

# CURRICULUM VITAE Pooran Chand, Ph.D. CEO Therachem Research Medilab (India), Pvt. Ltd.

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#### **EDUCATION**

1973: B.S. Agra University, Agra, India

1975: M.S. Organic Chemistry, Agra University, Agra, India

1979: Ph.D. Organic Chemistry, Rajasthan University, Jaipur, India

1980: Post-Doctoral Fellow, Rajasthan University, Jaipur, India with Professor K. C. Joshi

#### **EMPLOYMENT**

**2008-Present:** United Chem Resources, Birmingham, AL, USA & Therachem Research

Medilabs (India) Pvt. Ltd., Jaipur, India. (Both companies are same)

**Chief Executive Officer** 

1991-2008: BioCryst Pharmaceuticals Inc., Birmingham, AL, USA

**2006-2008:** Executive Director, Medicinal Chemistry

**1999-2005:** Director, Medicinal Chemistry

**1991-1999:** Various supervisory positions with increased responsibilities:

Chemist I, Chemist II, Chemist III, Senior Research Chemist,

Group Leader and Section Head.

1987-1989: *E.H.R.T.*, *Birmingham*, *AL*, *USA* 

**Assistant Director** 

1982-1986: Ballarpur Industries Ltd., Karwar, Karnataka, India.

Research Scientist

### ACADEMIC APPOINTMENTS

**2009-Present** Adjunct Professor *University of Alabama*, Chemistry Department, University of

Alabama, Tuscaloosa, AL, USA

**2009:** Adjunct Professor, *University of Alabama*, Chemistry Department, at Birmingham,

AL, USA

**1987-1990:** Post-Doctoral Fellow, *Southern Research Institute*, Birmingham, AL, USA **1986-1987:** Post-Doctoral Fellow, *University of Alabama*, Birmingham, Alabama with

Professor Koop Lammertsma.

1981: DANIDA Fellow at *Neurochemical Institute*, Copenhagen, Denmark

#### **CURRENT PROFESSIONAL AFFILIATIONS**

Member of The American Chemical Society (ACS)



#### RESEARCH EXPERIENCE

### BioCryst Pharmaceuticals, Inc.b Birmingham, AL, USA:

**Structure-based drug design**: Targets are selected for which the enzyme structure is known or being solved in-house or by the collaborators. The design of the molecules is carried out by a group of crystallographers and chemists. Successfully completed four projects and initiated a fifth project.

- 1. **Neuraminidase Inhibitors (For Flu):** Designed, synthesized and brought the target molecule (BCX-1812, Peramivir) to the IND stage. Research included intensive work to design a charged, multi-substituted cyclopentane derivative as well as the synthesis of a large number of pro-drugs. Developed a **commercial 5 step synthesis** for the selected molecule (BCX-1812) which has **5 chiral centers**, that was used for its GMP synthesis for phase-I trials. The project was licensed to Johnson & Johnson before returning back to BioCryst. The drug failed in phase-III clinical trials when used orally. Development was continued using intravenous and intramuscular routes. Peramivir was approved for treatment of influenza in Japan under the commercial name RAPIACTA®.
- 2. **Tissue Factor/ Factor VIIa Inhibitors (For Cardiovascular diseases):** Designed, synthesized and brought the target molecule to the IND stage. More than 2000 fully characterized new compounds and a number of pro-drugs were synthesized under my supervision. Developed a practical synthesis to prepare the molecule in Kg quantities. The sourcing and synthesis of the cheap starting materials were done in India. The product has been synthesized under c-GMP conditions.
- 3. **PNP Inhibitors:** Was involved in the discovery and large scale synthesis of BCX-4208, which was collaborated with Roche Pharmaceuticals. New compounds have been discovered which are under preclinical evaluations.
- 4. **Paramyxovirus Inhibitors (For Paraflu):** Designed, discovered and synthesized the target carbohydrate-based molecule.
- 5. **Hepatitis C viral polymerase Inhibitors (For HCV):** The project is in the discovery stage. A number of lead molecules based upon nucleosides have been discovered and the refining is under way. One molecule has been selected for toxicology studies.

