2. Scope Of The Study

Prevention of cardiovascular diseases, particularly atherosclerosis, remains a top concern on the global health agenda. Coronary care units, bypass operations and sophisticated heart catheterization procedures are conducive to people with chest pain, but do not provide wholesome appeasement to prevent future heart attacks and strokes. One of the discoveries of the 1990s was that giving drugs such as statins to lower LDL can reduce the risk of heart attacks and strokes by 25% to 40%. Magnetic resonance imaging and CT scanning brings up the possibility that removal of atherosclerotic plaque might be attained by using drugs that lower LDL and raise HDL, but this could lead to plaque stabilization not prevention. So, to study more about atherosclerosis, and exclusively about the key players of inflammation, the inflammatory mediators and the associated Notch pathway, may help in preventing heart attacks and strokes.

Inflammatory monocyte subset is a relevant biomarker for human inflammatory diseases, including cardiovascular diseases (Yang et al., 2014). Macrophages are specially designed to fight invading pathogens by initiating innate immune functions. Molecular activation signatures, which intend to eliminate invaders, also allow uptake of lipoproteins, the release of reactive oxygen species (ROS) and pro-inflammatory mediator formation that collectively foster atherosclerosis (Roman et al., 2006; Linton et al., 2015). Stimulation of an inflammatory reaction is considered to be a crucial event associated with most human pathologies like stroke and atherosclerosis (Elango and Niranjali, 2010; Jan et al., 2010). Understanding the mechanism of monocyte differentiation is likely to provide a potential therapeutic target for inflammatory monocytosis (Yang et al., 2014).

Interventions that target inflammatory molecules that enhance differentiation of monocyte into macrophage could prevent or retard the disease progression. Collective
data suggest that Notch pathway is important to inflammatory events involved in cardiovascular pathogenesis. The role of Notch signaling in atherosclerosis cannot be complete without analysing the key role of Notch in macrophages, which trigger the inflammatory response and subsequent plaque formation in atherosclerosis. Reports have revealed that diosgenin plays an important pharmacological role as an antidiabetic agent, an antioxidant, a plasma cholesterol lowering agent, an antineoplastic, anti-inflammatory agent, and as an anti-metastatic agent. In this study, the activation of inflammatory mediators and its molecular interaction with Notch signaling and the efficacy of diosgenin on inflammatory molecules and Notch signaling were investigated in particular reference to macrophage differentiation, to prevent the progression of atherosclerotic disease.

**Key hypothesis tested:**

*How does diosgenin modulate monocyte to macrophage differentiation?*

*How does diosgenin influence inflammatory mediators and Notch pathway?*

*Can targeting inflammatory mediator NFκBp65 have an impact on Notch and vice-versa in macrophage differentiation?*

*How does the antibiotic intake for common illness foster atherosclerosis?*
OBJECTIVES OF THE STUDY

1. To study the anti-inflammatory effect of diosgenin during the differentiation of monocyte into macrophage using an *in vitro* model.

2. To study the effect of diosgenin in atherogenic diet induced rat by analysing its anti-inflammatory properties.

3. To elucidate the expression of Notch pathway proteins.

4. To investigate the molecular interaction between inflammatory mediators and Notch intracellular domain (NICD) in progression of the disease.

5. To study the use of the antibiotic - Ciprofloxacin and its molecular link with atherosclerosis.