# DEVELOPMENT OF A TARGET METHOD BY UPLC-MS/MS FOR DETERMINING KYNURENINE PATHWAY METABOLITES IN PLASMA SAMPLES FROM PATIENTS WITH LEPROSY.

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Leprosy is an infectious disease caused by Mycobacterium leprae, a bacillus that has tropism for Schwann cells, leading to peripheral nerve damage. Furthermore, in leprosy there are acute inflammatory episodes, caused by an increase in pro-inflammatory cytokines, intensifying neural damage. The increase in pro-inflammatory mediators leads to greater activity of the enzyme Indoleamine 2,3-dioxygenase 1 (IDO1). IDO1 plays an active role in the human immune response by catalyzing the kynurenine pathway through the tryptophan degradation, which is an essential amino acid precursor of the kynurenine pathway. Tryptophan is an important metabolite for its function as intracellular messengers with neuroactive, pro-apoptotic and immunoregulatory properties. Previous data demonstrated that in patients with neural damage, IDO1 levels are even higher. However, studies involving the metabolites of the Kynurenine Pathway in the peripheral nervous system are still scarce.

Therefore, the present study aims to develop a new method using liquid chromatography coupled to mass spectrometry (LC-MS/MS) to determine metabolites of the kynurenine pathway in plasma samples from different clinical forms of leprosy, with or without neuropathy.

To extract the analytes 30?L of sample (plasma) was used and through LC-MS analysis 12 metabolites from Kynurenine Pathway were analyzed (Nicotinic Acid, Anthranilic acid, 3-Hydroxyanthranilic acid, 2-oxoadipic acid, 2,3-pyridinedicarboxylic acid, Kynurenic acid, L-tryptophan, Xanthurenic acid, L-Kynurenine, 3-Hydroxy-DL-kynurenine, Melatonin, Nicotinamide-Adenine-Dinucleotide). Eight metabolites were detected and quantified in plasma. The developed method presented a linear range between 0.0005-250 µg/mL.

In conclusion, the developed method proved to be selective and precise, allowing the quantification of metabolites from the kynurenine pathway in plasma.

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