#### E.H.R.T., Birmingham, AL, USA:

This is a 'Drugs of Abuse' (amphetamines, barbiturates, cocaine, phencyclidine, morphine and THC) testing company. The methods used were radioactive assay and GC/MS for the identification of drugs and drug metabolites in urine. I managed the drug testing program and developed a synthesis lab for the preparation of radioactive (C-14) compounds.

#### Southern Research Institute, Birmingham, AL, USA:

This is a non-profit drug discovery institute, which has licensed 7 drugs for treatment of cancer to different companies. I worked on carbohydrates (mono-, di- and trisaccharides) and radiolabeled (C-14) compounds.

### University of Alabama, Birmingham, AL, USA:

Conducted research aimed to study coal liquefaction and phosphorus-tungsten complexes.



### **Ballarpur Industries Ltd. Karwar (India):**

Developed the commercial processes for purifying technical grade phosphoric acid to food grade phosphoric acid; photographic grade KBr from Bromine and KOH and urea; Ethyl bromide from ethanol and bromine and developed some oil well chemicals.

### Neurochemical Institute, Copenhagen, Denmark:

Carried out research on the toxicity of industrial chemicals on rat brain and liver enzymes.

### Rajasthan University, Jaipur, India:

Research was focused on identification and synthesis of CNS active fluorine containing molecules, particularly indoles. The research encompassed other molecules including Aromatics (benzene, pyridine, naphthalene, benzodiazepine, pyrrole, etc.); carbohydrates (furanose, pyranose, acyclics, carbocyclics, nitrogen containing sugars, etc.), nucleosides of the same and nucleotides; peptides; radioactive molecules. More than **5000** new, fully characterized compounds resulting from this research were deposited into the library of BioCryst.

#### **PUBLICATIONS**:

- 1. Kotian, Pravin L.; Ghosh, Ajit; Lin, Tsu-Hsing; Wu, Minwan; Satish Kumar, V.; Babu, Yarlagadda S.; Chand, Pooran Synthetic approaches to imino sugar (2R,3R,4S)-2-(hydroxymethyl)-4-methylpyrrolidine-3,4-diol from naturally occurring sugar and amino acid. *Tetrahedron Letters* (2011), *52*(3), 365-368.
- 2. Bantia, Shanta; Parker, Cynthia; Upshaw, Ramanda; Cunningham, Amanda; Kotian, Pravin; Kilpatrick, J. Michael; Morris, Philip; Chand, Pooran; Babu, Yarlagadda S. Potent orally bioavailable purine nucleoside phosphorylase inhibitor BCX-4208 induces apoptosis in B- and T-lymphocytes-A novel treatment approach for autoimmune diseases, organ transplantation and hematologic malignancies. *International Immunopharmacology* (2010), 10(7), 784-790.
- 3. Kotian, Pravin L.; Krishnan, Raman; Rowland, Scott; El-Kattan, Yahya; Saini, Surendra K.; Upshaw, Ramanda; Bantia, Shanta; Arnold, Shane; Babu, Y. Sudhakar; Chand, Pooran Design, parallel synthesis, and crystal structures of biphenyl antithrombotics as selective inhibitors of tissue factor FVIIa complex. Part 1: Exploration of S2 pocket pharmacophores. [Erratum to document cited in CA151:147921] Bioorganic & Medicinal Chemistry (2010), 18(1), 460.
- 4. Alymova, Irina V.; Watanabe, Makiko; Boyd, Kelli L.; Chand, Pooran; Babu, Y. Sudhakara; Portner, Allen Efficacy of the novel parainfluenza virus hemagglutinin-neuraminidase inhibitor BCX 2798 in mice further evaluation. *Antiviral Therapy* (2009), *14*(7), 891-898
- 5. Kotian, Pravin L.; Krishnan, Raman; Rowland, Scott; El-Kattan, Yahya; Saini, Surendra K.; Upshaw, Ramanda; Bantia, Shanta; Arnold, Shane; Sudhakar Babu, Y.; Chand, Pooran Design, parallel synthesis, and crystal structures of biphenyl antithrombotics as selective inhibitors of tissue factor FVIIa complex. Part 1: Exploration of S2 pocket pharmacophores. *Bioorganic & Medicinal Chemistry* (2009), 17(11), 3934-3958.



