FABRICATION, OPTIMIZATION, AND IN VITRO/IN VIVO EVALUATION OF DICLOFENAC EPOLAMINE FLASH TABLET

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Abstract

Diclofenac epolamine (DE) flash tablets (FTs) intended to dissolve in the mouth saliva, thereby improving the DE bioavailability and reducing its first-pass liver metabolism. FTs were fabricated using lyophilization process. The results of the pharmacokinetic study performed in 6 human volunteers evidenced an increase in the maximum DE concentration in plasma and, consequently, an increased bioavailability of the FT formulation as compared with a reference formulation(Fr).

Introduction

Diclofenac epolamine (DE) is NSAIDs which selectively inhibits cyclooxygenase-2 (COX-2). It was developed in the last century to terminate the risk of gastrointestinal toxicity in the clinical settings. DE is the commonly used drug; it is used as analgesic and medicine in case of inflammatory conditions, including osteoarthritis and rheumatoid arthritis.

Objectives

The objective of the present study is to formulate FTs by the aid of Design-Expert software with utmost dissolving in the mouth saliva and auspicious bioavailability, moreover,avoidance of GIT complications.

Methods

Preparation of FTs.The required weight of gelatin was soaked in 100 mL water until complete hydration. The clear solution of gelatin was obtained using a magnetic stirrer (Thermolyne Stirring Hot Plate, Type 72200, USA). Weights of glycine, sorbitol, and 5 g of DE were dissolved in gelatin solution as illustrated in Table 2. The resulting dispersion was poured into the pockets of a tablet blister pack (1 ml in each pocket); consequently, DE dose of 50 mg in each tablet was obtained. The blister packs, each contained ten tablets, were transferred to a deep freezer at − 22 °C for 24 h. The frozen tablets were lyophilized for 24 h using a NL-Novalyphe 500 Freeze Dryer (Savant Instruments, Holbrook, NY) with a condenser temperature of − 52 °C and a pressure of 7 × 10–2 mbar. The flash tablets were kept in desiccators until use to avoid any atmospheric effect, especially moisture. The grittiness of flash tablets in the mouth cavity may be avoided by proper formulation .

Results

Table 1: Full factorial design ($3^1.2^2$) used for optimization of DE flash tablets

Factors (independent variables)	Levels
X1: gelatin	20 40 60
X2: sorbitol	10 - 70
X3: glycine	19 - 20
Dependent variable (response)	Desirability constraint
Dissolution (D)	Maximize

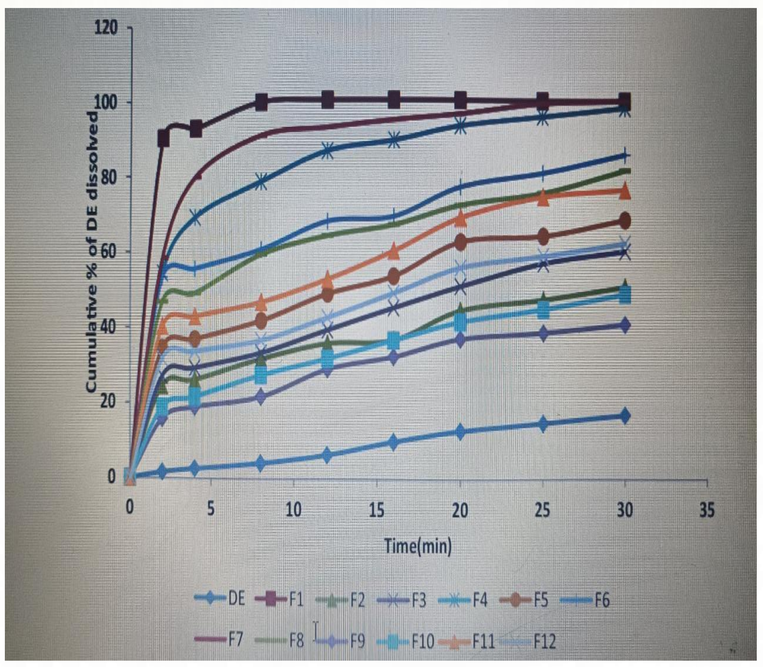

Fig. 1 Dissolution profile of different flash tablets runs in PBS (pH 6.8) at 37 ± 0.5 °C

