

Abstract

Introduction: The purpose of this study was to optimized betamethasone mucoadhesive patch by hot melt extrusion 3D printing method with box benken method, which was used to reduce pain and inflammation caused by aphthous stomatitis. The box benken design method was a set of techniques and mathematical equations that evaluates the appropriate conditions to achieved the ideal answer. With the help of this method, the relationship between answers and independent factors could be understood. Among the different forms of oral mucoadhesive dosage forms, films have sufficient flexibility and elasticity for the patient's comfort. It is also not easily washed away by saliva and had sufficient resistance to breakage caused by movements.

Materials and methods: In this study, four factors were investigated at three levels. The amount of polyvinyl alcohol (A), hydroxypropyl methyl cellulose (B), borax (C) and beeswax/paraffin ratio (D) as independent parameters, the effect of these four factors in 21 formulations on drug release (R1), open time patch formation (R2) and patch flexibility (R3) were investigated as the desired responses. The 3D printed patches were investigated in terms of physicochemical properties and drug release in vitro.

Results: The results showed that Hydroxypropyl methyl cellulose has the greatest effect on drug release, and the optimal patch was abled to release 88.8% of its drug in 100 minutes. Polyvinyl alcohol has the most effect on the opening time and flexibility of the patch and increases both of them. Polyvinyl alcohol is a flexible but strong material and has very good adhesion and biocompatibility and is not toxic. The optimal patch opens in 290 full minutes.

Discussion and conclusion: An important interaction effect between hydroxypropyl methyl cellulose and bisox/paraffin ratio on drug release can be seen. At the first because of hydroxypropyl methyl cellulose hydrophilicity the amount of drug release was decreased but after being solved, the amount of drug release was increased. The purpose of using hydroxypropyl methyl cellulose was to created a physical structure with polyvinyl alcohol and reduced the release slope.

Keywords: betamethasone mucoadhesive patch, aphthous stomatitis, Box Benken Design, Hot Melt 3D Printing, Optimization.