- 6. Alymova, Irina V.; Taylor, Garry; Mishin, Vasiliy P.; Watanabe, Makiko; Murti, K. Gopal; Boyd, Kelli; Chand, Pooran; Babu, Y. Sudhakara; Portner, Allen. Loss of the *N*-linked glycan at residue 173 of human parainfluenza virus type 1 hemagglutinin-neuraminidase exposes a second receptor-binding site. *Journal of Virology* (2008), 82(17), 8400-8410.
- 7. Babu, Y. Sudhakara; Chand, Pooran; Kotian, Pravin L. Influenza neuraminidase inhibitors as antiviral agents. Annual Reports in Medicinal Chemistry (**2006**), *41*, 287-297.
- 8. Krishnan, Raman; Kotian, Pravin L.; Chand, Pooran; Bantia, Shanta; Rowland, Scott; Babu, Y. S. Probing the S2 site of factor VIIa to generate potent and selective inhibitors: the structure of BCX-3607 in complex with tissue factor-factor VIIa, *Acta Crystallographica, Section D: Biological Crystallography* (2007), *D63*(6), 689-697.
- 9. Arnold, C. Shane; Parker, Cynthia; Upshaw, Ramanda; Prydz, Hans; Chand, Pooran; Kotian, Pravin; Bantia, Shanta; Babu, Y. Sudhakar. The antithrombotic and anti-inflammatory effects of BCX-3607, a small molecule tissue factor/factor VIIa inhibitor, *Thrombosis Research* (2006), 117(3), 343-349.
- 10. Chand, Pooran. Recent Advances in the Discovery and Synthesis of Neuraminidase Inhibitors. *Expert Opinion on Therapeutic Patents* (2005), *15*(8), 1009-1025.
- 11. Bantia, Shanta; Arnold, Shane, Parker, Cynthia; Upshaw, Ramanda; Chand, Pooran. Anti-influenza Virus Activity of Peramivir in mice with single intramuscular injection. *Antiviral Research* (2006), 69(1), 39-45.
- 12. Kotian, Pravin L.; Kumar, V. Satish; Lin, Tsu-Hsing; El-Kattan, Yahya; Ghosh, Ajit; Wu, Minwan; Cheng, Xiaogang; Bantia, Shanta; Babu, Yarlagadda S.; Chand, Pooran. An Efficient Regioselective Synthesis of Acyclic N7- And N9-Adenine Nucleosides Via Alkylation Using Secondary Electrophile to Introduce Versatile Functional Groups At The C-1-Position Of Acyclic Moiety. *Nucleosides, Nucleotides & Nucleic Acids* (2006), 25(2), 121-140.
- 13. Wu, Minwan; El-Kattan, Yahya; Lin, Tsu-Hsing; Ghosh, Ajit; Vadlakonda, Satish; Kotian, Pravin L.; Babu, Yarlagadda S.; Pooran Chand. Synthesis of 9-[1-(Substituted)-3-(Phosphonomethoxy) Propyl]Adenine Derivatives As Possible Antiviral Agents. *Nucleosides, Nucleotides & Nucleic Acids* (2005), 24(10-12), 1543-1568.
- 14. Wu, Minwan; El-Kattan, Yahya; Lin, Tsu-Hsing; Ghosh, Ajit; Vadlakonda, Satish; Kotian, Pravin L.; Babu, Yarlagadda S.; Chand, Pooran. Synthesis of 9-[1-(Substituted)-2-(Phosphonomethoxy) Ethyl]Adenine Derivatives As Possible Antiviral Agents. *Nucleosides, Nucleotides & Nucleic Acids* (2005), 24(10-12), 1569-1585.
- 15. Ghosh, Ajit; El-Kattan, Yahya; Wu, Minwan; Lin, Tsu-Hsing; Vadlakonda, Satish; Kotian, Pravin L.; Babu, Yarlagadda S.; Chand, Pooran. Synthesis Of 9-[1-(1-Hydroxyethyl)-3-(Phosphonomethoxy) Propyl]Adenine And Prodrug As Possible Antiviral Agents. *Nucleosides, Nucleotides & Nucleic Acids* (2005), 24(10-12), 1587-1595.
- 16. El-Kattan, Yahya; Lin, Tsu-Hsing; Wu, Minwan; Kumar, V. Satish; Kotian, Pravin L.; Ghosh, Ajit; Babu, Yarlagadda S.; Chand, Pooran. Synthesis Of N6-Substituted 9-[3-(Phosphonomethoxy)Propyl]Adenine Derivatives As Possible Antiviral Agents. *Nucleosides, Nucleotides & Nucleic Acids* (2005), 24(10-12), 1597-1611.



