1) Evaluation of efficacy of a polyherbal (Basant) anti-HIV vaginal microbicide in humanized mouse model and its mode of action.	
Principle Investigators	I. Dr Manoj Pastey, Assistant Professor, Oregon State University, USA. II. Dr Smita Kulkarni, Scientist E, Dept of Molecular Virology, NARI, Pune
Other investigators	Nil
Category/nature	Indo-US Joint Statement on prevention of HIV/AIDS and sexually transmitted diseases (R21)
Collaboration/participating centres	1.Oregon State University, Corvallis, Oregon 97331, USA. 2.National AIDS Research Institute, Pune, 411026, Maharashtra, India.
Funding agency(ies)/sponsors	National Institutes of Health, USA & Indian Council of Medical Research, India.
Budget	Rs.49,53,360/- (NARI).
Study period	November 2009 - December 2012.
Objectives	i. To confirm anti-HIV activity and to define the mechanism of action of Basant (OSU & NARI). ii. To evaluate the efficacy of Basant in preventing HIV transmission in humanized mouse model (OSU). iii. To evaluate efficacy of Basant against different clades of HIV (NARI).
Descriptions	Basant is a polyherbal topical microbicide candidate with demonstrated activity against CXCR4 tropic HIV-1, fungal, bacterial and viral sexually transmitted pathogens. Considering its broad-spectrum activity, Basant was further evaluated for activity against multiple HIV-1 clades using cell based assays, for determining the mechanism of action and for efficacy in preventing intra-vaginal HIV transmission in humanized mouse model. The results obtained at both institutes indicated that Basant is effective against HIV-1 CXCR4 as well as CCR5 tropic HIV-1 strains belonging to different clades. It inhibited HIV-1 by direct inactivation more effectively, however was also found to act at the post entry step. Molecular assays confirmed that Basant inhibited HIV-1 integration and provirus formation. Experiments in BLT mouse model indicated that Basant inhibited virus transmission without any toxicity.
Current status	The committed objectives have been achieved and project has been completed

	successfully in December 2012.
Publications	One manuscript submitted, one under preparation.
Presentations	Poster presentation: 3rd Biennial International Conference on New Developments in Drug Discovery from Natural Products and Traditional Medicines (DDNPTM), 23-25 November 12, NIPER, Mohali from. Basant, a polyherbal cream exhibits potent and broad anti-HIV1 activity Joshi Rupali, Pastey Manoj, Talwar GP and Kulkarni Smita.

2) Design, synthesis and biological evaluation of HIV-1 RT-inhibitors 4-Thioazolidinone compounds.	
Co-Principle Investigators	I. Dr S B Katti, Scientist G Central Drug Research Institute, Lucknow, India II. Dr Smita Kulkarni, Scientist E, Dept of Molecular Virology, National AIDS Research Institute, Pune, India
Other investigators	Nil
Category/nature	IN-SILICO Drug Discovery – Modeling, simulation and drug design using Bioinformatics tools and databases.
Collaboration/participating centres	Central Drug Research Institute, Lucknow, 226001, Uttar Pradesh, India National AIDS Research Institute, Pune, 411026, Maharashtra, India.
Funding agency(ies)/sponsors	Indian Council of Medical Research, Government of India
Budget	Rs. 20, 65,504/- (NARI) Rs 40,48,800/- (CDRI)
Study period	October 2009 - September 2012.
Objectives	i. Design and synthesis of 4-thiazolidinone (CDRI) ii. Screening of the synthesized 4-thiazolidinones using enzymatic RT inhibition assay (CDRI) iii. Cell based screening of selected 4-thiazolidinones (NARI) iv. Lead optimization using QSAR and Molecular modeling (CDRI)
Descriptions	2,3-diaryl-1,3-thiazolidin-4-one has emerged as an important chemical scaffold having promising anti-HIV activity. Based on the rational drug design approach, 72 of novel thiazolidin-4-ones bearing different aryl/heteroaryl moieties at position C-2 and N-3 were synthesizedand tested for anti-HIV activity using cell based and enzymatic RT inhibition assay. Four NCEs have been identified as leads. Further funcionalization of the lead NCEs may help in developing more effective NCEs.
Current status	The committed objectives have been achieved. The project has been completed successfully in September 2012.
Publications	1. Vanangamudi Murugesan, Vinay S. Tiwari, Reshu Saxena, Rajkamal

	Tripathi, Ramesh Paranjape, **Smita Kulkarni**, Nandini Makwana , Rahul Suryawanshi , Seturam B. Katti. Lead optimization at C-2 and N-3 positions of thiazolidin-4-ones as HIV-1 non nucleoside reverse transcriptase inhibitors. Bioorganic & Medicinal Chemistry, 19: 6919-26. 2. One manuscript under preparation
Presentations	Nil

