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Review article

Comprehensive review on method development of galantamine

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ABSTRACT

Galantamine is generally common in the treatment of Alzheimer's in old people. Galantamine is also used in combination treatments for Alzheimer. Different analytical techniques such as Liquid Chromatography-Mass Spectrometry, Reverse Phase-High Performance Liquid Chromatography,High Performance Liquid Chromatography, Ultra Performance Liquid Chromatography, and Ultraviolet Visible spectrometric method areused in the determination and validation of galantamine and its interactions. Different articles were reviewed and the results were found to be accurate and prudent in determining galantamine in human plasma and also other body fluids. Pharmacokinetic and bioequivalence investigations performed in different articles were summarized. All the methods stated in this article proves precise values and were found to be successful in determining and validating the drug galantamine and its interactions.Every method reviewed in this article are different from each other. This article summarizes few of the developed and validated analytical techniques available for the determination/ estimation/quantification and validation of Galantamine.

Keywords: Galantamine, Alzheimer disease, LC-MS, UV spectrometry, RP-HPLC.

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INTRODUCTION

Galantamine is an acetyl cholinesterase inhibitor that is taken orally to treat Alzheimer disease. The only acetyl cholinesterase inhibitor with both nicotinic receptor modification and acetyl cholinesterase inhibition [1-5]. It has been linked to a low rate of blood enzyme increases throughout treatment and has been linked to clinically obvious liver impairment [6-9]. Galanthus Nivalis is the plant source for the tertiary alkaloid, known to be identified in the early age of 1950s. The lectin obtained from the plant is studied to have activity potential against HIV. The phenanthridine alkaloid, lycorine is used as pharmaceutical drugs and herbal medicines.A finding in a study shows that the alkaloids present in the plant are majorly responsible for the inhibition of cholinesterase activities [10-12]. It was used to reverse the blockade in neuromuscular. It is also common in treating myopathies, a neuropathic disorder and also paralytics [13-15]. The medication to treat minor to moderate Alzheimer disease was authorised by the Food and Drug Administration (FDA) in the year 2001. It acts by inhibiting the enzyme that breaks down acetylcholine in the synaptic cleft, resulting in improved cholinergic neuron activity and signalling [16-20]. According to this proposed mode of action, galantamine's therapeutic benefits may wane as illness progresses and fewer cholinergic neurons remain functionally intact. As a result, it isn't regarded a disease modifying agent [21--24]. It is marketed as Razadyne an extended release, as oral tablet and also as solution [25]. The methods mentioned in this article are found to be safe and efficient for the determination of the drug. The methods mentioned below have used different internal standards, columns and their rate of flow has been varied. The analytical techniques reviewed in this article have two or more different methods and procedures to determine the drug. Different articles were reviewed to know varied methods and procedures available to be implemented in the single analytical technique [26-28].

Pharmacokinetics

Razadyne (Galantamine HBr)

Bioavailability- 80-100%

Half-life- 7 hours

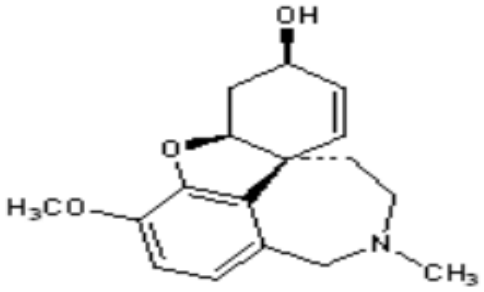
Volume of distribution- 175 L

Metabolism- partially metabolizes in the liver

Protein binding- Low 18%

It exhibits a linear pharmacokinetic ranging over 8-32 mg/day [29-32].

Figure 1: galantamine structure



Validated quantitative analytical methods

Liquid Chromatography-Mass Spectrometry

Method 1:

Using loratidine (IS), a quick, simple, selective and sensitive LC-MS/MS technique is devised for the measuring galantamine in human plasma. Following liquid-liquid extraction, the analytes are separated on a reverse phase C18 column with an isocratic mobile phase and analysed by mass spectrometry in the multiple reaction monitoring mode with the appropriate (M+H) +ions. Galantamine - M/z 288 to 213 & Loratidine- M/z 383, 337. In human plasma, a dynamic range that is linear was observed to be (0.5-100) ng/ml for galantamine. The relative SD was found to be >8%, the lowest limit of quantification in 0.5ng/ml. concentrations outside of the standard curve range provide acceptable precision & accuracy. With a sample run time of 2.5 minutes, more than 400 human plasma samples may be analysed every single day. Human plasma samples have been successfully analysed using the established technique for pharmacokinetic, bioavailability and bioequivalence investigations [33].

