2. Review of Literature:

Febuxostat Literature survey

Literature survey reveals that, few methods were reported for quantification of Febuxostat by using UV (17,18), Liquid chromatography (LC) (19-28), UPLC (29), UPLC-MS (30, 31), Liquid chromatography -Mass spectrometry (LC-MS) (32-34). These methods have been reported for the quantitative estimation of Febuxostat in pharmaceutical and biological fluids. Quantification of Febuxostat in biological matrices with LC-MS/MS were reported by Xitao ding and Wang H. et.al (33-34). Xitao ding et.al developed the method in rat plasma using protein precipitation extraction method by using acetonitrile as an precipitating agent. They developed with the linearity range of 10.00-2000.00 ng/mL for Febuxostat and used midazolam as internal standard and applied to determinate of Febuxostat in rat plasma for pharmacokinetic study. Wang H. et.al.,(34) developed the method in human plasma with protein precipitation extraction method and used acetonitrile as an precipitating agent. They developed the method with linear range of 10.00-5000.00 ng/mL for Febuxostat and used Febuxostat-d7 as an internal standard and performed the pharmacokinetic study in healthy Chinese volunteers.
Milnacipran Literature Survey

Literature survey reveals that, few methods were reported for quantification of MC in pharmaceutical (35-38) and biological fluids (39-41). They were quantified by several techniques such as, capillary electrophorics, micellar electro kinetic capillary, liquid chromatography (LC) and LC-MS/MS. However, LC-MS/MS has playing important role for the quantitative estimation of drugs in various biological matrices, including plasma, serum, urine, and ocular fluids, due to its high sensitivity, selectivity and reproducibility. Most of the published methods in the literature were liquid-liquid and solid-phase extraction (SPE) for quantification of MC in human plasma. Among all Shinozuka.et al (41) developed the most sensitive method in human plasma by using LC-MS/MS. However, it is required to develop the simplest, sensitive method with proper internal standard usage.
Mesalamine and N-Acetyl mesalamine Literature survey

Literature survey reveals that, only few methods were developed and validated for quantification of Mesalamine and N-Acetyl mesalamine by LC-MS (42-46), HPLC(47-61), micellar electrokinetic capillary chromatography (62), differential pulse voltammetry(63), Voltammetric studies(64). Among all, LC-MS methods were most accurate. These methods were developed in biological matrices by LC-MS, Pharmaceutical compounds by LC-MS. Gu GZ et.al., reported sulphasalazine and its main metabolite sulphapyridine and 5-aminosalicylic acid in human plasma by LC-MS/MS and established pharmacokinetic study. The reported method have some drawbacks in terms of sensitivity, repeatability and matrix effect issues. Hence it is required to develop most sensitive, rugged and reproducible method for quantification of Mesalamine and N-Acetyl mesalamine in human plasma.
Acamprosate Literature survey

Literature survey reveals that only a few methods were reported previously to determine Acamprosate by using proton emission tomography(65), LC-MS(66-69), HPLC(70), Capillary zone electrophorsis(71), LC-Flurometric electrochemical detection(72) in a variety of matrices like human plasma and dog urine, dog plasma, pharmaceutical. Among all the reported methods, LC-MS methods achieved best results.

Ghosh C, et.al explained more about matrix effect of acamprosate in biological matrices and they developed the method with Precipitation extraction method. Same authors (Ghosh C, et.al) reported for quantification acamprosate with the linearity range between 7.04-702.20 ng/ml with Precipitation extraction method by using LC-MS/MS in human plasma. Hammerberg A et.al reported the method, both in human plasma and CSF(Ceribro spinal fluid) with LC-MS/MS and they quantified the drug with the linearity range between 9-33 ng/ml in CSF and 25 times higher than CSF in human plasma. Rhee YS et.al reported the method in dog plasma by precipitation extraction method with LC-MS/MS with the linearity range between 200-10000 ng/mL. Chabenat.C et.al, reported the method in dog urine by using HPLC.
The reported methods do not provide stable, reproducible extraction methods in terms of matrix effect, and with high sensitive method. Hence it is required to develop most sensitive, rugged and reproducible method for quantification of Acamprosate in human plasma.