البحث الثامن

Glucosamine-paracetamol spray-dried solid dispersions with maximized intrinsic dissolution rate, bioavailability and decreased levels of in vivo toxic metabolites

Drug Des Devel Ther. (2018); Vol. 12: P. 3071–3084

Ahmed Mahmoud Abdelhaleem Ali, Ahmed Khames, Majed Mansour Alrobaian, Mohammad Hamaidi, Mohammed AS Abourehab

Purpose: This study is aimed at preparing and testing physicochemical, pharmacokinetic and levels of toxic metabolites of paracetamol and glucosamine solid dispersions intended for multiple deliveries via the parenteral or per oral route.

Methods: Solid dispersions were prepared using the spray drying technique at different molar ratios of paracetamol and glucosamine. Characterization of the solid dispersions was carried out using differential scanning calorimetry (DSC), Fourier transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), scanning electron microscopy (SEM), equilibrium solubility and intrinsic dissolution rate. In vivo pharmacokinetics and toxic metabolites of the prepared dispersions were evaluated and compared to those of pure drugs and physical mixtures.

Results: Instant water solubility and more than 7-fold increase in dissolution rate led to significantly high plasma drug concentration (.6.5-fold) compared to paracetamol alone. More than 2-fold increase in area under the curve from 0 to 24 h from the dispersions was noticed on the third day of oral dosing to animals. Lower number and concentration followed by the complete disappearance of toxic pathway metabolites were observed on second and third days of dosing with solid dispersions and physical mixtures, respectively.

Conclusions: The spray-dried dispersions support safer and more effective delivery of multiple doses of paracetamol, leading to an acceleration of its analgesic actions. Synergism between the analgesic actions of paracetamol and joint protective actions of glucosamine in this combination is expected to facilitate effective treatment of persistent pain-related illnesses such as osteoarthritis.