Method 2:

The measurement of galantamine in human plasma using commercially available chemical glimepiride as an IS was devised and confirmed utilising a simple, quick and selective LC-MS. Following a one-step liquid- liquid extraction with ethyl acetate, the analytes are separated on a reverse phase C18 Column. Acetonitrile&ammonium acetate (0.001m)is the mobile phase (isocratic) & analysed by mass spectrometry in multiple reaction monitoring mode using the transitions of respective M & H ions, and were found to be within (4 – 240) nanogram/ml, the SCC indicate acceptable linearity. Quantification is limited to 4ng/ml at the lowest level. Galantamine and IS had retention durations of 1.1 & 0.71 minutes respectively, indicating the suggested methods great throughput potential. Furthermore, no important metabolic chemicals were discovered to cause the study to fail. For concentration over the standard curve range, acceptable accuracy & precision are attained. Pharmacokinetic & bioequivalence investigations of 24mg of galantamine hydrobromide capsule in 32 healthy Korean participants were successfully completed using established technique [34].

Spectrophotometry

For the measurement of galantamine hydrobromide in bulk medication and tablet dosage form a two unique, new, low cost and easy UV spectrophotometric method and first order derivative approaches were devised and verified. In distilled water, Galantamine Hydrobromide was measured at 289nm. It had an amplitude of 284.8nm and a minimum of 290.4 nm in the first order derivative, with a zero crossing point of 286.4 nm. For the UV spectrophotometric approach (y=0.007x -0.002, r2= 0.999) and the first order derivative spectrophotometric method (Y= 0.0012x =0.00045; r2= 0.999) respectively, linearity was determined to be I the range of 20-100 g/ml. according to USP requirements, these procedures were examined and verified for numerous validation factors. For the UV spectrophotometric approach, the quantitation limits were determined to be 0.50 and 1.54 g/ml respectively. For the first order derivative approach, the concentration were 3.3 & 10 g/ml. the described procedures were used to successfully determine galantamine hydrobromide in tablet dosage forms. The technique is proved to be easy, accurate, cost-effective and repeatable (RSD 2%), and that it can be used to estimate Galantamine Hydrobromide in various dose forms [35].

RP-HPLC

Galantamine hydrobromide is determined using an easy and prudent validated RP-HPLC technique. The analysis was performed using a shimadzu HPLC system with a Phenomenex C18 Column (250 x 4.6mm i.d, 5 m particle size) it is done in Isocratic mode, the rate of flow was(0.4 ml.min-10, using 1mm ammonium formate: acetonitrile (30:70) as the mobile phase A and a flow rate of 0.4ml.min-1. A UV detector tuned 289 nm was used to do the detection. Beers law is followed in this approach for concentration of galantamine hydrobromide ranging from 100-1000 gml-1. The proposed technology has been used to analyse drug in bulk and pharmaceutical formulation with great success. For the brand formulation, the mean percent recoveries were determined to be 99.8-0.13. In terms of linearity, the approach was proven to be reliable [36].

HPLC

Galantamine, donepezil and rivastigmine are cholinesterase inhibitors used to treat patients with Alzheimer disease. In this technique, the Donepezil, Rivastigmine and Galantamine in Cerebrospinal fluid, blood serum and urine have all been produced and verified using an HPLC-DAD technique. The drug retention durations were 1.5, 2.2, &3.1 minutes respectively, while the total analysis time was 5 minutes. Linearity, accuracy, selectivity,

precision and stability were all tested throughout the validation. The approach was tested on clinical samples after it was validated. The newly established approach is a reliable tool for monitoring galantamine, donepezil and rivastigmine levels in urine and serum Cerebrospinal fluid in patients who are taking these medications [37].

UPLC-MS

In order to determine, quantify galantamine a UPLC-MS method was developed. The column used C18 column kept at 40°C, chromatographic separation was obtained. Solution A & B acetonitrile water is used as mobile phase and both contained 2mm ammonium formate, formic acid for 2%. The mobile phase was given using 3 minutes gradient programme that began with 95% A/5 % B and ended with 95 % A/5 %B at rate of flow of 0.6ml/min. the analyte& IS galantamine 3 were identified using the selected ion monitoring mode. According to FDA bioanalytical instructions, the procedures was validated. (2-2000) ng/ml was the observed range of analysis, the technique was selective & linear. With intraday and interday accuracies between 96.8% and precisions lesser than 4.88%, accuracy and precision were satisfactory. In the series of preclinical bioavailability experiments for the assessment of new galantamine formulations, the approach was effectively used to quantify galantamine plasma levels.

CONCLUSION

Galantamine is used with interactions like galantamine hydro bromide, galantamine benzyl ester etc. The drug is usually taken orally to treat Dementia/ Alzheimer disease. This article comprises few different analytical methods available for the determination of Galantamine with its interactions. The methods were validated using ICH & FDA guidelines. The analytical methods mentioned above are extremely accurate, prudent and permits the determination and validation of the drug galantamine.

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Conflict of interest

The authors declare no conflicts of interest for this study.

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