Abhishek Mondal

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Indian Institute of Science Education and Research (IISER), Pune
Sustainable Supramolecular Systems Lab
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Gender: Male | Date of Birth: 1st July 1994 | Nationality: Indian

EDUCATION & TRAINING

PhD in chemistry

August 2018 – Present
Department of Chemistry, Indian Institute of Science Education and Research (IISER) Pune, India
PhD Thesis Supervisor: Prof. Pinaki Talukdar
PhD Thesis Title: Development of Artificial Anion Transport Systems and Evaluation of Their Biological Activity

MS in chemistry

August 2018
Department of Chemistry, Indian Institute of Science Education and Research (IISER) Pune, India. CGPA: 9.2/10
MS Thesis Supervisor: Prof. Pinaki Talukdar
MS Thesis Title: Synthesis of Small Molecule Hydrazones as Photoresponsive Anion Transporters

Bsc in chemistry

June 2016
University of Calcutta, India. 76%

WORK EXPERIENCE

Teaching Activities (2020-2021)

IR Spectroscopy (*Fergusson College*, Pune)
Molecular Rearrangements (*Fergusson College*, Pune)
Chromatographic Techniques for Purification (*Fergusson College*, Pune)

Teaching Assistant (2019)

CHM 101: Chemical Principles-I (*IISER*, Pune)
CHM 121: Chemistry Lab I (*IISER*, Pune)
CHM 331: Self-Assembly in Chemistry (*IISER*, Pune)

TECHNICAL PROFICIENCY

Research Expertise

Synthesis: Retro-synthetic analysis, multi-step organic synthesis, isolation and purification

Host-guest binding studies of synthetic receptors with various ions; Self-assembly and development of artificial Ion channels

Electrophysiological conductance measurement across bilayer membrane (BLM experiments)

Studies of supramolecular polymer and channels via morphology, solid-state, and solution phase analysis

Analytical experiments across lipid vesicle-based systems: Ion transport and water transport across vesicular membrane

Molecular biology experiments: Cell culture, western blotting, live-cell imaging, immunostaining.

Characterisation Methods

Strong background in the spectroscopic analysis including 1D-NMR, 2D-NMR, FT-IR, Stopped-flow light scattering, UV-Visible, and Fluorescence spectroscopy; Mass spectrometry; SCXRD studies for characterization; AFM, FESEM, and HRTEM analysis for the characterization of self-assembled behavior of supramolecular system.

Software Skills

Well versed with various supramolecular chemistry research related computer packages viz. Chemdraw, Origin, MarvinSketch, Gaussian, Apex-XShell, Mercury, Discovery Studio, MestReNova, SciFinder, Endnote, pClamp, Prism, Image J, Blender, etc.

ADDITIONAL INFORMATION

Languages Known

English, Hindi, Bengali

Communication Skills

Ability to interact and communicate with people from diverse backgrounds.

Mentoring Activities

Experienced in instructing the junior researchers (PhD and Master students) with much positive feedback.

AWARDS & ACHIEVEMENT

Awards

1. Prestigious *Prime Minister's Research Fellowship* (PMRF) Award (2019)
2. *Infosys Foundation Scholarship* for academic excellence (2018)
3. *Best Teaching Assistant* award, *IISER*, Pune (2019)
4. *DST-INSPIRE Scholarship* Award, *Govt of India*. (Reg. No. 12256/2012)

National and State-Level Qualifications

1. Qualified IIT-JAM, (2016)
2. CSIR-UGC National Eligibility Test (NET) (2019)
3. West Bengal State Eligibility Test (WB-SET) (2020)

PUBLICATIONS

1) Mondal, A.; Save, S. N.; Sarkar, S.; Mondal, D.; Mondal, J.; Sharma, S.; Talukdar, P*. A Benzohydrazide-based Artificial Ion Channel that Modulates Chloride Ion Concentration in Cancer Cells and Induces Apoptosis by Disruption of Autophagy. *J. Am. Chem. Soc*. Just Accepted.

2) Mondal, A.; Malla, J. A.; Paithankar, H.; Sharma, S.; Chugh, J.; Talukdar, P*. A Pyridyl-Linked Benzimidazolyl Tautomer Facilitates Prodigious H+/Cl– Symport through a Cooperative Protonation and Chloride Ion Recognition. *Org. Lett.* 2021, *23*, 6131-6136.

