ANKARA UNIVERSITY
FACULTY OF PHARMACY

ISOPS 13th International SYMPOSIUM ON PHARMACEUTICAL SCIENCES

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JUNE 22-25, 2021
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Dear Participants and Guests,

I would like to express my sincere appreciation for the valuable contributions of all the participants of 13th International Symposium on Pharmaceutical Sciences (ISOPS). As we all know, the COVID-19 pandemic is still ongoing and the vaccination programmes are proceeding throughout the world. However, during 2021 we continue to face travel bans, governmental and contract restrictions in many countries. Therefore, the symposium was organized as a virtual event for the first time in its history.

ISOPS, initiated in 1989, has successfully brought international scientists, researchers, students together from pharmaceutical sciences and related areas. This symposium was organized biannually until 1997 and then every three years.

Ankara University, Faculty of Pharmacy is the first faculty of pharmacy in Turkey and was established in nineteen sixty (1960). Since the establishment, the institution rapidly progressed and now has very advanced scientific and physical infrastructure. Pharmaceutical science refers to a category of scientific fields and has followed important development processes, mainly in line with the developments in Biotechnology, Nanotechnology and Health Technologies, which are among the priority of the technology fields of today. While realizing the modern requirements, our Faculty has a 5-year undergraduate education programme since 2005 and besides Turkish; it provides an instruction programme in English language since 2015. Our faculty has 6689 graduates since its establishment and the current number of students is 1267. Present educational and scientific resources allow a total of 138 faculty members, 45 professors, 22 associate professors, 5 assistant professors, 51 research assistants in our faculty. Moreover, 66 administrative staff members and other personnel are working at different offices.

The mission of 13th International Symposium of Pharmaceutical Sciences was to perform a broad scientific perspective by the invitation of distinguished scientists having national / international reputation in their areas, so most recent advances were discussed interactively, and to empower the knowledge-based drug research development and multidisciplinary collaborations. It was our intention to make this symposium a memorable event.

This year, scientists from 24 countries registered to ISOPS-13. Our programme consisted of 40 plenary lectures, 212 oral and 200 poster presentations. Excellent research works were presented in different sessions. The speakers in the programme were uniquely placed in accordance to their area of expertise.

I would like to refer also to other initiatives that took place in our symposium. A workshop on "Employability of the Graduates of the Faculty of Pharmacy in Europe" was held with the contribution of Prof. Luciano Saso, Prof. Claire Anderson, Prof. Lilian M. Azzopardi, Prof. Sibel Süzen, Prof. İlkay Erdogan Orhan and Pharm. Nilhan Uzman. This workshop was interesting in terms of discussing the priorities and developments on this topic from local, regional and international respects.

On June 25, our panel on "University-industry-public sector cooperation in drug and vaccine development processes" was carried out by Prof. Dr. Asuman BOZKIR. The heads and *senior representatives of relevant institutions* including; Prof. Hasan Mandal, Assoc. Prof. Tolga Karakan, Pharm. Dr. Nihan Burul Bozkurt, Prof. Erhan Akdoğan, Assoc. Prof. Rabia Çakır Koç, Prof. Mayda Gürsel, Prof. Rana Sanyal, Prof. Hülya Ayar Kayalı, Dr. Süha Taşpolatoğlu, Dr. Hasan Ersin Zeytin, and Pharm. Dr. Ferhat Farşi were with us. This event has been a great platform to discuss the existing practices and requirements, and to propose solutions.

On behalf of the Organizing Committee, I would like to mention my gratitude to the President of Ankara University who gave full support for the Symposium Organization. ISOPS-13 was organized successfully, without any professional support, with the contribution of all our faculty members, especially our symposium secretary Assoc. Prof. Zerrin Sezgin-Bayındır. I congratulate the organizing committee and all the other committees with all my heart, as well as all academic and managing personnel because of their extensive work.

Prof. Dr. Asuman BOZKIR

Chair of ISOPS-13

Honory President of the Symposium

Prof. Dr. Necdet ÜNÜVAR

President of Ankara University

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CONTENTS

POSTER PRESENTATIONS

Materials and Methods: A modular capillary electrophoresis analyzer EA-102 (Villa Labeco, Spišská Nová Ves, Slovakia), assembled in the column-coupling configuration of the separation unit, was used in this work for performing the ITP-CZE runs. This CE analyzer was coupled to the triple quadrupole mass spectrometry detector (Agilent Technologies, Santa Clara, CA) via an elution block developed by Foret et al. (2).

Results: The optimized composition of electrolyte systems was: a) ITP stage – leading electrolyte (LE) = 10 mM NH4Ac + 20 mM HAc, terminating electrolyte (TE) = 10 mM HAc; b) CZE stage – background electrolyte (BGE) = 20 mM HAc. The limit of detection was predicted at pg/ml concentration level.

Conclusions: Two dimensional capillary electrophoresis based on on-line combination of capillary isotachophoresis and capillary zone electrophoresis hyphenated with mass spectrometry is an effective and sensitive tool for serotonine determination at very low concentration levels in real biological samples.

Acknowledgements

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P127: DETERMINATION AND POSSIBLE MECHANISMS OF FORMATION LUMACAFTOR DEGRADATION PRODUCTS WITH USING LCMS-IT-TOF

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Introduction: Lumacaftor (LUMA) is used as a combination therapy in cystic fibrosis, especially for homozygous for the F508del mutation patients (aged ≥12 years) (1). In the current study forced degradation products of LUMA were obtained, determined and possible formation mechanisms were proposed using high-resolution mass spectrometric data.