- 17. Kotian, Pravin L.; Pooran Chand. An Efficient Stereoselective Synthesis Of (3S,4R)-4-(Hydroxymethyl)Pyrrolidin-3-ol from (S)-Diethylmalate. *Tetrahedron Letters* (2005), 46(19), 3327-3330.
- 18. Kotian, Pravin L.; Lin, Tsu-Hsing; El-Kattan, Yahya; Pooran Chand. A Practical Large-Scale Synthesis of (3*R*,4*R*)-4-(Hydroxymethyl)pyrrolidin-3-ol Via Asymmetric 1,3-Dipolar Cycloaddition. *Organic Process Research & Development* (**2005**), *2*, 193-197.
- 19. Arnold, C. Shane; Parker, Cynthia; Upshaw, Ramanda; Prydz, Hans; Chand, Pooran; Kotian, Pravin; Bantia, Shanta, Babu, Y. Sudhakar. The Antithrombotic and Anti-Inflammatory Effects of BCX-3607, A Small Molecule Tissue Factor/Factor VIIa Inhibitor. *Thrombosis Res.* (2006), 117(3), 343-349.
- 18. Chand, Pooran; Kotian, Pravin L.; Morris, Philip E.; Bantia, Shanta; Walsh, David A.; Babu, Yarlagadda S. Synthesis and Inhibitory Activity of Benzoic Acid and Pyridine Derivatives on Influenza Neuraminidase. *Bioorganic & Medicinal Chemistry* (2005), *13*, 2665-2678.
- 19. Chand, Pooran; Bantia, Shanta; Kotian, Pravin L.; El-Kattan, Yahya; Lin, Tsu-Hsing; Babu, Yarlagadda S. Comparison of the anti-influenza virus activity of cyclopentane derivatives with oseltamivir and zanamivir in vivo. *Bioorganic & Medicinal Chemistry* (2005), *13*(12), 4071-4077.
- 20. Chand, Pooran; Babu, Y. Sudhakar; Bantia, Shanta; Rowland, Scott; Dehghani, Ali; Kotian, Pravin L.; Hutchison, Tracy L.; Ali, Shoukath; Brouillette, Wayne, El-Kattan, Yahya; Lin, Tsu-Hsing. Syntheses and Neuraminidase Inhibitory Activity of Multisubstituted Cyclopentane Amide Derivatives. *J. Med. Chem.* (2004), *47*, 1919-1929.
- 21. Alymova, Irina V.; Taylor, Garry; Takimoto, Toru, Lin, Tsu-Hsing; Chand, Pooran; Babu, Y. Sukhakara; Li, Chenghong; Xiong, Xiaoping; Portner, Allen. Efficacy of Novel Hemagglutinin-Neuraminidase Inhibitors BCX 2798 and BCX 2855 against Human Parainfluenza Viruses In Vitro and In Vivo. *Antimicrobial Agents and Chemotherapy* (2004), 48 (5), 1495-1502.
- 22. Sweet, Clive; Jakeman, Kenneth J.; Bush, Karen; Wagaman, Pamela C.; Mckown, Linda A.; Streeter, Anthony J.; Desai-Krieger, Daksha; Chand, Pooran, Babu, Yarlagadda S. Oral Administration of Cyclopentane Neuraminidase Inhibitors Protects Ferrets against Influenza Virus Infection. *Antimicrobial Agents and Chemotherapy* (2002), 46 (4), 996-1004.
- 23. Chand, Pooran; Kotian, Pravin L.; Dehghani, Ali; El-Kattan, Yahya; Lin, Tsu-Hsing; Hutchison, Tracy L.; Babu, Y. Sudhakar; Bantia, Shanta; Elliott, Arthur J.; Montgomery, John A. Systematic Structure-Based Design and Stereoselective Synthesis of Novel Multi-Substituted Cyclopentane Derivatives with Potent Anti-influenza Activity. *Journal of Medicinal Chemistry* (2001), 44(25), 4379-4392.
- 23. Bantia, S.; Parker, C. D.; Ananth, S. L.; Horn, L. L.; Andries, K.; Chand, P.; Kotian, P. L.; Dehghani, A.; El-Kattan, Y.; Lin, T.; Hutchison, T. L.; Montgomery, J. A.; Kellog, D. L.; Babu, Y. S. Comparison of the anti-influenza virus activity of RWJ-270201 with those of oseltamivir and zanamivir. *Antimicrobial Agents and Chemotherapy* (2001), 45(4), 1162-1167.
- 24. Babu, Y. Sudhakar; Chand, Pooran; Bantia, Shanta; Kotian, Pravin; Dehghani, Ali; El-Kattan, Yahya; Lin, Tsu-Hsing; Hutchison, Tracy L.; Elliott, Arthur J.; Parker, Cynthia D.; Ananth, Sandya L.; Horn, LaShun L.; Laver, Graeme W.; Montgomery, John A. Bcx-1812 (RWJ-270201):