3) In vitro testing of indigenously developed active principles for identification andcharacterization of candidate anti-retroviral microbicides.	
Principle Investigator	Dr Smita Kulkarni, Scientist E, Dept of Molecular Virology, NARI, Pune
Co-Principle Investigators	1. Dr. S P Joshi, Scientist F, NCL, Pune. 2. Dr. K K Singh, Principal, C U Shah College of Pharmacy, Mumbai. 3. Dr. KVR Reddy, Scientist F, NIRRH, Mumbai.
Other Co-investigator/s	1. Dr. Jayanta Bhattacharya, Scientist D, NARI 2. Dr. Arun Risbud, Scientist F, NARI
Category/nature	Research and Development/Programme Support Microbicide Development and related areas
Collaboration/participating centres	1. National AIDS Research Institute, Pune, India 2. National Chemical Laboratory, Pune. 3. National Institute for Research in Reproductive Health, Mumbai. 4. C U Shah College of Pharmacy, SNDT Women's University, Mumbai.
Funding agency(ies)/sponsors	Department of Biotechnology and Indian Council of Medical Research, Government of India.
Budget	Rs. 2, 41, 19,000/-
Study period	October 2006 - July 2011.
Objectives	1. Selection and development of candidate lead compounds (NCL, Pune; NIRRH, Mumbai and CU Shah College of Pharmacy, Mumbai) 2. Screening of lead preparations for anti-HIV activity using cell based high throughput TZM-bl assay (NARI). 3. Evaluation of anti-HIV activity using additional *in-vitro* models (NARI). a. Evaluation of activity using PM-1 cells. b. Evaluation of toxicity and efficacy using cervical explants cultures. c. Toxicity testing using Transwell Epithelial model system. d. Evaluation of lead compounds against other STIs (*C. albicans, N. gonorrhoeae, H. ducreyi* and HSV-2). 4. Identification of lead compounds
Descriptions	Under this project, we developed and tested indigenous preparations (herbal and AMPs) for anti-HIV and anti-STI activity. The outcomes are as follows • The project has created facility that comprises necessary *in vitro* models for testing microbicide candidates. • It has created bioactivity profile of 79 natural products including their HPLC

	and HPTLC profiles. • Seven lead extracts showing anti-HIV and anti-STI activities have been identified that would be further taken for identification of active principles and determination of mechanism of action (Reference: Porject No II in Ongoing projects).
Current status	The committed objectives have been achieved. The project has been completed successfully in July 2011.
Publications/patents filed	• A patent application has been submitted in collaboration with NCL, Pune. (1342DEL2012). • One manuscript submitted, other manuscripts under preparation.
Presentations	**1.** Screening of indigenous plant products as potential candidate microbicides. Navin Pathare, Swati Joshi, Nutan Jadhav, Sunayana Shelar, Arati Mane, Roshan Kulkarni, Arun Risbud and Smita Kulkarni. Abstract: 114 Pg. No: 107. Poster presented at the International Microbicides Conference (M2010), Pittsburgh, USA, 22-25 May 2010 **2.** RVF H a promising protein having Anti-STI and Anti-HIV activities identified in Rabbit Vaginal Fluid. M Patgaonkar, R.D Yedery, S. Kulkarni, K. V .R .Reddy Abstract: 134 Pg. No: 115. Poster presented at the International Microbicides Conference (M2010), Pittsburgh, USA, 22-25 May 2010. **3.** Novel Lead for HIV Microbicide from Plant Origin. D. Palshetkar, Navin Pathare, Balaji Deshmukh, P. A. Tatke, Nutan Jadhav, Megha Pawar, S.S.Kulkarni, K. K. Singh. Oral presentation at the South Asian Chapter of American College of Clinical Pharmacology. Oral presentation at the 4th International Conference on Innovations in Translating Technologies through Clinical Pharmacology, Mumbai, 10-12 December 2010. **4.** Design and Evaluation of Anti HIV Microbicidal Herbal Vaginal Gel. A. D. Palshetkar, Navin Pathare, Balaji Deshmukh, P. A. Tatke, Nutan Jadhav, Megha Pawar , S. S. Kulkarni, K. K. Singh. Poster presented at the Controlled Release Society-Indian Chapter 11th International Symposium on, Advances in Technology and Business potential of New Drug Delivery Systems, Mumbai, 16th-17th Feb 2011.

4) Design and Development of anti-viral compounds as inhibitors of HIV replication	
Principle Investigator	Dr. R K Singh, Assistant Professor, University of Allahabad, Allahabad, India
Co-Investigator	Dr Smita Kulkarni, Scientist E, Dept of Molecular Virology, NARI, Pune, India
Other investigator	Nil
Category/nature	Research & Development/Programme Support Medical Sciences and allied areas
Collaboration/participating centres	1. Univ of Allahabad, Allahabad, India 2. National AIDS Research Institute, Pune, India
Funding agency(ies)/sponsors	Department of Biotechnology and Indian Council of Medical Research, Government of India.
Budget	Rs 8,64,000/- (NARI) Rs 26,62,253/- (UoA)
Study period	2006-2011
Objectives	1. Design and synthesis of NNRTIs, NRTIs and Pro drugs of active NRTs (UoA). 2. Anti-HIV testing of synthesized NNRTIs, NRTIs and Pro drugs of active NRTs using cell based assays (NARI)
Descriptions	A total of 64 NCEs were tested for anti-HIV activity. Analysis indicated that Therapeutic Indices of these NCEs were low; hence the NCEs were not taken further. However the chemical structures of these NCE's may be referred as a guideline to develop more effective RT inhibitors.
Current status	Completed
Publications	Manuscript under preparation
Presentations	Poster presented at the Microbicide 2010 Conference held in Pittsburgh, USA. Design and development of novel NNRTIs against HIV-1 R.K.Singh, G. Kumari, D.Yadav, S.S.Kulkarni, S.K.Gupta