Methods: LCMS-IT-TOF analyses were performed using a hybrid IT-TOF mass spectrometer with ESI interface (Shimadzu, Japan). Analysis conditions were as follows: Nebulizing gas flow: 1.5 L/min; high voltage probe: -3.5 kV, drying gas pressure: 200 KPa, heat block temperature and CDL temperature: 200 °C. CID parameters are chosen 50% for collision gas parameter, 50% for CID energy and argon gas for CID. In addition, the detector voltage of TOF was set to 1.6 kV. The degradation conditions to which the active ingredient is exposed are made according to the ICH Q2 (R1) guideline (2).

Results: The results of forced degradation experiments revealed two new compounds in alkali and acid conditions, and three compounds in oxidation conditions. On the other hand, LUMA had no degradation in forced heat, moisture and UV-light conditions. Three of obtained degradation products had ionization in mass detector and their structure and possible formation mechanisms were proposed. The others had no ionization in mass detector, however detected using DAD detector.

Conclusion: LCMS-IT-TOF method was developed and examined for forced degradation products of LUMA. In addition to the above, new degradation products were added in to the literature.

Acknowledgements

This study was supported by a grant of Anadolu University Scientific research Projects Commission (Project No: 2005S039).

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P128: THE NOVEL APPROACH TOWARDS GRADIENT ELUTION HPLC METHOD DEVELOPMENT

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Introduction: Gradient elution HPLC finds its purpose in simultaneous analyses of solutes covering wide range of polarities. However, the instrument related factors, especially dwell volume,

are frequently responsible for fizzy transfer and short life cycle of the gradient elution method. Therefore, it is advisable to incorporate dwell volume into the optimization stage and avoid transfer related failures. The chemometric approach would enable selection of optimal chromatographic conditions for different HPLC instruments. The aim of this study was to propose and test this approach in gradient elution method's development.

Materials and Methods: The experiments were carried out on three chromatographic systems (UPLC, UHPLC and HPLC), while the separation was achieved on Kinetex C18 Core-shell column (100 mm × 2.1 mm, 2.6 µm particle size). Design of experiments was constructed in Design-Expert 11.0. Indirect modeling, grid point search and graphical presentations were done in Matlab 7.10.0.

Results: Dabigatrane etexilate mesylate and nine structurally related compounds were selected as suitable model mixture due to its complexity and polarity. Method development was supported with experimental design methodology, Placket – Burman for screening and D-optimal design for optimization purposes. Dwell volumes were included in the optimization phase and in this way the same optimal chromatographic conditions for all three instruments were selected.

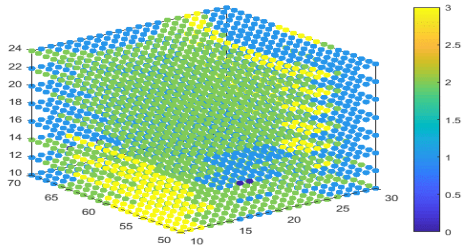

Fig 1: Experimental space overlap of instruments: yellow – 3 instruments, green – 2 instruments, light to dark blue 0 – 1 instrument

They included 10 mM ammonium acetate buffer with pH set to 4.9 using acetic acid, and acetonitrile. The components of the mobile phase were pumped into chromatographic system with flow rate of 400 µL min^{-1} in a linear gradient mode: at 0 minutes 24% (v/v) acetonitrile and 76% (v/v) of buffer solution, at 15 minutes 54% (v/v) acetonitrile and 46% (v/v) buffer solution. At 16 minutes the acetonitrile content was back to 24% (v/v) and 76% (v/v) of buffer solution. The re-equilibration time was set to 5 minutes. The examined chromatographic region is graphically presented and optimal conditions are noticed as the cross sections (yellow dots). The method was validated and confirmed its utility on all instruments.

Conclusions: The proposed methodology demonstrated its ability to predict joint optimal chromatographic conditions for instruments with different values of dwell volume. The potential was confirmed on complex model mixture and instruments significantly differing in dwell volume values. In this way the gap between developing and routine needs could be overwhelmed, followed by facilitated transfer of methods.

Acknowledgements

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P129: CHEMOMETRICALLY SUPPORTED OPTIMIZATION OF RP/WCX-HPLC METHOD

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Introduction: Active pharmaceutical ingredients (APIs) are often used in salt form, which is why the inclusion of weak cation exchange (WCX), in addition to reverse-phased (RP) hydrophobic interactions, could improve APIs' separation (1). Due to the limited knowledge about the RP/WCX bimodal system, the aim was to elucidate the experimental factors' influence on the retention of diverse ionized APIs, and provide efficient method optimization.

Materials and Methods: Acidic (ibuprofen (IB), aceclofenac (AC)) and basic (escitalopram (ES), aripiprazole (AR), atomoxetine (AT)) analytes were tested. Chromatography experiments were performed on Thermo Acclaim Mixed Mode WCX-1 (5 µm, 3x10 mm) column. Mobile phase consisted of ACN (30-50% (v/v)) and acetic buffer (pH 3.8 - 5.6; ionic strength (I) 20-40 mM). Temperature (T) was varied in range 30–38 °C. Variations of these factors were conducted according to Full Factorial Design 2^4. Optimization phase was executed by using face-centered Central Composite Design (Design-Expert 7.0.0).

Results: Screening results showed that %ACN had the greatest impact on analytes' retention factors (k), so increasing in %ACN caused a decrease in k. T had the same effect, but much less pronounced. Changes in mobile phase pH affected k, with the opposite effect on anionic and cationic