BIODATA OF POORAN CHAND, PhD

Education : M.S. (1975) and Ph.D. (1979) in Organic Chemistry

Positions Held

Present Position	: CEO, United Chem Resources, 509 Creekwood Place, Birmingham, AL-35226 and CEO, Therachem Research Medilabs (India) Pvt. Ltd., Jaipur, India. Both companies are merging. Adjunct Professor at Chemistry Department, University of Alabama at Birmingham, Alabama Adjunct Professor at Chemistry Department, University of Alabama, Tuscaloosa, Alabama
2006- August, 2008	: Executive Director, Medicinal Chemistry at Biocryst Pharmaceuticals Inc.
1999- 2005	: Director, Medicinal Chemistry at BioCryst
1991-1999	: Various positions at BioCryst, like Section Head, group leader, senior research chemist, chemist III, II and I. All the positions at BioCryst were supervisory positions
1987-1989	: Assistant Director at E.H.R.T., Birmingham, Alabama.
1987-1990	: Post-doctoral fellow at Southern Research Institute, Birmingham, Alabama with Dr. John Montgomery and John A. Secrist.
1986-1987	: Post doctoral Fellow at University of Alabama, Birmingham, Alabama with Dr. Koop Lammertsma.
1982-1986	: Research Scientist at Ballarpur Industries Ltd., Karwar, Karnataka in India.
1981	: DANIDA Fellow at Neurochemical Institute, Copenhagen, Denmark with Prof. Clausen.
1975-1980	: Junior Research Fellow, Senior Research Fellow and Post Doctoral fellow at Rajasthan University, Jaipur, India with Prof. K.C. Joshi.

Type of Research Experience at Different Places

BIOCRYST PHARMACEUTICALS, INC.: It is a structure-based drug design company. The 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 done by a group of crystallographers and chemists. Successfully did 4 projects and the fifth one was under way.

1. **Neuraminidase Inhibitors (For Flu):** Designed, synthesized and brought the target molecule (BCX-1812, Peramivir) to the IND stage. The project was collaborated with Johnson & Johnson. Heavily worked on a charged, multi-substituted cyclopentane derivatives. A large number of pro-drugs were synthesized. Developed a **commercial 5 step synthesis** for BCX-1812 which has **5 chiral centers**. Synthesized the compound under GMP for phase-I trials. Have 7 patents on this target. The drug failed in phase-III clinical trials when used orally. It is being reevaluated by intravenous and intramuscular routes.
2. **Tissue Factor/ Factor VIIa Inhibitors (For Cardiovascular diseases):** Designed, synthesized and brought the target molecule to the IND stage. Heavily worked on C-C coupled, charged molecules. More than 2000 fully characterized new compounds synthesized under my supervision in this project. Made a number of pro-drugs also. Developed a synthesis which has yielded the molecule in Kg quantities. The sourcing and synthesis of the cheap starting materials was done in India. The product has been synthesized under GMP.
3. **PNP Inhibitors:** Was involved in the large scale synthesis discovery 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 molecules. The molecules are based upon carbohydrates. The selected compound is being tested for preclinical tox, etc.
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. A number of provisional patent applications have been filed.

E.H.R.T., Birmingham: 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: This is a non-profit drug discovery institute, which has licensed 7 drugs (in market) for cancer to the companies. I worked on carbohydrates (mono-, di- and tri-saccharides) and radiolabeled (C-14) compounds.

University of Alabama, Birmingham: Worked on coal liquefaction and phosphorus- tungston 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): Worked on the toxicity of industrial chemicals on rat brain and liver enzymes.

Rajasthan University, Jaipur (India): Worked on CNS active fluorine containing molecules, particularly Indoles.

The overall experience includes- Aromatics (benzene, pyridine, naphthalene, indole, benzodiazepine, pyrrole, etc.); carbohydrates (furanose, pyranose, acyclics, carbocyclics, nitrogen containing sugars, etc.), nucleosides of the same and nucleotides; peptides; radioactive molecules. Deposited more than **5000** new, fully characterized compounds in the library of BioCryst.

