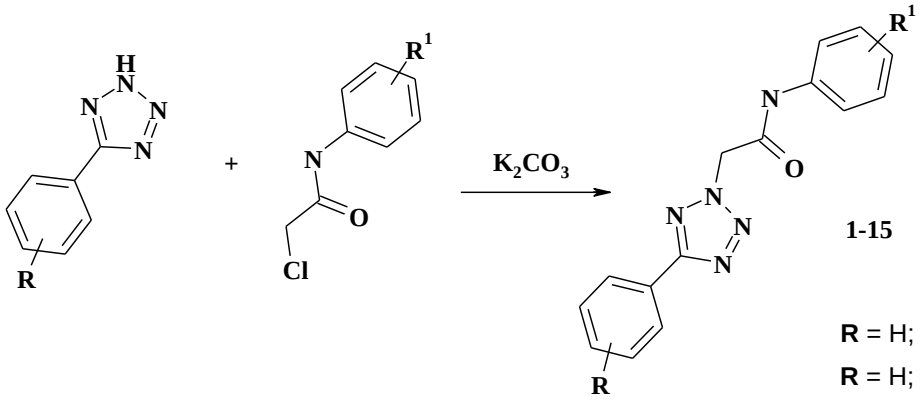
SYNTHESIS AND ANTICANCER PROPERTIES OF SOME *N*-ARYL-2-(5-ARYLTETRAZOL-2-YL)ACETAMIDES

Chaban T.I., Matiichuk Y.E., Myrko I.I., Chaban I.G., Matiychyk V.S.
[1]Danylo Halytsky Lviv National Medical University, Lviv, Ukraine
[2]Ivan Franko National University of Lviv, Lviv, Ukraine
chabantaras@ukr.net

The problem of finding effective low-toxic antitumor drugs is one of the most important in modern medicine and pharmacy. According to World Health Organization, more than 10 million new cancer patients appear annually. In recent years, pharmacotherapy of tumor pathology has been enriched with numerous new drugs that increase its effectiveness and safety. However, despite significant advances in the chemotherapy of malignant tumors, many types of cancer remain incurable, and the available of antitumor drugs is clearly insufficient. Therefore, the search for new organic compounds with anticancer activity is an urgent problem of our time.

Tetrazole and their derivatives are present in many of the bioactive heterocyclic compounds that are of wide pharmacological interest. Among the specified class of compounds were researched antimicrobial, anti-fungal, anti-viral, antitubercular, antiproliferative, anti-inflammatory, antioxidant, anticancer, anti-hypertension activities. Taking all mentioned above into account, in this paper, we present work was to synthesize a series of novel *N*-aryl-2-(5-aryltetrazol-2-yl)acetamides by means with further pharmacological screening on anticancer activity.

The desired compounds (**1-15**) were prepared by reacting 5-phenyl-2*H*-tetrazole or 5-p-tolyl-2*H*-tetrazole with appropriate 2-chloro-*N*-arylacetamides. This nucleophilic substitution reaction was carried out in the presence of potassium carbonate.



R = H; **R$_1$** = H (**1**);
R = H; **R$_1$** = 3-CH_3 (**2**);
R = H; **R$_1$** = 2,3 -$(CH_3)_2$ (**3**);
R = H; **R$_1$** = 2,5 -$(CH_3)_2$ (**4**);
R = H; **R$_1$** = 3,4 -$(CH_3)_2$ (**5**);
R = H; **R$_1$** = 2 -OCH_3 (**6**);
R = H; **R$_1$** = 2 -OC_2H_5 (**7**);
R = H; **R$_1$** = 4 -OC_2H_5 (**8**);
R = H; **R$_1$** = 4 -Br (**9**);
R = H; **R$_1$** = 2 -CH_3, 3-Cl (**10**);
R = H; **R$_1$** = 2 -CH_3, 5-Cl (**11**);
R = H; **R$_1$** = 3 -CH_3, 4-Cl (**12**);
R = 4-CH_3; **R$_1$** = 3-CH_3 (**13**);
R = 4-CH_3; **R$_1$** = 4-Cl (**14**);
R = 4-CH_3; **R$_1$** = 4-OC_2H_5 (**15**).

The structures of the obtained compounds were confirmed by 1H-NMR spectroscopy and elemental analysis. In 1H-NMR spectra it was found that the signals for the protons of all the structural units were observed in their characteristic ranges.

The synthesized compounds were selected by the National Cancer Institute (NCI) Developmental Therapeutic Program (www.dtp.nci.nih.gov) for the *in vitro* cell line screening

to investigate their anticancer activity. Primary anticancer assay was performed at approximately sixty human tumor cell lines panel derived from nine neoplastic diseases, in accordance with the protocol of the Drug Evaluation Branch, National Cancer Institute, Bethesda (USA). The results for each tested compound were reported as the percent of growth of the treated cells when compared to the untreated control cells. The percentage growth was evaluated spectrophotometrically versus controls not treated with test agents.

As the experiment showed, all compounds showed low or moderate activity against most malignant tumor cells. But in case of compounds **1**, **6**, **8**, **10**, **11**, **12** against several cancer cell lines the high activities was observed. The most sensitive were PC-3 Prostate cancer cell lines (GP = 34.42 %) and RXF 393 Renal cancer cell line (GP = 39.32%) to the compouds **6** and **8**. The compound **8** stimulate growing of NCI-H522 Non-Small Cell Lung Cancer, IGROV1 Ovarian Cancer and HOP-92 Non-Small Cell Lung Cancer. It should also be noted that compounds **1**, **10**, **11** and **12** effectively promote growth of UO-31 Renal Cancer cell line. Further optimization of the structure to improve biological activity is currently in progress.