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Article

A smart approach for delivery of aripiprazole via oro-soft palatal mucosal route for improved therapeutic efficacy

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Effective management of schizophrenia, acute mania, mixed episodes associated with bipolar disorders, and depression can be managed with aripiprazole moiety. In the present research work an attempt was made to minimize the dose related side effects thus improving the quality life of the patients. A novel biopolymer was isolated from the fruits of *Trachyspermum ammi*. Ten optimized nanosized aripiprazole loaded formulations were prepared in 1-5% concentration of biopolymer (FA1-FA5) and sodium CMC (FM1-FM5) by solvent casting technique. The formulated flexy films were evaluated for thickness, folding endurance, weight uniformity, surface pH, mucoadhesivity, *In-vitro* drug release studies, *In-vivo* pharmacodynamic study and stability studies. The isolated biopolymer showed inbuilt fimability and mucoadhesivity and consists of carbonyl, hydroxyl and thiocarbonyl functional groups. All formulations showed folding endurance from 153 to 170, mucoadhesion time in the range of 24-48hrs., and in-vitro drug release was performed using dynamic Franz Diffusion cell and analyzed using BIT-SOFTWARE. The experimental animals showed improved activity score on actophotometer. The formulated nanosized aripiprazole loaded bio-flexy films showed pharmacotherapeutic response. Conclusion can be drawn that optimized formulation showed effective Pharmacodynamic activity and can be used as for improving therapeutic efficacy of aripiprazole through this platform.

Keywords: Aripiprazole/therapeutic efficacy. Nanosized. Mucoadhesive. Schizophrenia. Oro-soft palatal mucosal route.

INTRODUCTION

Schizophrenia is self-disorder characterized by complementary distortions of the act of awareness i.e. hyperreflexivity and diminished self-affection (Sass, Parnas, 2003). Studies had suggested that the etiology of schizophrenia is yet unclear but it is believed that dopaminergic neural network has major role in its pathophsiology (Nekovarova *et al.,* 2014). The symptoms of schizophrenia are positive and negative symptoms, and cognitive effects. The positive symptoms are conceptual disorganization, abnormal thought contents and hallucinations. Negative symptoms are reduction in normal functioning, flattened emotions, decrease of social behavior and anhedonia. Cognition is affected in several arena such as vigilance, psychomotor speed, impairment of memory functioning, social cognition (Green *et al.,* 2004).

Aripiprazole is used for the treatment of schizophrenia, bipolar disorder, major depressive disorder, autism, and Tourette's syndrome (USFDA approved label of ABILIFY). It is a second generation atypical antipsychotic which belongs to the benzisoxazole derivatives and has serotonin 5-HT1A-receptor partial agonist as well as 5- HT2A-receptor antagonist properties like a partial agonist at dopamine D2 receptors. It has a pKa value of 7.6 in 20% aqueous ethanol (Ardiana, Lestari, Indrayanto, 2013). Aripiprazole is a poorly soluble and poorly permeable compound with BCS class IV (Laszcz, Witkowska, 2016). It is weak alkaline drug which thus imparts pH-dependent solubility to it (Xu *et al.,* 2012).

Aripiprazole is categorized under black box warning drugs as it increases the risk of death in geriatric patients having dementia-related psychosis when treated with antipsychotic drugs. This may be due to collapse,

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