S2 P 102

Reverse phase LC method for in vitro dissolution test for determination of Bromazepam from tablet formulations

Authors
Irena Brchina[1], Biljana Gjorgjeska[2]*

Affiliations
1Irena Brchina,AD Jaka 80,Prvomajska 75A,Macedonia

2* Biljana Gjorgjeska, Ph.D,UGD,K. Misirkov bb,Macedonia

e-mail address of presenting author
biljana.gorgeska@ugd.edu.mk

Session
Pharmacoeconomics/Social Pharmacy/Drug information

Introduction
Disorders that involve anxiety are the most common mental disturbances. Many of the anti-anxiety drugs also cause some sedation, so the same drug is often functioning clinically as both, anxiolytic and hypnotic agent. Benzodiazepines are the most widely used anxiolytic drugs. They have largely replaced barbiturates in the treatment of anxiety, because the benzodiazepines are safer and more effective.

Anxiety is an unpleasant state of tension, apprehension, a fear that seems to arise from a sometimes unknown source. The physical symptoms of severe anxiety are similar to those of fear (such as tachycardia, sweating, trembling, and palpitations) and involve sympathetic activation. Episodes of mild anxiety are common life experiences and do not warrant treatment.

However, the symptoms of severe, chronic, debilitating anxiety may be treated with antianxiety drugs (sometimes called anxiolytic or minor tranquilizers) and/or some form of behavioral or psychotherapy.

Bromazepam is a benzodiazepine (BZD) generally used for a number of medical reasons, it is an intermidiate-acting tranquiliser (Ashton H, 2005), prescribed for the treatment of moderate to severe anxiety and panic attacks for the short-term treatment of insomnia.

It has been widely used in psychiatry disorders for four decades, with selective anxiolytic, anticonvulsant, myorelaxant and hypnotic actions. It acts on the central neural system as an inhibitor of the neurotransmitter gamma aminobutyric acid (GABA). (Guilherme Nobre Lima do Nascimento et al. 2012)

It is a drug that belongs to class of 1,4-benzodiazepine and chemically corresponds to 7-bromo-1,3-dihydro-5-(2-pyridyl)-2H-1,4-benzodiazepine-2-one, $C_{14}H_{10}BrN_3O$. (Ph.Eur 7th, 2010). It is a controlled psychotropic

substance-B1 class according National Agency of Sanitary Vigilance in Brazil (ANVISA), with the DCB identification numbers: 01366, DCI: 2692 and CAS: 1812-20-2. The solid form is the widespread used and prescribed in clinical practice. The solid form shows problems associated to the bioavailability, (FDA, 2003) indeed; the absorption of oral drugs in the solid form depends on the solubility and dissolution in physiologic liquids and its permeability through the gastrointestinal tract, factors that influence directly its bioavailability and subsequent pharmacological effects. The biotransformation from solid into absorbable form depends on its dissolution in organic liquids; therefore, dissolution tests became an essential parameter to determine the properties of biopharmaceutical formulations in order to predict their quality. The quality of pharmaceutical formulations is important in financial and ethical terms because it is directly associated with the patient's health. Thus, there is a real need for the development of dissolution tests able to predict in vivo physiological behavior.

Materials and Methods

Tablet dissolution test is a standardized method for measuring the rate of drug release from a dosage form, (FDA, 1997). For dissolution medium 0.1 M HCl was chosen, in volume of 500 ml, at 37ºC, performed on ERWEKA DT 700, apparatus 2 (paddle), with 75 rpm for 45 minutes.

An analytical method for Dissolution by using High Performance Liquid Chromatography technique was validated for content of Bromazepam and the validation was carried out on Shimadzu Nexera HPLC system.

To optimize chromatographic parameters several mobile phase compositions were tested in this method. A satisfactory separation, good peak symmetry and optimal retention time was obtained with mobile phase consisting a mixture of methanol, acetonitrile and potassium dihydrogen phosphate buffer (KH_2PO_4) (pH 7.0; 11.33g/l of KH_2PO_4) in ratio of 45:5:50 (v/v/v) that was set at flow rate of 1.0 ml/min was found to be optimum and further optimized by adjusting pH 7.0 by adding KOH 0.5M. A LiChrospher RP Select B column (125 × 4.0 mm, 5µm) is used as stationary phase with temperature of column oven, 50ºC.

Results and Discussion

A simple reverse phase HPLC method for in vitro dissolution test was developed and validated for the determination of Bromazepam and release from pharmaceutical dosage form. The elution was monitored at 239 nm. Chromatogram showed a peak of Bromazepam (BZP) at retention time of 3.50 ± 0.1 min. The linearity of Bromazepam was confirmed with correlation coefficient of 0.999.

The suitability of the mobile phase determined on the basis of the sensitivity of the dissolution, time required for the analysis, easy way of preparation and use of readily available cost effective solvents are benefits of the proposed method. The method was validated as per ICH guidelines with respect to specificity, linearity, accuracy, precision, robustness, solution stability and filter paper compatibility. All results of validation parameters meet the limits of ICH guidelines-(ICH Q2, 2005)

Conclusion

The proposed method is simple, rapid, accurate, precise, and specific without interference of excipients. Its chromatographic run time of 3.50 min allows the analysis of a large number of samples in short period of time. Therefore, it is suitable for the routine analysis of Bromazepam in pharmaceutical dosage forms. So it could be used for the rapid and reliable determination of Bromazepam in tablet formulations. Several high-performance liquid chromatographic (HPLC) methods have also been reported for the determination of Bromazepam and other BZDs-(Sruthi P, 2013) The present study is focused on minimizing limitations and developing a simple precise accurate and economic method for estimation of Bromazepam in tablet dosage form.

References

1. Ashton H. The diagnosis and management of benzodiazepine dependence, Curr Opin Psychiatry, 18, 2005, 249–255.

2. Guilherme Nobre Lima do Nascimento, Eurico Viegas Montalvão and Tales Alexandre Aversi-Ferreira, 2012, Study of the Pepsin Enzymatic Activity in in-vitro Dissolution Test of Bromazepam Tablets by UV/VIS Spectrophotometry, Journal of Applied Pharmaceutical Science Vol. 2 (10), pp. 011-015, October, 2012
3. European Pharmacopoeia 7 th Edition, 2010, 1507-1508
4. FDA (Food and Drug Adiministration) Guidance for industry. Bioavailability and Bioequivalence Studies for orally administred drug products–general considerations.
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070124.pdf, 2003
5. FDA (Food and Drug Adiministration) Guidance for industry. Dissolution Test of immediate release solid dosage forms.
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070237.pdf, 1997
6. ICH Q2. Validation of analytical procedures: text and methodology, International Conference on Harmonization Geneva, 2005, 1-13.
7. Sruthi P, Tejaswi N, Thanuja D, Sudheer Kumar P, Vivek Sagar. Simple RP- HPLC method for estimation of diazepam in tablet dosage form, Journal of Pharmacy Research, 1, 2013, 140-144.