

Serenex and MolecularNature will share in intellectual property and revenue opportunities arising from the collaboration.

"MolecularNature has a library of potentially important pharmaceutical compounds," said Richard S. Kent, MD, Serenex president and CEO. "Serenex technology will help fast-forward the drug discovery process, determining compounds with the most value and propelling commercial development. Both companies will benefit under this agreement."

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Drug Discovery

HIV-1 integrase inhibitory substances extracted from *Coleus parvifolius*

2003 MAY 23 - (NewsRx.com) -- Scientists in Japan report that ethyl alcohol extracts of the herbaceous plant *Coleus parvifolius* "showed potent activity against HIV-1 integrase" in their studies.

"For the purpose of discovering anti-HIV-1 agents from natural sources, water and EtOH [ethyl alcohol] extracts of 50 Thai plants were screened for their inhibitory activity against HIV-1 integrase (IN), an enzyme essential for viral replication. Of these plants, an EtOH extract of *Coleus parvifolius* Benth. (aerial parts) showed potent activity against HIV-1 IN with an IC₅₀ value of 92 mcg/mL," said S. Tewtrakul and colleagues, Toyama Medical & Pharmaceutical University, Institute of Natural Medicine.

They isolated 11 compounds from the *C. parvifolius* extract: "luteolin 5-O-beta-D-glucopyranoside (1), luteolin (2), luteolin 7-methyl ether (3), luteolin 5-O-beta-D-glucuronide (4), 5-O-beta-D-glucopyranosyl-luteolin 7-methyl ether (5), rosmarinic acid (6), rosmarinic acid methyl ester (7), daucosterol (8), a mixture of alpha- and beta-amyrin (9, 10), and phytol (11)."

The researchers reported that "rosmarinic acid methyl ester (7), rosmarinic acid (6), luteolin (2), and luteolin 7-methyl ether (3) exhibited inhibitory activities against HIV-1 IN with IC₅₀ values of 3.1, 5.0, 11.0, and 11.0 microM, respectively.

"Among rosmarinic acid derivatives, the HIV-1 IN inhibitory activity increased in turn for a dimer (IC₅₀ = 5.0 microM), a trimer (IC₅₀ = 1.4 microM), and a tetramer (IC₅₀ = 1.0 microM)," Tewtrakul and colleagues said.

They published their findings in *Phytotherapy Research* (HIV-1 integrase inhibitory substances from *Coleus parvifolius*. *Phytother Res*, 2003;17(3):232-239).

For more information, contact M. Hattori, Toyama Med & Pharmaceutical University, Institute Nat Med, 2630 Sugitani, Toyama 9300194, Japan.

Publisher contact information for the journal *Phytotherapy Research* is: John Wiley & Sons Ltd., Baffins Lane Chichester, W Sussex PO19 1UD, UK.

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Drug Discovery

Novel mechanism for inhibition of HIV-1 reverse transcriptase reported

2003 MAY 23 - (NewsRx.com) -- University of Michigan pharmacologists say they've identified "potent and selective HIV-1 reverse transcriptase (RT) inhibitors that may work by a mechanism distinct from that of current HIV drugs."

Writing in the journal *Bioorganic Chemistry*, A.G. Skillman and colleagues reported that "the most potent of these compounds (Compound 4: 2-naphthalenesulfonic acid, 4-hydroxy-7-[5-hydroxy-6-[(4-cinnamylphenyl)-azo]-7-sulfo-2-naphthalenyl]amino]carbonyl]amino]-3-[(4-cinnamylphenyl)-azo], disodium salt) has an IC₅₀ of 90 nM for inhibition of polymerase chain extension, a K_d of 40 nM for inhibition of DNA-RT binding, and an IC₅₀ of 25-100 nM for inhibition of RNaseH cleavage.

"The parent compound was as effective against 10 nucleoside and non-nucleoside resistant HIV-1 RT mutants as it was against the wild-type enzyme," the researchers said.

"Compound 4 inhibited HIV-1 RT and murine leukemia virus (MLV) RT, but it did not inhibit T-4 DNA polymerase, T-7 DNA polymerase, or the Klenow fragment at concentrations up to 200 nM," they continued (A novel mechanism for inhibition of HIV-1 reverse transcriptase. *Bioorg Chem*, 2002;30(6):443-458).

Skillman's group reported that their "Compound 4 protected cells from HIV-1 infection at a concentration more than 40 times lower than the concentration at which it caused cellular toxicity."

Additional information can be obtained by contacting G.L. Kenyon, University Michigan, College Pharmacy, 428 Church St., Ann Arbor, MI 48109, USA.

The publisher of the journal *Bioorganic Chemistry* can be contacted at: Academic Press Inc. Elsevier Science, 525 B St., Ste. 1900, San Diego, CA 92101-4495, USA.

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Drug Hypersensitivity

Effective tolerance induction protocol reported for HIV patients

2003 MAY 23 - (NewsRx.com) -- An effective tolerance induction protocol for HIV patients with hypersensitivity to sulfonamides and antiretroviral drugs was outlined in the journal *Revue Francaise d'Allergologie et d'Immunologie Clinique*.

"HIV infected patients are at greater risk for drug hypersensitivity than non-HIV infected patients. Sulfonamides and antiretroviral drugs are most often the responsible agents," said D. Messaad and colleagues, CHU Montpellier, INSERM, France (Tolerance-induction protocol in HIV-infected patients with drug hypersensitivity. *Rev Fr Aller Immunol Clin*, 2002;42(8):757-762).

