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Formulation and Optimization of Self Nanoemulsifying Drug Delivery System of Rutin for Enhancement of Oral Bioavailability Using QbD Approach

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Abstract : Introduction: Rutin is a naturally occurring strong antioxidant molecule belonging to bioflavonoid category. Due to its free radical scavenging properties, it has been found to be beneficial in the treatment of various diseases including inflammation, cancer, diabetes, allergy, cardiovascular disorders and various types of microbial infections. Despite its beneficial effects, it suffers from the problem of low aqueous solubility which is responsible for low oral bioavailability. The aim of our study was to optimize and characterize self-nanoemulsifying drug delivery system (SNEDDS) of rutin using Box-Behnken design (BBD) combined with a desirability function. Further various antioxidant, pharmacokinetic and pharmacodynamic studies were performed for the optimized rutin SNEDDS formulation. Methodologies: Selection of oil, surfactant and co-surfactant was done on the basis of solubility/miscibility studies. Sefsol+ Vitamin E, Solutol HS 15 and Transcutol P were selected as oil phase, surfactant and co-surfactant respectively. Optimization of SNEDDS formulations was done by a three-factor, three-level (33)BBD. The independent factors were Sefsol+ Vitamin E, Solutol HS15, and Transcutol P. The dependent variables were globule size, self emulsification time (SEF), % transmittance and cumulative percentage drug released. Various response surface graphs and contour plots were constructed to understand the effect of different factor, their levels and combinations on the responses. The optimized Rutin SNEDDS formulation was characterized for various parameters such as globule size, zeta potential, viscosity, refractive index , % Transmittance and in vitro drug release. Ex vivo permeation studies and pharmacokinetic studies were performed for optimized formulation. Antioxidant activity was determined by DPPH and reducing power assays. Anti-inflammatory activity was determined by using carrageenan induced rat paw oedema method. Permeation of rutin across small intestine was assessed using confocal laser scanning microscopy (CLSM). Major findings:The optimized SNEDDS formulation consisting of Sefsol+ Vitamin E - Solutol HS15 -Transcutol HP at proportions of 25:35:17.5 (w/w) was prepared and a comparison of the predicted values and experimental values were found to be in close agreement. The globule size and PDI of optimized SNEDDS formulation was found to be 16.08 ± 0.02 nm and 0.124±0.01 respectively. Significant (p□0.05) increase in percentage drug release was achieved in the case of optimized SNEDDS formulation (98.8 %) as compared to rutin suspension. Furthermore, pharmacokinetic study showed a 2.3-fold increase in relative oral bioavailability compared with that of the suspension. Antioxidant assay results indicated better efficacy of the developed formulation than the pure drug and it was found to be comparable with ascorbic acid. The results of anti-inflammatory studies showed 72.93 % inhibition for the SNEDDS formulation which was significantly higher than the drug suspension 46.56%. The results of CLSM indicated that the absorption of SNEDDS formulation was considerably higher than that from rutin suspension. Conclusion: Rutin SNEDDS have been successfully prepared and they can serve as an effective tool in enhancing oral bioavailability and efficacy of Rutin.

Keywords : rutin, oral bioavilability, pharamacokinetics, pharmacodynamics
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