Patents and Publications: About one dozen US applications granted. Numerous applications are pending. More than 50 publications in various peer reviewed journals.

PATENTS

Neuraminidase Inhibitors:

1. Chand, Pooran; Elliott, Arthur J. **Preparation of substituted cyclopentane and cyclopentene compounds and certain intermediates.** PCT Int. Appl. (2001), 53 pp., WO 01/00558 A1
USP 6,672,316

2. Chand, Pooran; Babu, Yarlagadda S.; Bantia, Shanta. **New cyclopentane and cyclopentene compounds and use for detecting influenza virus.** PCT Int. Appl. (2000), 42 pp., WO 00/28328 A1
USP 6,503,745

3. Babu, Yarlagadda S.; **Chand, Pooran**; Montgomery, John A. **Substituted cyclopentane and cyclopentene compounds useful as neuraminidase inhibitors.** PCT Int. Appl. (1999), 196 pp., WO 99/33781 A1
USP 6,562,861

4. Babu, Yarlagadda S**.; Chand, Pooran**; Montgomery, John A. **Substituted cyclopentane compounds useful as neuraminidase inhibitors.** PCT Int. Appl. (1997), 206 pp., WO 9747194 A1
USP 6,410,594

5. Babu, Yarlagadda S.; **Chand, Pooran**; Walsh, David A. **Substituted benzene derivatives useful as neuraminidase-inhibitors.** PCT Int. Appl. (1996), 109 pp., WO 96/30329 A1
USP 5,602,277

6. **Chand, Pooran;** Kotian, Pravin L.; Babu, Yarlagadda S. **Substituted pyrrolidine compounds useful as neuraminidase inhibitors.**
USP 6,518,299

In addition to these, there are two following patents, which, after filing by J & J were handled by me for all correspondence with the patent attorney and the examiners.

- Process for Preparing Substituted Cyclopentane Derivatives and Novel Crystalline Structures Thereof.
  USP 6,576,786

- Process for Preparing (-)-(1S, 4R)-N-Protected 4-Amino-2-cyclopentene-1-carboxylate Esters.
  USP 6,495,711

- Two more provisional application on use have been filed recently.

Tissue Factor/ Factor VIIa Inhibitors:

7. Babu, Yarlagadda S.; Rowland, Scott R.; **Chand, Pooran;** Kotian, Pravin L.; El-Kattan, Yahya; Niwas, Shri. **Preparation of [(carboxybiphenyl)carboxamido]- benzamidines and analogs as serine protease inhibitors.** PCT Int. Appl. (2002), 341 pp., WO 02/34711 A1
USP 6,699,994

8. Babu, Yarlagadda S.; Rowland, Scott R.; **Chand, Pooran;** Kotian, Pravin L.; El-Kattan, Yahya; Niwas, Shri. **Preparation of [(carboxybiphenyl)carboxamido]- benzamidines and analogs as serine protease inhibitors.** .
USP 6,936,719

Paraflu:

9. Babu, Yarlagadda S.; Rowland, Scott R.; **Chand, Pooran. Compounds Useful for Inhibiting Paramyxovirus Neuraminidase.**
USP 7,045,535

Hepatitis C viral polymerase inhibitors:

10. Babu, Yarlagadda S.; **Chand, Pooran**; El-Kattan, Yahya; Wu, Minwan. Nucleosides, preparation thereof and use as Inhibitors of RNA viral polymerases.
USP 7,388,002

11. Chand, Pooran; Wu, Minwan. Therapeutic Furopyrimidines and Thienopyrimidines.
Has been granted in US but not published yet.

There are eighteen provisional applications filed, which are pending. A number of these applications have been published.