3) Mondal, A.; Barik, G. K.; Sarkar, S.; Mondal, D.; Ahmad, M.; Vijayakanth, T.; Mondal, J.; Santra, M. K.; Talukdar, P*. Nontoxic Artificial Chloride Channel Formation in Epithelial Cells by Isophthalic Acid-Based Small Molecules. *Chem. Eur. J.* 2023, 29, e202202887.

4) Mondal, A.; Ahmad, M.; Mondal, D.; Talukdar, P*. Progress and prospects toward supramolecular bioactive ion transporters. *Chem. Commun.* 2023, *59*, 1917-1938.

5) Mondal D.; Ahmad, M.; Dey, B.; Mondal, A.; Talukdar, P*. Formation of supramolecular channels by reversible unwinding-rewinding of bis(indole) double helix via ion coordination. *Nat. Commun.* 2022, 13, 6507.

6) Malla, J. A.; Upadhyay, A.; Ghosh, P.; Mondal, D.; Mondal, A.; Sharma, S.; Talukdar, P*. Chloride Transport across Liposomes and Cells by Nontoxic 3-(1H-1,2,3-Triazol-1-yl)benzamides. *Org. Lett.* 2022, 24, 4124-4128.

7) Mondal, D.; Dandekar, B. R.; Ahmad, M.; Mondal, A.; Mondal, J.; Talukdar, P*. Selective and rapid water transportation across a self-assembled peptide-diol channel via the formation of a dual water array. *Chem. Sci.* 2022, 13, 9614-9623

8) Mondal, A.; Siwach, M.; Ahmad, M.; Radhakrishnan, S.; Talukdar P*. Pyridyl-Linked Hetero Hydrazones: Transmembrane H+/Cl– Symport with Efficient Antibacterial Activity. *Manuscript under communication.*

9) Mondal, A.; Save, N. S.; Sarkar, S.; Mondal, J.; Sharma, S.; Talukdar P*. A Pyrrole-linked Benzimidazolyl Hydrazone Self-Assembles to Form HCl Channel and Induces Apoptosis in Cancer Cells. *Manuscript under preparation.*

10) Mondal, A.; Mondal, D.; Sarkar, S.; Mondal, J.; Talukdar P*. A Benzohydrazide-Based Artificial Channel: Rapid Transport of Water with Rejection of Proton and Salts. *Manuscript under preparation.*

11) Mondal, A.; Barik, G. K.; Sarkar, S.; Mondal, D.; Mondal, J.; Santra, M. K.; Talukdar, P*. Apoptosis-Inducing Activity by a Hydroxyphenyl-based Self-Assembled Chloride Channel. *Manuscript under preparation.*

CONFERENCES & EVENTS

1. Participation: *ACS on Campus events*, IISER, Pune (2017)
2. Participation: *Chemsymphoria*, IISER, Pune (2017, 2018, 2019, 2022)
3. Poster Presentation: International Conference On. Disease Biology: Diagnostics and Therapeutics (DBDT-2020). Poster Title: Benzimidazolyl hydrazones as prodigious H+/Cl− cotransporters.
4. Poster Presentation: PMRF Annual Symposium 2023, A Benzohydrazide-based Artificial Ion Channel that Modulates Chloride Ion Concentration in Cancer Cells and Induces Apoptosis by Disruption of Autophagy.
5. Oral Presentation: Chemsymphoria, IISER, Pune, 2021. Presentation Title: A Pyridyl-Linked Benzimidazolyl Tautomer Facilitates Prodigious H+/Cl– Symport through a Cooperative Protonation and Chloride Ion Recognition.
6. Oral Presentation: International Conference on Noncovalent Interactions (ICNI), 2022, Strasbourg, France. Presentation Title: Nontoxic Artificial Chloride Channel Formation in Epithelial Cells by Isophthalic Acid-Based Small Molecules.
7. *EMBO Workshop* on Communicating Research (2023): Paper Writing and Research Integrity.

REFERENCES

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DOCTORAL RESEARCH SUMMARY

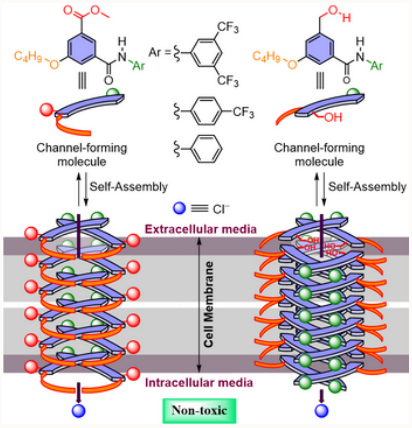
The thesis entitled "**Development of Artificial Anion Transport Systems and Evaluation of Their Biological Activity**" comprises of four chapters.

