Македонски Фармацевтски билтен

Macedonian Pharmaceutical Bulletin

волумен **62** (додаток) 2016 / volume **62** (supplement) 2016

Македонско фармацевтско друштво, ул. Маршал Тито 13б/8, Скопје, Македонија
Macedonian Pharmaceutical Association, Marshal Tito 13b/8, Skopje Macedonia

It is our great pleasure to present this Supplement Issue on "*Macedonian Pharmaceutical Bulletin*" to the scientific and professional community. This supplement includes the short communications from the *Sixth Congress of Pharmacy in Macedonia with International participation*, as the largest gathering for the pharmacy profession held in the Republic of Macedonia. The main theme of the Congress was "Modern pharmacist - bridging science with practice".

A broad spectrum of topics within the pharmaceutical sciences and practice carefully selected for this special occasion in order to build up a highly interesting and comprehensive program were covered. The contributions submitted to the Congress included 6 plenary lectures, 84 section lectures, and more that 240 posters. This Congress, followed the excellent international tradition, was attended by close to 1000 domestic and foreign participants. We received 326 short paper submissions from more than 25 countries. These numbers show that our Congress is aiming for the highest scientific standards, and that it can be considered a well-established venue for researchers in the broad fields of Pharmaceutical sciences and practice.

We would like to thank all internationally prominent researchers for their contribution to reinforcing the overall quality of the Congress. They give the state of the art of the recent advances in the field of pharmacy research.

Sincere thanks to the hosts of the Sixth Congress of Pharmacy in Macedonia with International participation, Macedonian Pharmaceutical Association and Faculty of Pharmacy, Ss Cyril and Methodius University in Skopje for their vision and commitments.

We acknowledge the sponsoring companies: the platinium sponsor AD ALKALOID, Skopje, the golden sponsor PLIVA, the silver sponsor EUROFARM and the bronze sponsor SEPTIMA, for the permanent support to our efforts during the organization.

We would also like to thank our members of the Scientific Committee for their volunteer time and dedication to the critical peer review process and in the organization of the program. We also wish to thank all the members of the Organizing Committee, whose work and commitment was invaluable.

On behalf of the Advisory and Scientific Committees, we would like to especially thank the authors, whose work was the essential part of the congress and contributed to a very successful event. Besides the many academic staff and professionals who contributed to the success of the Congress, we are grateful to the students who participated with oral presentations and posters.

The pharmaceutical sciences continue to grow as dynamic scientific interdisciplinary fields. We believe that published short communications will be an excellent source of scientific material in the fast evolving fields in Pharmaceutical sciences and practice.

Chair of the Scientific committee

Prof. Marija Glavas Dodov

Chair of the Organizing committee

Prof. Rumenka Petkovska

Your hosts
Macedonian Pharmaceutical Association
and
Faculty of Pharmacy, Ss Cyril and Methodius University in Skopje

Organizing Committee

Rumenka Petkovska, Ss Cyril and Methodius University, Faculty of Pharmacy / Chair
Zoran Sterjev, Ss Cyril and Methodius University, Faculty of Pharmacy / Co-Chair
Nikola Geskovski, Ss Cyril and Methodius University, Faculty of Pharmacy / Secretary
Jelena Acevska, Ss Cyril and Methodius University, Faculty of Pharmacy
Aleksandra Kapedanovska Nestorovska, Ss Cyril and Methodius University, Faculty of Pharmacy
Arlinda Haxhiu Zaimi, The State University of Tetovo, Faculty of Medical Sciences
Katerina Smilkov, Goce Delcev University, Faculty of Medical Sciences
Gjorge Stojadinovic, Alkaloid AD Skopje

Advisory Board

Svetlana Kulevanova - Macedonia, Suzana Trajkovic Jolevska - Macedonia,
Aleksandar Dimovski - Macedonia, Aneta Dimitrovska - Macedonia, Atila Hinchal –Turkey,
Biljana Bauer - Macedonia, Borut Bozic - Slovenia, Carmen Fernández – Sweden,
Dominik Duchene - France, Jerka Dumic – Croatia, Katerina Goracinova - Macedonia,
Lidija Petrusevska Tozi - Macedonia, Lilian Azzopardi - Malta, Ljubica Suturkova - Macedonia,
Nada Kovacevic - Serbia, Renata Slaveska Raicki – Macedonia, Slobodan Apostolski – Serbia,
Vasia Bankova – Bulgaria, Zoran Kavrakovski - Macedonia

