**Aripiprazole loaded *in situ* forming implant; an innovative alternative for treatment of schizophrenia**

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**Purpose:** Multiple applications of antipsychotic agents are the main obstacle upon treatment of schizophrenia. Due to behavioral abnormalities, low compliance is observed in the most of psychotic patients. *In situ* forming implants (ISFI) are a suitable choice for delivery of antipsychotic agents due to its easy administration process and sustained release kinetics [1, 2]. In this study, a novel poly(hydroxybutyrate-co-hydroxyvalerate) (PHBV) based *in situ* implant system was developed for aripiprazole (APZ); an atypical antipsychotic agent [3].

**Methods:** The aim of this study was to develop an *in situ* forming implant for delivery of APZ. The solubility of APZ was assessed. Using D-optimal design, important experimental parameters such APZ feed and PHBV feed were analyzed. Afterwards, polymer-drug interactions were studied by Forier transform infrared spectroscopy (FTIR). Scanning electron microscopy revealed morphological characteristics of developed ISFI system. Rheological aspects of implants such as viscosity were assessed. *In vitro* release studies clarified release pattern of APZ in the developed system.

**Results:** Experimental design modeling demonstrated that increasing initial APZ feed lead to an increase of Entrapment Efficiency (ER%) and Drug Loading (DL%). ER% and DL% were optimized at 99.32% and 75.23%, respectively. Rheological analyses demonstrated that the developed formulation is highly cross-linked gel with possible capability for controlled delivery of APZ. According to FTIR studies, APZ was intact within polymer networks. Release studies demonstrated a biphasic pattern of release. After initial burst release, a sustained pattern was observed for the next 18 days. The initial burst release was decreased by increasing initial polymer feed. According to SEM analysis, porosity of PHBV network is increased significantly compared to first day of release study. SEM morphological studies authenticated the hypothesis that APZ is mainly released by gradual disintegration of PHBV networks, in second phase of release test. The release data fitted to Korsmeyer-Peppas model and release pattern found out to be non-fickian.

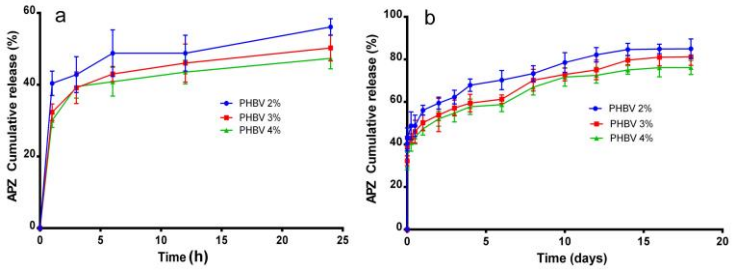


Figure 1. *In vitro* release profile of APZ in PBS (pH =7.4) medium.

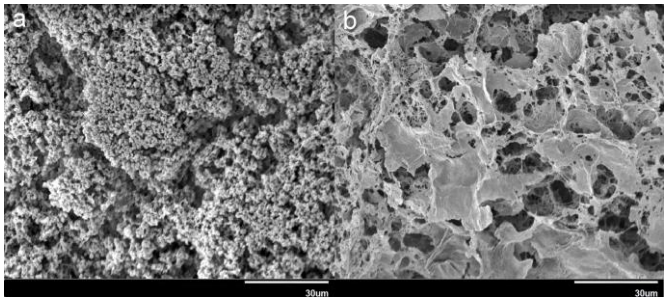


Fig 2. SEM image of APZ loaded implant (a) first day (b) 18th day of release analysis.

**Conclusions:** APZ loaded implants seems to be an innovative alternative instead of common treatments of schizophrenia due to its optimal physicochemical characteristics.

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**References:**

1. Wang, L., et al.. International journal of pharmaceutics. 2012.
2. Kempe, S. and K. Mäder.. Journal of Controlled Release. 2012.
3. Shapiro, D.A., et al. Neuropsychopharmacology. 2003.