN enzymatic activity (3′-P IC_{50}: 1.9 ± 0.451 μg/ml and ST IC_{50}: 1.4 ± 0.3 μg/ml).

Conclusions: Indole derivatives such as isatin, indirubin, indigotin and tryphanthrin are the principle active constituents of *W. tinctoria*, which may responsible for HIV-1 IN inhibitory activity. The results presented herein substantiate the basis for the discovery of novel natural product IN inhibitors and elucidate the combined usage of medicinal plants in AIDS treatment by Indian traditional practitioners.

Table 1

Extracts	IC_{50} 3′-P, mg/ml	IC_{50} ST, mg/ml
CWT	13.0 ± 3.0	12.0 ± 2.0
MWT	8.7 ± 1.2	4.6 ± 0.4
AWT	1.9 ± 0.5	1.4 ± 0.3
ETWT	2.3 ± 0.4	2.2 ± 0.5
EWT	5.3 ± 0.6	4.6 ± 1.0

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Preliminary Evidence of Rapid HBsAg Seroconversion in Patients with Chronic Hepatitis B (CHB) Treated with a DNA-based Amphipathic Polymer

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Background: REP 9AC is a DNA-based amphipathic polymer that targets viral glycoproteins important for viral entry and/or release. REP 9AC has been previously shown to result in the rapid clearance of surface antigen and the development of protective immunity in DHBV infected ducks which results in 56% of treated ducks achieving SVR (DHBV DNA negative) at 16 weeks post-treatment. The ability of REP 9AC to treat human patients with CHB is currently being evaluated in a proof of concept trial.

Methods: Patients with CHB were subjected to REP 9AC therapy administered by slow continuous infusion. Safety and virologic response (HBV DNA, HBsAg, anti-HBs) were assessed weekly, either at the trial site or by confirmatory testing (HBsAg, HBeAg, anti-HBs, anti-HBe) of frozen serum samples at a separate location using the Architect™ testing platform.

Results: All patients treated to date have cleared HBsAg and developed protective immunity (anti-HBs) which was observed as early as 7 days following initiation of treatment at higher doses. At the time of abstract submission, one patient has already exhibited clear signs of a sustained virologic response (HBV DNA−, HBsAg−, HBeAg−, anti-HBs+, anti-HBe+) for 12 continuous weeks off treatment after receiving only 23 weeks of treatment with REP 9AC.

Conclusions: These results demonstrate that amphipathic polymers are effective in rapidly reducing HBsAg levels in CHB patients which is a critical event for allowing patients to achieve a rapid seroconversion. Subsequent rapid appearance of anti-HBs and anti-HBe antibodies observed in these patients are the best indicators for achieving SVR and suggest that amphipathic polymers could become an important new tool in the treatment of CHB.

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