ABSTRACT

BCS Class II drug may behave as a BCS Class I drug if correct formulation strategy is adopted. Solid dispersions have tremendous potential in increasing the dissolution rate but are not popular commercially because of problems like poor stability, poor compressibility and difficulty in process scale up. These can be overcome by converting the solid dispersion into a free flowing powder form by adsorbing it onto a porous adsorbent. So, with this hypothesis the aim of the present research work was to enhance the dissolution rate of selected BCS Class-II drugs by employing the hybrid technology of melt adsorption and solid dispersion.

Three drugs were selected for the dissolution enhancement i.e. ritonavir, lamotrigine and febuxostat. Candesartan cilexetil was used as check-point API to validate the hypothesis. Surfactant based carriers were used like Lutrol F127, Transcutol and Labrsol. Neusilin is used as adsorbent due to its high porous structure, good adsorbing capacity, large surface area and improving stability. The target was set to achieve at least 85% drug release in 60 min of the selected drugs as per the FDA guidelines except for Ritonavir where the dissolution criteria was set for >70% drug release in 10 min. Following the development process according to the QbD guidelines different design have been applied for each selected drug for the optimization of the formula. The optimized formulations were then subjected to physical characterization like flow properties, FTIR, DSC and XRD analysis. Convolution modeling was done of the three drugs to predict in vivo plasma concentration profile. Stability studies were also carried out for three months under accelerated conditions and all the developed formulations were found to be stable.

The optimized SDA of ritonavir, lamotrigine and febuxostat showed around 2.5, 3.4 and 3.3 fold increase in the dissolution rate respectively as compared to untreated API. This can be attributed to hydrogen bonding between the drug and carrier and the drug and adsorbent as seen from FTIR results, and/or improvement in the wetting characteristics due to molecular dispersion/solubilization of drug in the surfactant based carrier and/or decrease in the crystallinity of the drug as seen from the DSC and XRD results.
The physicochemical properties of the drug (dose and molecular weight) were then correlated with the amount of carrier needed for dissolution enhancement and a mathematical relationship was derived for determining amount of carrier needed for BCS Class-II drugs. Candesartan cilexetil SDA were prepared using the above relationship. Also, the developed technique was validated using another surfactant based carrier Vitamin E-TPGS and the results showed significant enhancement. This study thus, can be used to resolve the issue of chemical incompatibility on a drug-to-drug basis and for cost adjustments.

In conclusion, formulated SDAs of selected drugs showed noticeable improvement in drug dissolution as compared to untreated API. Due to simplicity in processing, developed technology could be utilized for dissolution enhancement of other BCS Class-II drugs and surfactant based carrier could be used to improve its dissolution. The formulated SDA can be commercialized in form of tablets and capsules indicating its future potential in an industry.