Abstract

The developed bioanalytical methods for estimation of novel pharmaceutical drugs like febuxostat, clebopride, darifenacin, cycloserine and carbocisteine from human plasma employing protein precipitation, solid phase extraction and liquid liquid extraction as extraction technique. In these methods sample preparation is faster, simple and easy for the determination of all these novel drugs in human plasma. These methods developed are accurate and precise validated as per regulatory guideline. These methods are rugged and the interferences from the plasma did not affect the peak response at the retention time of internal standard. These methods has resulted all validation parameter as per regulatory guidelines and thus can be of use in the clinical studies. Stability of all drugs determined at room temperature and at freezing temperature.

The validated method for febuxostat allows determination in the linearity range 49.896 to 10060.888 ng/ml. Lansoprazole was used as internal standard. The m/z of febuxostat was 317.1>261.0 and for lansoprazole was 370.1>251.9. The protein precipitation was used as extraction method. The Hypurity C18 (100x4.6mm), 5 µ column were used for chromatographic separation. The run time was 3.3 minutes and volume ofr injection was set 2 µl.

The validated method for clebopride allows determination in the linearity range 0.051 to 10.352 ng/ml. Cinitapride was used as internal standard. The m/z of febuxostat was 374.2>184.1 and for cinitapride was 403.3>209.2. The extraction method was solid phase extraction. The injection volume was 15 µl and runtime was 2.2 minutes. The Hypersil Gold C18 (50 x 4.6mm), 5 µ column were used for chromatographic separation.

The validated method for darifenacin allows determination in the linearity range 018 to 10025.334 pg/ml. Darifenacin-d4 was used as internal standard. The m/z of febuxostat was 427.400>431.500 and for darifenacin-d4 was 147.100>151.100. The liquid-liquid extraction was used as extraction method. The volume foe injection was set 15 µl and runtime was 2.6 minutes. The Zorbax XDB-C18 (50 x 4.6 mm), 5 µ column was used for chromatographic separation.

The validated method for cycloserine allows determination in the linearity range 0.3064 to 25.1100 µg/ml. Niacin was used as internal standard. The m/z of febuxostat was
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103.100>124.000 and for niacin was 75.000>80.100. The extraction method was solid phase extraction. The injection volume was 2 µl and runtime was 3.0 minutes. The Hiber Purospher STAR RP18e (100 x4.6 mm), 3 µ column were used for chromatographic separation.

The validated method for carbocisteine allows determination in the linearity range 50.069 to 6008.310 ng/ml. Rosiglitazone was used as internal standard. The m/z of febuxostat was 180.000>89.000 and for niacin was 358.100>135.100. The protein precipitation was used as extraction method. The volume for injection was set 5 µl and runtime was 4.5 minutes. The Symmetry shield RP8 (150 x 3.9 mm), 5 µ column were used for chromatographic separation.

These all methods are suitable for determination concentrations in pharmacokinetic studies or in drug monitoring investigations and for the bioavailability.