

## *Real-Time Oral Biodistribution of Fluorescent Labelled Olmesartan Medoxomil SMEDDS*

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### *Abstract*

Statement of the Problem: Nowadays, the use of fluorescent labeled molecules with near infrared (NIR) dye at in vivo imaging, are increasingly common in the pharmaceutical field. Several studies were conducted using in vivo imaging technique to determine the biological characteristics, biodistribution and toxicity of different drug carriers like microbubbles [1], nanobubbles, nanocapsules, nanodevices, polymer-shelled agents and nanoparticles [2]. Although there were many studies on the imaging of the drugs after iv injection, there have been no oral biodistribution studies similar to our study. BCS Clas II type, antihypertensive drug Olmesartan Medoxomil (OM) is a prodrug which is converted to olmesartan with low bioavailability in the gastrointestinal tract. The aim of this work was to prove increased oral biodistribution of Olmesartan by fluorescent labelled Self-Microemulsifying Drug Delivery System (SMEDDS). In this study, VivoTag® 680 XL was chosen for the determination of the biodistribution of OM-SMEDDS because SMEDDS includes nano and microsize of droplets and small molecules. The second dye, lipophilic infrared fluorescent cyanine Xenolight® DiR was selected due to the lipid characteristics of SMEDDS. Labelled OM-SMEDDS and control dye administered group of mice visualised and emission values were recorded during the experiment [3]. Preparation of OM-SMEDDS: The experiments were carried out using our previous standardized and optimized SMEDDS and validated HPLC method that reported in our previous article [4]. The precipitated OM-SMEDDS was transferred to another ependorf and the remaining washed portion was administered with 150 µl of oral gavage to the mice [3]. Findings: The fluorescent efficiency was calculated with Living Image® 4.4 software. Because the stomach has a dominant luminescence, the measurements were made with and without stomach. Representing the real-time biodistribution of OM-SMEDDS in vivo region of interest (ROI) values and ex vivo findings were recorded at predetermined times. (Figure 1). The results were statistically evaluated with one-way ANOVA (Analysis of variance) method. Differences in p values were considered significant ( $p < 0.05$ ). Conclusion & Significance: In this present study, a biocompatible imaging technique that can pass through

the gastrointestinal tract has been developed for the first time. Real-time in vivo imaging of oral biodistribution of fluorescence labeled OM-SMEDSS was performed successfully.



### *Biography:*

In 2017, Yelda Komesli completed her PhD degree program in Biopharmaceutical and Pharmacokinetics at Ege University Institute of Health Sciences. She worked as a Pharmacist in Konak-Izmir, Hereke-Izmit, Etlik-Ankara SSI Directorates. In 2018, she assigned as Assist Prof. Dr. in Van Yüzüncü Yıl University Faculty of Pharmacy. Since October-2019, she has been working as an Assist Prof. Dr. at the Department of Pharmaceutical Biotechnology, Faculty of Pharmacy, Department of Pharmacy Technology, Altınbaş University in Istanbul-TURKEY

### *Speaker Publications:*

1. Å. Barrefelt et al., "Fluorescence labeled microbubbles for multimodal imaging," *Biochem. Biophys. Res. Commun.*, vol. 464, no. 3, pp. 737–742, 2015.
2. B. Semete et al., "In vivo evaluation of the biodistribution and safety of PLGA nanoparticles as drug delivery systems," *Nanomedicine Nanotechnology, Biol. Med.*, 2010.

3. V. Kalchenko et al., "Use of lipophilic near-infrared dye in whole-body optical imaging of hematopoietic cell homing," *J. Biomed. Opt.*, vol. 11, no. 5, p. 050507, 2006.
4. Y. Komesli, A. Burak Ozkaya, B. Ugur Ergur, L. Kirilmaz, and E. Karasulu, "Design and development of a self-microemulsifying drug delivery system of olmesartan medoxomil for enhanced bioavailability," *Drug Dev. Ind. Pharm.*, vol. 45, no. 8, 2019.
5. S. D. Hellyer et al., "In vitro labelling of muscle type nicotinic receptors using a fluorophore-conjugated pinnatoxin F derivative," *Toxicon*, 2014.
6. J. J. Mulvey, E. N. Feinberg, S. Alidori, M. R. McDevitt, D. A. Heller, and D. A. Scheinberg, "Synthesis, pharmacokinetics, and biological use of lysine-modified single-walled carbon nanotubes," *Int. J. Nanomedicine*, vol. 9, pp. 4245–4255, 2014.
7. K. Thell et al., "Oral activity of a nature-derived cyclic peptide for the treatment of multiple sclerosis," *Proc. Natl. Acad. Sci.*, 2016.

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