The main objective of this thesis is to develop artificial ion transport systems and explore their potential applications in the field of biomedicine. During my doctoral research, I focused on designing, synthesizing, and characterizing biomimetic artificial ion channels and ion carriers that have shown promising biological applications for future therapeutics. Specifically, this thesis primarily focuses on the supramolecular architecture of artificial ion channels that can selectively transport chloride ions across cell membranes.

Chapter 1 introduces isophthalic acid-based small molecules that self-assemble to form chloride ion channels, which are non-toxic to cells even at elevated concentrations. Such non-toxic chloride channels hold realistic potential for their application in the treatment of "channelopathies". In chapter 2, we present a benzohydrazide-based artificial chloride channel which is capable of inducing apoptosis as well as disrupting autophagy, a combination seldom seen in cancer-targeting drugs. As an important contribution to the field, chapter 3 of the thesis reports the highest active artificial HCl symporter *hithertho* reported in literature. Chapter 4 presents a rare example of HCl channel which is highly toxic toward cancer cells while remaining relatively non-toxic to healthy cells. The compound also shows better efficacy when compared to the commercially available anticancer drug, Doxorubicin, in inhibiting the growth of MCF-7 3D spheroid cultures, indicating that it may be a promising candidate for combating cancer in due course.

CHAPTER 1

Nontoxic Artificial Chloride Channel Formation in Epithelial Cells by Isophthalic Acid-Based Small Molecules



Artificial channels that are capable of facilitating chloride ion transport across cell membranes, while remaining non-toxic to cells, are a rarity. They have the potential to replace defective ion channels and treat channelopathies, by mimicking the functions of membrane transport proteins. In this study, we developed a series of isophthalic acid-based small molecules, which self-assemble into supramolecular nanochannels that enable selective transport of chloride ions. Our findings revealed that intermolecular hydrogen bonding and π-π stacking interactions govern the self-assembly, as confirmed by single-crystal X-ray diffraction analysis. Electrophysiological studies, in addition to Molecular dynamics simulation, demonstrated the formation of stable chloride channel assembly in the lipid membrane and efficient chloride transport through them. The efficacy of the compounds in delivering chloride ions into cells was demonstrated through the MQAE assay, while the MTT assays confirmed that the compounds are non-toxic to cells, even at a concentration of 100 μM.

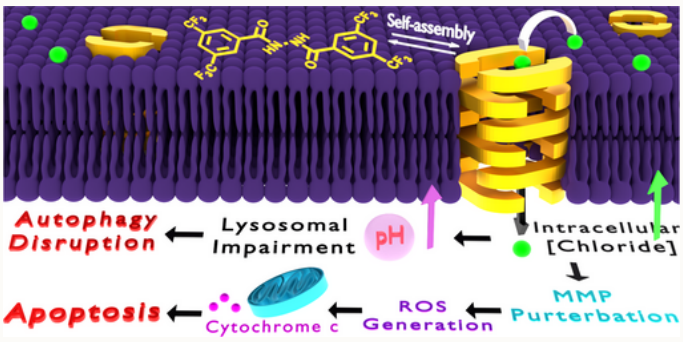
Mondal. A., et. al., *Chem. Eur. J.* 2023, 29, e202202887.

CHAPTER 2

A Benzohydrazide-based Artificial Ion Channel that Modulates Chloride Ion Concentration in Cancer Cells and Induces Apoptosis by Disruption of Autophagy

Previous research has shown that changes in the concentration of chloride ions within cells, induced by synthetic ion transporters, can cause cell death by disrupting the balance of ions within the cell. However, the effects of these transporters on autophagy, the process by which cells break down and recycle their own components, have not been extensively studied.

