Introduction
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World Health Organization (WHO) 2013 report shows that *Mycobacterium tuberculosis* (*M. tuberculosis*) infection caused tuberculosis (TB) in 8.6 million people and 1.3 million deaths in 2012 and remains a major health concern in the developing world and among HIV-positive people. This situation is further intensifying by the coming out of drug-resistant strains, multidrug-resistant (MDR), extensively drug-resistant (XDR) and totally drug-resistant strains. These drug-resistant *Mtb* strains infected patients require much longer treatment courses and have lower success rates compared to susceptible strains (Gandhi et al., 2010; Dye et al., 2013; Muller et al., 2013). The WHO has developed the Directly Observed Therapy Short course (DOTS) strategy to optimize response and adherence to TB treatment. However, DOTS is long and expensive, so the shortening of the duration of treatment without compromising the cure and relapse rates still remains a major goal for control policies. Evidence that the addition of fluoroquinolones to present treatment regimens might shorten their duration has been provided by studies of experimental murine tuberculosis. Further clinical trials of fluoroquinolones aimed at shortening treatment, with backing in the United States (O’Brien, 2003) and from the European Commission (Mitchison, 2004), are proceeding.

The fluoroquinolones have been used to treat a variety of infections including gonococcal, enteric, respiratory tract infections and osteomyelitis and they are also used as prophylaxis in neutropenic patients, or to prevent spontaneous bacterial peritonitis in cirrhotic patients (Sharma et al., 2009). Among the fluoroquinolones, those with the greatest activity in tuberculosis are ofloxacin (OFX), levofloxacin (LFX), and the newer quinolones such as 8-methoxy derivatives gatifloxacin (GFLX) and moxifloxacin (Hu et al., 2003). The two drugs at advanced stage of clinical trials to treat tuberculosis are gatifloxacin and moxifloxacin. Gatifloxacin is 3-methylpiperazine at position 7 of the quinolone ring and a methoxy group at position 8 being developed by a group of public and private sector partners for pulmonary TB. It is being evaluated in combination with isoniazid, rifampin and pyrazinamide in a four-month course of therapy against paradigm six-month therapy in phase 3 trial in Africa (Ginsberg and Spigelman, 2007). Despite having excellent
bactericidal properties gatifloxacin treatment leads to having specific side effects that includes increased risk of dysglycemia, primarily in adults and diabetics (Park-Wyllie et al., 2006c). Sanchez-Morillas, 2010 also reported a case of anaphylaxis due to moxifloxacin which suggest, an IgE-mediated mechanism (Benator et al., 2002).

In this study we have investigated the possible effects of quinolone antibiotics gatifloxacin on insulin release in rat pancreatic islets in order to elucidate the involvement of mRNA degradation in their actions. These drugs were reported to induce hypoglycaemia and hyperglycaemia in one cohort of patients (Park-Wyllie et al., 2006b; Park-Wyllie et al., 2006a; Happe et al., 2004). In one of those reports, the serum level of immunoreactive insulin (IRI) was found to be higher than the normal range. In addition, quinine with some structural resemblance to quinolones was reported to increase insulin release by decreasing the K⁺ permeability (Yamada et al., 2006).

TB is chronic infectious disease that is characterized by ongoing inflammation and responsible for excessive mortality and morbidity worldwide. The past decades have witnessed considerable efforts toward the elucidation of the immune mechanisms underlying protection and pathogenesis in TB (Kaufmann, 2006; Philips and Ernst, 2012). It is thoroughly recognized that Mtb infects macrophages and dendritic cells (DCs). The dual role of mononuclear phagocytes as effectors against and habitats of Mtb is well accepted (Philips and Ernst, 2012). The potent antigen presenting activity of DCs regulates adaptive immune response in response to inflammatory stimuli like lipopolysaccharides (LPS) (Steinman and Banchereau, 2007; Banchereau and Steinman, 1998). DCs are the most efficient at initiating antigen-specific responses and naive T cell differentiation among all antigen presenting cells. DCs begins maturation process after stimulation, branded by cytokine production or antigen presentation capacity up regulation (Reis e Sousa, 2006). TLR-4 senses LPS and activates 2 canonical pathways resulting in DC maturation. The first pathway results via MyD88-IRAK-TRAF6 in IKK, JNK and p38 MAPK stimulation pathway. The second pathway involves the Toll-IL-1 receptor domain-containing adapter- inducing IFN-γ (TRIF) and IRF3, which leads to type I IFN expression and costimulatory molecules up-regulation (Kawai and Akira, 2006). Both pathways are requisite for finest NF-κB activation and the formation of
cytokines such as IL-12 or IL-1β (Shen et al., 2008). Activation of DC results the enhanced ability to stimulate and polarize T cells in vitro and in vivo (Dudziak et al., 2007).

More recently, microRNAs (miRNAs) have emerged as a major class of gene expression regulators linked to most biological functions. The Post-transcriptional gene expression controlled by miRNAs in the course of imperfect pairing in 3’ untranslated region (3’ UTR) sequence of target mRNAs that results in induction of mRNA degradation or prevention of protein accumulation and translation repression (Liu, 2008). More than 800 miRNAs have been identified in mammals (miRBase v.12.0), even if their functions are only now being elucidated. The enzyme responsible for regulatory RNA biogenesis, Dicer, is required for lymphocytes function, which suggests regulatory roles for miRNAs in the immune system (Otsuka et al., 2007). However, the relationship between inflammation, innate immunity, and miRNA expression is just beginning to be explored (Baltimore et al., 2008; Hoefig and Heissmeyer, 2008). miRNAs regulates immune response towards various infectious microorganisms at post-transcriptional level and the role of miRNAs as regulator of cytokine is also documented so they emerged as key player in immunity system (Asirvatham et al., 2009a). The role of miRNA during virulent Mtb. Infection shown that lipomannan (LM) is a potent inhibitor of TNF-α in human macrophage via inositol phosphatase SHIP-1 (Asirvatham et al., 2009b). Taking together, these data advocate the correlation between miRNA expression and cytokine regulation during Mtb infection.

Several miRNA expressions are known to be altered during Mtb infection such as mir155. We investigated the possible alteration in miRNA and mRNA expression and the possible role of those genes in Mtb infection establishment.

The objectives of present study were:

- Elucidating the mechanism of quinolone induced disruption in cellular signalling of host.
- What are the microRNAs and genes which differentially expressed in dendritic cell isolated from healthy controls and Mtb infected patient blood?
- How these microRNA and differential expression of gene regulates immunereresponse in Monocytes derived dendritic cells (moDCs)?