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Formulation and Evaluation of Bio-Flexy Strips of Aripiprazole for Brain Targeting Through Soft Palatal Mucosa

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ABSTRACT: The aim of research work was to deliver Aripiprazole to the brain via trans-soft palatal route. Soft palatal mucosa is composed of non-keratinized stratified squamous epithelium with thickness of about 100–200 μm and enriched with innervations like facial, trigeminal, vagus nerve which are linked into the brain. It is also enriched with rich blood supply by the lesser palatine and ascending palatine arteries. Apart from this, the soft palatal region is flexible and mobile tissue can be easily accessed for placing the dosage form and it remain intact for long period in order to achieve a controlled drug release. The biopolymer was isolated from the natural edible source by addition of optimized quantity of non-solvent and was tested for mucoadhesivity and mucoretentibility. Six optimized aripiprazole bio-flexy strips were formulated of concentration 4%, 5%, 6% using biopolymer and standard polymer (Sodium CMC) by solvent casting method. Evaluation parameters tested were weight variation, thickness, mucoadhesivity and content uniformity, surface pH, folding endurance, *In-vitro* and *In-vivo* studies. The formulation FL2 was found to be the best formulation on the basis of mucoretentibility, amount of drug reached to brain, $t_{50\%}$(4.4 hrs), $t_{80\%}$(21hrs), and pharmacodynamics studies like locomotors activity with R^2 value 0.9913. According to the release kinetics the best fit model **Higuchi matrix** with **Anomalous Transport** as the mechanism of drug release. The research work was focused to explore a route for brain specificity and In vitro/in vivo studies reveal reduction in the drug dosing up to 10 folds. Based on above research work a conclusion was drawn that the environment of soft palatal mucosa is the most interesting factor to explore its unique novelistic platform for brain targeting by formulating suitable drug loaded dosage form.

Keywords: Bio-flexy strips, Aripiprazole, Nelumbo nucifera, Sodium CMC.

1. Introduction

Depression is the third leading cause (350 million people affected worldwide) of global disease burden worldwide (WHO 2012). Aripiprazole is second generation atypical antipsychotic drug that is primarily used in brain disorders (Tanahashi et al., 2012). It comes with Black Box warning and is a partial agonist at dopamine D2, D3 receptors and serotonin $5HT_{1A}$ and antagonist at $5HT_{2A}$ receptors come in BCS Class IV (Tsai et al., 2011). Soft palate has a promising non-keratinized histology with a unique thickness as compared which offers more permeability (Shakya et al., 2011). The soft palatal mucosa possesses various advantages like it does not with regular activities like talking; eating, drinking, etc, region is flexible, bypass of first pass metabolism, ease of administration and removal, better patient compliance. It also provides greater surface area and longer contact time for delivery of API over extended period of time (Reddy et al., 2013). *Nelumbo nucifera* isolated biopolymer belongs to Nymphaeaceae family and also known as Lotus root. Fresh rhizome contains carbohydrate, crude protein, starch, and vitamins (Mukherjee et al., 2008).