- discovery of a novel, highly potent, orally active, and selective influenza neuraminidase inhibitor through structure-based drug design. *Journal of Medicinal Chemistry* (**2000**), *43*(19), 3482-3486.
- 25. Atigadda, Venkatram R.; Brouillette, Wayne J.; Duarte, Franco; Babu, Yarlagadda S.; Bantia, Shanta; Chand, Pooran; Chu, Naiming; Montgomery, John A.; Walsh, David A.; Sudbeck, Elise; Finley, James; Air, Gillian M.; Luo, Ming; Laver, Graeme W. Hydrophobic benzoic acids as inhibitors of influenza neuraminidase. *Bioorganic & Medicinal Chemistry* (1999), 7(11), 2487-2497.
- 26. Atigadda, Venkatram R.; Brouillette, Wayne J.; Duarte, Franco; Ali, Shoukath M.; Babu, Yarlagadda S.; Bantia, Shanta; Chand, Pooran; Chu, Naiming; Montgomery, John A.; Walsh, David A.; Sudbeck, Elise A.; Finley, James; Luo, Ming; Air, Gillian M.; Laver, Graeme W. Potent Inhibition of Influenza Sialidase by a Benzoic Acid Containing a 2-Pyrrolidinone Substituent. *Journal of Medicinal Chemistry* (1999), 42(13), 2332-2343.
- 27. Chand, Pooran; Babu, Yarlagadda S.; Bantia, Shanta; Chu, Naiming; Cole, L. Brent; Kotian, Pravin L.; Laver, W. Graeme; Montgomery, John A.; Pathak, Ved P.; Petty, Sandra L.; Shrout, David P.; Walsh, David A.; Walsh, Gerald M. Design and Synthesis of Benzoic Acid Derivatives as Influenza Neuraminidase Inhibitors Using Structure-Based Drug Design. *Journal of Medicinal Chemistry* (1997), 40(25), 4030-4052.
- 28. Sudbeck, E. A.; Jedrzejas, M. J.; Singh, S.; Brouillette, W. J.; Air, G. M.; Laver, W. G.; Babu, Y. S.; Bantia, S.; Chand, P.; Chu, N.; Montgomery, J. A.; Walsh, D. A.; Luo, M. Guanidinobenzoic acid inhibitors of influenza virus neuraminidase. *Journal of Molecular Biology* (1997), 267(3), 584-594.
- 29. Niwas, Shri; Chand, Pooran; Pathak, Ved P.; Montgomery, John A. Structure-Based Design of Inhibitors of Purine Nucleoside Phosphorylase. 5. 9-Deazahypoxanthines. *J. Med. Chem.* (1994), 37(15), 2477-80.
- 30. Hung, Jui-Te; Yang, Suh-Wan; Chand, Pooran; Gray, Gary M.; Lammertsma, Koop. Olefin Reactivities toward the Ph-P-W(CO)5 Phosphinidene. J. Am. Chem. Soc. (1994), 116(24), 10966-71.
- 31. Hung, Jui Te; Chand, Pooran; Fronczek, Frank R.; Watkins, Stephen F.; Lammertsma, Koop. Addition of a terminal phosphinidene complex to norbornadiene. *Organometallics* (1993), *12*(4), 1401-5.
- 32. Lammertsma, Koop; Hung, Jui Te; Chand, Pooran; Gray, Gary M. Addition of a terminal phosphinidene complex to a conjugated diene. Thermal rearrangement of a vinylphosphirane to a 1,4 adduct. *J. Org. Chem.* (1992), *57*(24), 6557-60.