Scientific Committee

Marija Glavas Dodov / Chair
Maja Simonoska Crcarevska / Secretary

Aleksandra Grozdanova - Macedonia
Ana Poceva Panovska - Macedonia
Antonio Makris - Greece
Arijana Meštrović -Croatia
Balázs Hankó - Hungary
César Viseras Iborra - Spain
Dea Baricevik - Slovenia
Dinko Vitezic – Croatia
Dragana Vujanović – Serbia
Ela Hoti - Albania
Emilija Janjevik - Macedonia
Giangiacomo Beretta - Italy
Gjose Stefkov - Macedonia
Jasmina Tonic Ribarska - Macedonia
Jelena Filipovich Grchic - Croatia
Johanes Novak - Austria
Katerina Ancevska Netkovska - Macedonia
Katerina Brezovska - Macedonia
Kristina Mladenovska - Macedonia
Margarida Caramona – Portugal
Marija Hiljadnikova Bajro - Macedonia
Michaele Montagne - USA
Milen I. Georgiev - Bulgaria
Milenko Tanasijevic – USA
Mitko Efremov - Italy
Nasir Behxheti - Macedonia
Nebojsa Menkovic - Serbia
Neda Mimica Dukić - Serbia
Ran Balicer - Israel
Rok Dreu – Slovenia
Rubin Zareski - Macedonia
Rumenka Petkovska - Macedonia
Sasha Baumgartner- Slovenia
Sema Calis – Turkey
Slavica Razic – Serbia
Suela Kellici - Albania
Tatjana Kadifkova Panovska - Macedonia
Vesna Kuntic - Serbia
Vilma Papajani - Albania
Zbigniew Fijałek - Poland
Zoran Sterjev - Macedonia

The present issue *of Macedonian Pharmaceutical Bulletin* is a special issue of the 6th Congress of Pharmacy in Macedonia with international participation.

This issue of *Macedonian Pharmaceutical Bulletin* contains short papers accepted by the scientific committee for the presentation at the Congress.

The authors are fully responsible for the contents of their short papers.

All reviewers that were involved in the short papers revision process are sincerely acknowledged.

Opening lecture

Macedonian pharmaceutical bulletin, **62** (suppl) 161 - 162 (2016)
ISSN 1409 - 8695
UDC: 615.214.24.074:543.544.5.068.7
Short communication

A rapid and validated reverse phase liquid chromatographic method for *in vitro* dissolution test for determination of bromazepam in tablet formulations

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

[1]*AD Jaka 80,Prvomajska 75A, Macedonia*
[2] *Department of Pharmacy, Faculty of Medical Sciences, Goce Delcev University, str. "Krste Misirkov" no.10-A, 2000 Stip, Republic of Macedonia*

Introduction

Disorders that involve anxiety are the most common mental disturbances. Many of the anti-anxiety medicines also cause some sedation, so the same medicine is often functioning clinically as both, anxiolytic and hypnotic agent. Benzodiazepines are the most widely used anxiolytic medicines. 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 medicines (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, 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) (Nascimento et al., 2012).

Bromazepam is an active substance 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., 2010). It is a controlled psychotropic substance-B1 class according to the National Agency of Sanitary Vigilance in Brazil (ANVISA), with the DCB identification numbers: 01366, DCI: 2692 and CAS: 1812-20-2. The solid dosage form (tablet) is the widespread used and prescribed in clinical practice. The solid dosage form presents problems associated to the bioavailability (FDA, 2003). The absorption of active substance from the solid dosage form for oral application 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 conditions.