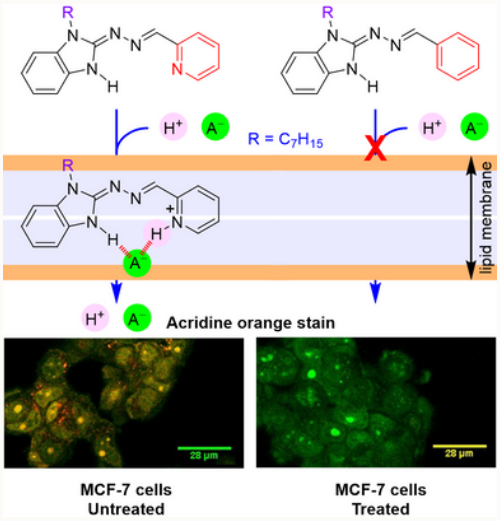
In this chapter, we introduced a benzoylbenzohydrazide molecule that can assemble into a supramolecular nanochannel within cell membranes. This nanochannel selectively transports chloride ions, disrupting the balance of ions within cancer cells and causing them to undergo programmed cell death (apoptosis). Importantly, this transporter did not cause significant harm to non-cancerous cells. We also found that the transporter disrupts autophagy in cancer cells by causing lysosomes (organelles involved in autophagy) to become less acidic. These results demonstrate a novel approach for specifically targeting cancer cells by disrupting autophagy and inducing apoptosis using an artificial ion channel.



Mondal. A., et. al., *J. Am. Chem. Soc.* Accepted.

CHAPTER 3

A Pyridyl-Linked Benzimidazolyl Tautomer Facilitates Prodigious HCl Symport through a Cooperative Protonation and Chloride Ion Recognition

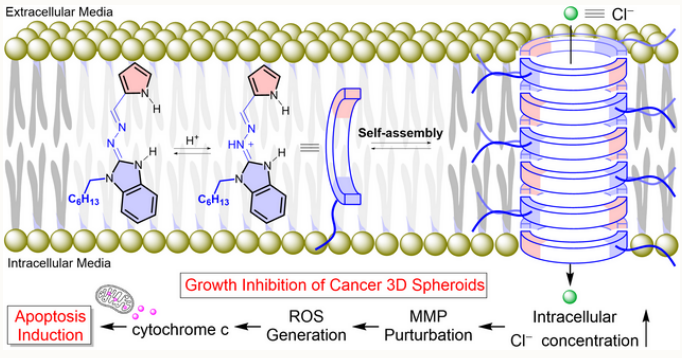


In this chapter, we introduced two pyridyl-linked benzimidazolyl hydrazones that exhibit superior HCl cotransporting ability compared to prodigiosin, a natural product whose synthetic counterparts have never achieved such high transport efficiency. These hydrazones possess a cooperative protonation and chloride ion recognition mechanism that facilitates the binding of HCl. The transport of HCl by the most potent compound results in the deacidification of lysosomes. Viability assays indicated that these compounds induce cytotoxicity in human breast cancer MCF-7 cells while exhibiting relatively low toxicity towards noncancerous HEK293T cells. These findings suggest that these hydrazone-based HCl transporters hold promise as potential therapeutic agents for cancer treatment.

Mondal. A., et. al., *Org. Lett.* 2021, 23, 6131-6136.

CHAPTER 4

A Pyrrole-linked Benzimidazolyl Hydrazone Self-Assembles to Form HCl Channel and Induces Apoptosis in Cancer Cells



Modulation of intracellular chloride ion concentration by artificially developed ion transporters has been known to cause apoptosis in cancer cells. However, most of these transporters cause harm to healthy cells as well, limiting their applicability in real systems. In this chapter, we report a pyrrole-linked heterohydrazone that self-assembles to form a nanochannel assembly across the membrane for the selective translocation of HCl; a system which is rarely reported in the literature. We also demonstrate solid-state evidence that the compound self-assembles in the presence of HCl to produce organized arrays that include chloride-filled and water-filled

channels. When tested on cellular systems, the compound showed extremely high toxicity toward cancerous cell lines while remaining relatively nontoxic to cell lines of non-cancerous origin. The compound also showed better efficacy when compared with the commercially available anticancer drug, Doxorubicin, in inhibiting the growth of MCF-7 3D spheroid cultures.

Manuscript under preparation

WORK NOT INCLUDED IN MY DOCTORAL THESIS

1) Mondal, A.; Siwach, M.; Ahmad, M.; Radhakrishnan, S.; Talukdar P*. Pyridyl-Linked Hetero Hydrazones: Transmembrane HCl Symport with Efficient Antibacterial Activity. *Manuscript under communication.*

2) Mondal, A.; Mondal, D.; Sarkar, S.; Mondal, J.; Talukdar P*. A Benzohydrazide-Based Artificial Channel: Rapid Transport of Water with Rejection of Proton and Salts. *Manuscript under preparation.*

3) Mondal, A.; Barik, G. K.; Sarkar, S.; Mondal, D.; Mondal, J.; Santra, M. K.; Talukdar, P*. Apoptosis-Inducing Activity by a Hydroxyphenyl-based Self-Assembled Chloride Channel. *Manuscript under preparation.*