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- hydroxypropiophenone and salicylaldehyde, 2-hydroxyacetophenone, pentane-2,4-dione or 1,3-diphenylpropane-1,3-dione. *J. Indian Chem. Soc.* (1990), 67(2), 91-4.
- 35. Lammertsma, Koop; Chand, Pooran; Yang, Suh Wan; Hung, Jui Te. The reactivity of a terminal phosphinidene complex toward styrenes. *Organometallics* (1988), 7(8), 1875-6.
- 36. Joshi, Krishna C.; Pathak, Vijai N.; Chand, Pooran. Mass spectral studies on heterocyclic compounds. Part-I. Fragmentation of some fluorine containing indole derivatives under electron impact. *J. Indian Chem. Soc.* (1987), 64(2), 111-113.
- 37. Joshi, Krishna C.; Jain, Renuka; Chand, Pooran. Indoles with C-3 as spiro atom. *Heterocycles* (1985), 23(4), 957-96.
- 38. Joshi, Krishna C.; Patni, R.; Chand, P.; Sharma, V.; Bhattacharya, S. K.; Rao, Y. V. Synthesis and central nervous system activities of certain fluorine-containing 3-substituted indol-2-ones. *Pharmazie* (1984), 39(3), 153-5.
- 39. Joshi, Krishna; Chand, Pooran; Dandia, Anshu. Studies in spiroheterocycles: part II reactions of fluorine containing indole-2,3-diones with 1,2-phenylenediamines and 2,3-diaminopyridine in different media. *Indian J. Chem., Sect. B* (1984), 23B(8), 743-5.
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- 41. Joshi, Krishna C.; Jain, Renuka; Chand, Pooran; Garg, Saroj. Studies in spiro heterocycles. Part III: Synthesis of fluorine containing spiro[3H-indole-3,2'-thiazolidine]-2,4'(1H)-diones as antifertility agents. *J. Indian Chem. Soc.* (1983), 60(8), 760-1.
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### **ISSUED PATENTS**

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- 2. Babu; Yarlagadda S., Chand; Pooran, Wu; Minwan, Kotian; Pravin L., Kumar; V. Satish, Lin; Tsu-Hsing, El-Kattan; Yahya, Ghosh; Ajit K. Hepatitis C therapies, US patent: **US 7,514,410**, April **2009**.
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- 13. Babu, Yarlagadda S.; Chand, Pooran; Montgomery, John A. Substituted cyclopentane compounds useful as neuraminidase inhibitors. US Patent: US 6,410,594, June 2002.
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### RECENT PENDING PATENT APPLICATIONS

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### **EXAMPLES OF DISCOVERED MOLECULES**

Examples of the many novel structures resulting from several discovery project; the molecules were designed, optimized for activity, selected and advanced to the development stage.