Materials and methods

Dissolution test is a standardized method for measuring the rate of active substance release from a dosage form (FDA, 1997). The test was performed on ERWEKA DT 700, apparatus 2 (paddle), using 0.1 M HCl as a dissolu-

* biljana.gorgeska@ugd.edu.mk

tion medium, in volume of 500 ml, at 37°C, with 75 rpm for 45 minutes.

The quantity of the dissolved bromazepam was determined using analytical method based on High Performance Liquid Chromatography (HPLC). Validation of the method was performed 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 using mobile phase consisting of a mixture of methanol, acetonitrile and potassium dihydrogen phosphate buffer (11.33 g/l of KH_2PO_4, pH 7.0 adjusted with KOH, 0.5 M) in ratio of 45:5:50 (v/v/v), at flow rate of 1.0 ml/min. A LiChrospher RP Select B column (125 × 4.0 mm, 5µm) was used as stationary phase with temperature of column oven, 50 °C. The elution was monitored at 239 nm.

Results and discussion

A simple reverse phase HPLC method for *in vitro* dissolution test was developed and validated for the determination of bromazepam and its release from pharmaceutical dosage form. Several high-performance liquid chromatographic (HPLC) methods have also been reported for the determination of bromazepam and other BZDs (Sruthi et al., 2013). Chromatogram showed a peak of bromazepam (BZP) at retention time of 3.50 ± 0.1 min. The most suitable mobile phase was selected on the basis of time required for the analysis and the sensitivity of the method. The method was validated according to ICH Q2 guideline with respect to specificity, linearity (with correlation coefficient of 0.999), accuracy, precision, robustness, solution stability and filter paper compatibility. All results of the validation parameters were within the limits of ICH guidelines (ICH, 2005). The benefits of the proposed method include simple preparation of the solutions for the analysis and usage of readily available solvents.

Conclusion

The proposed method is simple, rapid, accurate, precise and specific without interference of excipients. The short chromatographic run time 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 and it could be used for the rapid and reliable determination of dissolved bromazepam in tablet formulations. The present study was focused on minimizing method limitations and developing a simple and economic method for determination of dissolved bromazepam from tablet dosage form.

References

Ashton, H., 2005. The diagnosis and management of benzodiazepine dependence. Curr. Opin. Psychiatry. 18(3), 249-255.

European Pharmacopoeia Commission, 2010. European Pharmacopoeia 7th Edition . Directorate for the Quality of Medicines & HealthCare of the Council of Europe (EDQM). Strasbourg, France. pp.1507-1508.

International conference on harmonisation of technical Requirements for registration of pharmaceuticals for human use (ICH), 2005. ICH Q2. Validation of analytical procedures. Harmonized tripartite guideline.

Nascimento, G. N. L., Montalvão, E. V., Aversi-Ferreira, T. A., 2012. Study of the pepsin enzymatic activity in *in-vitro* dissolution test of bromazepam tablets by UV/VIS spectrophotometry. J. App. Pharm. Sci. 2(10), 011-015.

Sruthi, A., Tejaswi, P., Thanuja, N., Sudheer Kumar, D., Vivek Sagar P., 2013. Simple RP-HPLC method for estimation of diazepam in tablet dosage form. J. Pharm. Res. 6, 140-144.

U.S. Department of Health and Human Services, Food and Drug Administration (FDA), Center for Drug Evaluation and Research (CDER). 1997. Dissolution Testing of Immediate Release Solid Oral Dosage Forms. Guidance for Industry.

U.S. Department of Health and Human Services, Food and Drug Administration (FDA), Center for Drug Evaluation and Research (CDER). 2003. Bioavailability and Bioequivalence Studies for orally administred drug products. Guidance for Industry.

CONTENTS

Opening lecture

Closing lecture

Plenary lectures

Pharmacoeconomy / Social pharmacy / Drug information

Pharmaceutical analysis / Quality assurance / Regulatory affairs

Clinical biochemistry / Toxicology / Food and nutrition

Pharmaceutical technology and biotechnology/ Cosmetology / Biopharmacy

Medicinal and aromatic plants

Clinical pharmacy / Pharmaceutical chemistry / Biomolecular sciences

Continual professional development

Student session