Optimization of Diclofenac Sodium Orodispersible Tablets with Natural Disintegrants using Response Surface Methodology

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ABSTRACT

Traditionally experimental methods in the pharmaceutical formulation development involve significant amount of time and efforts to get an optimized dosage form. It is very much desirable as per industrial perspective to obtain suitable, optimized and stable formulation with minimum amount of time and effort. The purpose of this study was to study the synergic effect of natural disintegrants and central composite design in optimization of diclofenac sodium orodispersible tablets. In this study, central composite design was applied to study the effect of natural disintegrant as independent variables i.e. seed mucilage of Plantago ovata, and seed mucilage of Ocimum basilicum. Diclofenac sodium orodispersible tablets were prepared by direct compression method on Cadmech single punch machine using flat 8-mm punches and characterized for the dependent variables like disintegration time and cumulative percent drug released after 25 minutes. Optimization study by multiple regression analysis revealed that, 6% of Plantago ovata and 5% Ocimum basilicum was found to be optimum which has disintegrated in 36 secs and cumulative percent drug released was 99.2% at 25 minutes. A checkpoint formulation was prepared to prove the validity of the evolved mathematical model. These findings suggest that synergic effect of natural disintegrants of Plantago ovata and Ocimum basilicum employed with systematic experimental design approach have greater influence in optimization of diclofenac sodium orodispersible tablets. It is likely that this formulation technology can be exploited for commercial production of dispersible tablets.

KEYWORDS: Oro-dispersible tablet; natural disintegrant; plantago ovata; ocimum basilicum; Central composite design.

Introduction

Diclofenac sodium, a phenyl acetic acid derivative is a NSAID with a potent cyclooxygenase inhibiting action, prescribed for long term treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. Diclofenac when administered orally is well absorbed and undergoes extensive first pass metabolism resulting a terminal half life of 1 to 2 hours, which requires frequent administration of 50 mg thrice a day. Gastrointestinal side effects such as bleeding, ulceration or perforation of the intestinal wall are commonly seen when the drug is administered orally (Todd and Sorkin, 1988).

The orodispensible tablets are solid dosage form containing active therapeutic agent, which disintegrates rapidly, usually within a matter of seconds, even without need of water or chewing, usually superdisintegrants are added in formulation to facilitate break-up and disintegrate rapidly into smaller particles. Super-disinteggrant is an excipient, which is added in lower concentrations to a tablet or capsule blend to aid in the breakup of the compacted mass when it is put into a fluid environment (Ainley and Paul, 1994; Shirsand et al., 2010). The response surface designs (RSM) are most widely used statistical experiment designs in optimization experiments. It explores the relationship between several independent variables and one or more response of dependent variables. RSM is a collection of both statistical and mathematical techniques, which is useful for developing, improving and optimizing of processes. Different types of RSM designs include 3 level full factorial design, Central composite design, Box-Benken design, D-Optimal design etc. RSM is employed when only few significant factors are involved in optimization of a process. The techniques involve minimum experimentation and time. This experiment was done by central composite design using Design expert 8.0.4 U.S.A software (Dave et al., 2004; Singh et al., 2005; Mukerjee, 2006).

Central composite design is one of the best tools available for studying the effect of different variables to determine the evaluation parameters of any formulation. The multiple regression analysis of the results gave equation which described the influence of the independent variables on the selected responses. According to central composite design in the present study, two independent factors of formulation were evaluated, each at 3 levels (low, medium, high) and experimental trials were performed in all 13 formulations. The amounts of seed mucilage of Plantago ovata (X1) and seed mucilage of Ocimum basilicum (X2)