

# Pharmacy

## Department Seminar

Date: 29<sup>th</sup> May  
2017

Time: 5pm

Venue: S4A Level 3  
Room A & B

## Delineating the mechanisms of cardiac adverse effects of dronedarone: A role of CYP2J2



Aneesh graduated with a Bachelor of Pharmacy (B. Pharm) Hons from BITS Pilani, India. He is pursuing his PhD studies under the supervision of A/P Eric Chan. His research explores the roles of CYP2J2 in cardiac adverse reactions especially focusing on specific pathways that distinguish the cardiac adverse effects between dronedarone and amiodarone.

Cytochrome P450 (CYP450) enzymes are crucial for the metabolism of xenobiotics and endobiotics. CYP2J2, a predominantly cardiac CYP450 enzyme catalyses the metabolism of arachidonic acid (AA) to downstream cardioprotective secondary molecule; however the role of this pathway in drug-induced cardiotoxicity remains undefined.

In this project, we focused on amiodarone and dronedarone as two model anti-arrhythmic drugs with structural and pharmacological similarities. However, dronedarone exacerbates cardiac failure and is contraindicated in such patients, while amiodarone lacks this adverse effect. This prompted us to raise the following questions: (1) Why does dronedarone but not amiodarone cause cardiac failure exacerbation? (2) What are the possible mechanisms that address this difference? (3) Could CYP2J2 inhibition and perturbation of AA metabolism play a role?

In this seminar, we will explore the links between CYP2J2, AA metabolic pathway and dronedarone-induced cardiac failure exacerbation.