

Review

of the domestic scientific supervisor

Candidate of Chemical Sciences, PhD, professor Uralbekov Bolat
for the thesis of Gurin Andrey Nikolaevich

«Development of a radiopharmaceutical based on Lu-177 labelled elagolix for therapy and
diagnosis»

submitted to the degree of Doctor Philosophy (PhD) in the specialty 6D060600 – Chemistry

The development of method for therapy and diagnosis is relevant task in Chemistry, especially in multidisciplinary field such as radiopharmaceutical chemistry. In work done by Gurin, one of the lutetium isotope (Lu-177) and its complexation were studied by advanced methods such as neutron-activation analysis, gamma-spectrometry, thin-layer chromatography, liquid chromatography and other research methods.

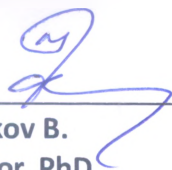
First of all, I need to mention about the compound, which was labelled by the isotope in the presented dissertation work. This compound entitled as elagolix, was described in 2005, while its clinical trials was carried out for the treatment of endometriosis just recently in 2016. Thus, this elagolix is a gonadotropin-releasing hormone antagonist (GnRH antagonist) medication which is used in the treatment of pain associated with endometriosis in women. However, to the best of my knowledge, there is no detail studies related to its labeling by proper radioisotopes to further application this as a radiopharmaceutical for cancer therapy and treatment.

The goal of Gurin Andrey Nikolaevich's dissertation work was to study radiolabelling of elagolix by Lu-177 and to find optimal condition of this process. The problem of this goal associated with that fact that lutetium cannot be bonded to elagolix directly, so first it was need to prepare the so called DATOELA composite, which has proper site to be bonded by such complexing agent as lutetium. And this work has been done in association with leading radiochemical laboratory in Oslo University, under Prof. Patrik Riss supervision. This substance was successfully delivered to Almaty for further investigation.

Secondly, it was necessary to prepare radioactive source with proper nuclear characteristics such as specific activity, and purity. And this task was successfully implemented on the basis of Almaty nuclear physics institute within ministry project AP 05134384 «Determination of the optimal technological parameters for preparation of a new radiopharmaceutical for diagnosis and therapy of thrice-negative breast cancer (TNBC) with an elagolix-¹⁷⁷Lu of antagonistic mechanism of action.» (2018-2020 yy.). In these experiments Andry Gurin with co-workers showed that source of Lu-177 with suitable activity can be prepared by the neutron activation reaction through $^{176}\text{Lu} (n, \gamma)^{177}\text{Lu}$ at the WWR-K reactor under thermal neutron flux of $1.2 \cdot 10^{14} \text{ cm}^{-2} \cdot \text{s}^{-1}$. Due to small amount of DATOELA available to study, it was possible to investigate only major parameters like complexation and its stability, an attempt was made to purify the Lu-DATOELA coordination compound. Andrey Nikolaevich also suggested a block-scheme to prepare the radiopharmaceuticals, including the preparation step, characterization and synthesis.

With regards of Gurin Andrey Nikolaevich personal attributes, I need to mention the following: responsibility, independence, thoughtfulness and ability to solve assigned tasks. He published (co-authored) two paper in peer-reviewed journals such as Pharmaceutical Chemistry Journal and Revista de Chimie. He undertaken internship to University of Oslo, and got experience to do radiochemistry and radiolabeling.

I should mention that all obtained results is of great relevance due to study the labeling of new compound, which is of great interests within pharmacy scientific community. Contribution to the chemistry is obvious and can be expressed as study the chemistry of coordination compounds of lutetium radioisotope. Taken into consideration abovementioned, I consider that Gurin Andrey Nikolaevich's dissertation work fully complies the qualification requirements for PhD thesis in the specialty 6D060600 – Chemistry and may be submitted to be considered at the Dissertation Council.



Uralbekov B.
Professor, PhD
Chair, general and inorganic chemistry
Faculty, chemistry and chemical technology
al-Farabi Kazakh National University

РАСТАВЕРЖАЮЩИЙ
ал-Фараби атындағы Қазақ Ғылыми кадрларды
даярлау және аттестаттау басқармасының басшысы
ЗАВЕРЯЮ
Начальник управления подготовки и аттестации
научных кадров КазНУ им. аль-Фараби

Р.Е. Кудайбергенова

20 ж.т.