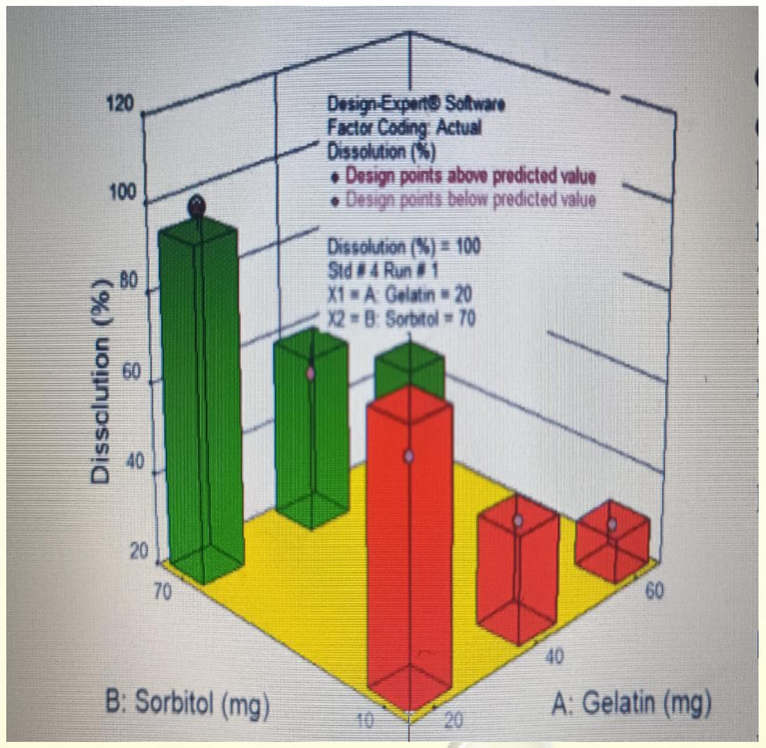

Fig. 2 3D surface plot of sorbitol and gelatin against dissolution

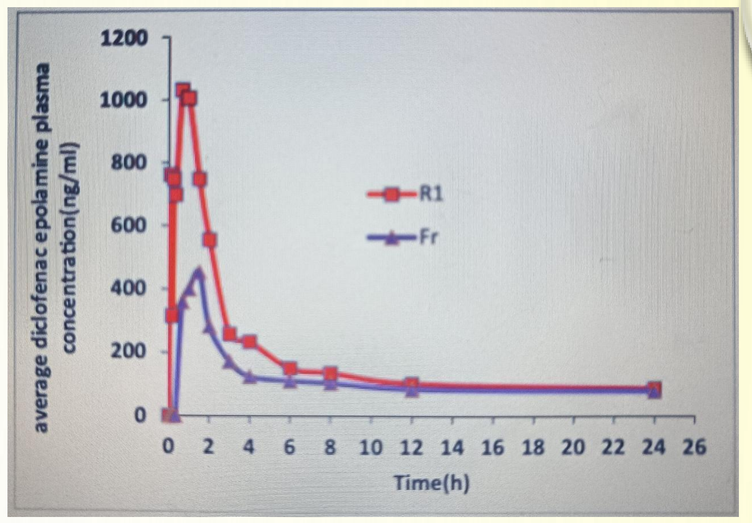

Fig.3 Profile of the mean plasma concentration time of six human volunteers following administration of reference formulation (Fr 50 mg)and flash tablet (R1)

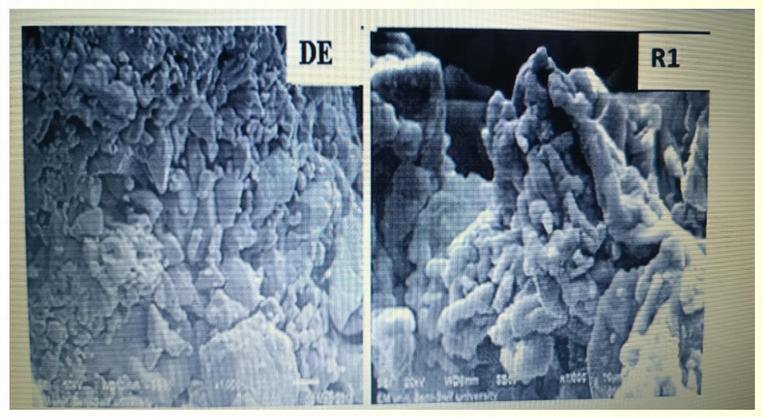

Fig.4 XRPD of Drug and R1

Conclusions

The prepared lyophilized diclofenac epolamine tablets made of safe and highly water-soluble excipients were necessary for escalating the dissolution; consequently, an auspicious drug bioavailability could be achieved. The promising results obtained were ascribed to reduction in particle size and solidsolid transition of drug from crystalline to amorphous state in freeze-dried matrix. Multilevel categoric software was truly important to detect the optimized formulation (R1). The promising formulation (R1) depicted the highest dissolution compared with other formulations and higher bioavailability compared with reference formulation (Fr). Therefore, it could bepossible to fabricate diclofenac epolamine in lyophilized tablets having a minimized therapeutic dose with reduced gastrointestinal complications. The composition of R1 is gelatin
20 mg, sorbitol 70 mg, and glycine 19 mg.

References

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