PUBLICATIONS/PRESENTATIONS:

Medicinal chemistry publications:

- Chand, Pooran. Recent Advances in the Discovery and Synthesis of Neuraminidase Inhibitors. Expert Opinion on Therapeutic Patents (2005), 15(8), 1009-1025.
- Bantia, Shanta; Arnold, Shane, Parker, Cynthia; Upshaw, Ramanda; Chand, Pooran. Anti-influenza Virs Activity of Peramivir in mice with single intramuscular injection. Antiviral Research (2006), 6991), 39-45.
- 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.
- 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.
- 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.
- 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.
- 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.
- Kotian, Pravin L.; Pooran Chand. An Efficient Stereoselective Synthesis Of (3S,4R)-4-(Hydroxymethyl)Pyrrolidin-3-ol from (S)-Diethylmalate. Tetrahedron Letters (2005), 46, 3327-3330.
- 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.
- 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.
- 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.
- 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, 4071-4077.
- 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.
- 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.
- 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.

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- 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.
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- 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.
- 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.
- 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.
- 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.
- 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.
- 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.
- Joshi, Krishna C.; Chand, Pooran. Biologically active indole derivatives. Pharmazie (1982), 37(1), 1-12.
- Joshi, Krishna C.; Pathak, Vijai N.; Chand, Pooran. Possible psychopharmacological agents. Part XI: Synthesis and CNS activity of some fluorine containing indole derivatives. J. Indian Chem. Soc. (1980), 57(4), 423-5.
- Joshi, K. C.; Pathak, V. N.; Chand, P. Possible psychopharmacological agents. X. Synthesis of some fluorine-containing indole-2,3-dione derivatives. J. Prakt. Chem. (1980), 322(2), 314-20.
- Joshi, Krishna C.; Pathak, Vijai N.; Arya, Pramila; Chand, Pooran. Possible psychopharmacological agents. Part 7: Synthesis and CNS activity of some fluorinated 2,4,7/8-trisubstituted-3H-1,5-benzodiazepinium monoperchlorates. Pharmazie (1979), 34(11), 718-20.
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bis[5-fluoro-2-(4-fluorophenyl)indol-3-yl]methanes. Indian J. Chem., Sect. B (1978), 16B(10), 933-6.

- Joshi, Krishna C.; Pathak, Vijai N.; Chand, Pooran. Possible psychopharmacological agents. Part V. Synthesis and CNS activity of some fluorine containing 3-indolylglyoxamides and tryptamines. Agric. Biol. Chem. (1978), 42(9), 1723-6.
- Joshi, Krishna C.; Pathak, Vijai N.; Chand, Pooran. Possible psychopharmacological agents. IV. Synthesis of some fluorine-containing indoles and related compounds. J. Prakt. Chem. (1978), 320(4), 701-4.

Toxicology publications:

- Langner, Jeffrey G.; Gan, B. K.; Liu, Ray H.; Baugh, L. Diane; Chand, Pooran; Weng, J. L.; Edwards, Cinnamon; Walia, Amrik S. Enzymic digestion, solid-phase extraction, and gas chromatography/mass spectrometry of derivatized intact oxazepam in urine. Clin. Chem. (Winston-Salem, N. C.) (1991), 37(9), 1595-601.
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- Chand, P.; Clausen, J. Effects of toluene on cytochrome P 450 mixed-function oxygenase and glutathione S-transferase activities in rat brain and liver. Bull. Environ. Contam. Toxicol. (1982), 28(5), 542-5.

Organometallics publications:

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General publications:

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Presentations:

- Chand, P; Ghosh, A. K.; Kotian, P. L.; Lin, T.H.; El-Kattan, Y.; Wu, M.; Sadlakonda, S.; Babu, Y. S. Synthesis of (2S,3S,4R,5R)-2-(4-amino-5H-pyrrolo[3,2-d]pyrimidin-7-yl)-5-(hydroxymethyl)-3-methylpyrrolidine-3,4-diol, an analog of potent HCV inhibotor. Collection Symposium Series (2005), 7(Chemistry of Nucleic Acid Components), 329-332.
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