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RESEARCH ARTICLE

Paliperidone-Loaded Mucoadhesive Microemulsion in Treatment of Schizophrenia: Formulation Consideration

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Abstract
Purpose This paper describes formulation considerations and in vitro evaluation of a microemulsion drug delivery system designed for intranasal administration of Paliperidone.
Methods Drug-loaded microemulsions were successfully prepared by a water titration. Prepared formulations were subjected to physicochemical characterization, and evaluated for in vitro diffusion, nasal cilio toxicity, and in vitro mucoadhesion.
Results The microemulsion, containing 4 % oleic acid, 30 % surfactant mixture of [Labrasol/Cremophor RH 40 (1:1)]/[Transcutol P] (3:1) and 66 % (wt/wt) aqueous phase, that displayed a 99.93 % optical transparency, globule sizes of 20.01±1.28 nm, and a polydispersity index of 0.117±0.034 was selected for the incorporation of polyelectrolytic polymer (polycarbophil) as the mucoadhesive component. The mucoadhesive microemulsion formulation of Paliperidone that contains 0.5 % by weight of polycarbophil displayed higher in vitro mucoadhesive potential (18.0±2.5 min) and diffusion coefficient ($3.83\times10^{-6}\pm0.019\times10^{-6}$) than microemulsion. Also, they were found to be free from nasal ciliotoxicity and had stability for 6 months.
Conclusion The in vitro studies demonstrated the potential of developing mucoadhesive microemulsion formulation for intranasal delivery of Paliperidone.

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Keywords Intranasal delivery · Microemulsion · Paliperidone · Schizophrenia

Introduction

Paliperidone (PPD), a benzisoxazole derivative and the principal active metabolite of risperidone, is commonly referred to as 9-hydroxyrisperidone. Chlorpromazine and other first-generation antipsychotics are effective against psychosis, but they do not improve and may even exacerbate the negative symptoms of schizophrenia and are associated with dose-limiting extrapyramidal symptoms. PPD represents the most recent second-generation atypical antipsychotic indicated for the short- and long-term treatment of schizophrenia. PPD blocks both dopamine and serotonin D_2/5-HT_{2A} receptors [1–4].

Atypical antipsychotic agents are a heterogeneous class of medications. Individual agents vary substantially in efficacy and incidence of side effects, which may be related to differences in their receptor binding and pharmacokinetic characteristics. The need for treatment options has been emphasized by the recent Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study in which 74 % of 1,493 patients with schizophrenia discontinued study medication within 18 months. The reasons for discontinuation included lack of efficacy, intolerability, and patient decision. The CATIE study has increased awareness for new treatment options tailored to the choice of the individual patient and clinician. Until new agents with novel mechanisms of action become available, improved delivery of the existing treatment class may enhance clinician- and patient-reported outcomes. Innovation of the delivery system allows an optimal, controlled pharmacokinetic profile to be achieved over appropriate dosing intervals [3]. Thus, PPD can be a possible candidate for the development of a nasal formulation for therapeutic prompt action to rapidly control agitation and disturbed behaviors in patients with schizophrenia.