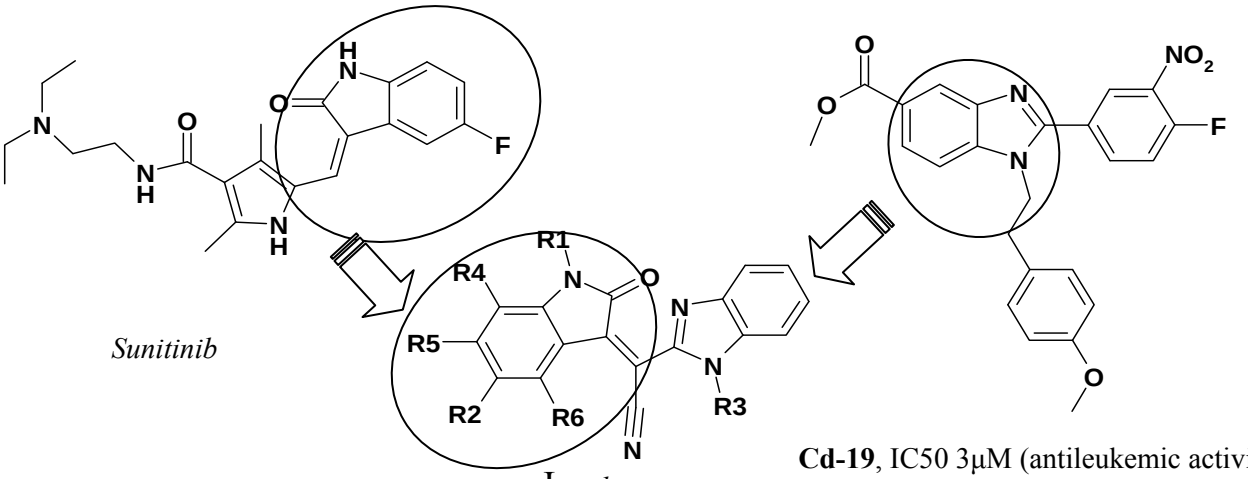
CONSTRUCTION FOCUS LIBRARY OF 2-BENZIMIDAZOLE OXINDOL NUCLEI EXHIBITING ANTITUMOR PROPERTIES POTENTIAL

Novikov V.A., Redkin R.G., Shemchuk L.A., Chernykh, V.P.
The National University of Pharmacy, Kharkiv, Ukraine
v-novikov-naydar@mail.ru

It is known that a number of diseases including autoimmune, cancer starts activating protein kinases that play a key role in the regulation of a wide variety of cellular processes, including metabolism, cell proliferation, cell differentiation, cell survival, angiogenesis and immune response. Therefore, identification of inhibitors of protein kinases that can potentially be effective as therapeutic agents against these diseases is an important task of the modern pharmaceutical science.



I *de novo*

Cd-19, IC50 3μM (antileukemic activity)

The greatest practical importance, such studies have to design de novo, synthesis and search for new molecules drug substances. The purpose of this paper is de novo design and the search for new drug-like molecules – potential inhibitors of kinases 2-oxindolin 3-acrylonitrile benzimidazole nuclei. To design focus library of new compounds we used Chemoinformatics methods. The initial platforms chosen synthetic 2-oxindolin metyliden fragment characteristic of already known kinase inhibitor Sunitinib, allowed for the treatment of renal carcinoma and gastrointestinal tumors. As a reference drug used as an experimental compound CD-19 high antileukemic activity. All calculations of molecular descriptors were taken with a software system Molinspiration Cheminformatics v2013.09, 2013 (University of Bratislava, Slovakia). As a result of variation over a 6-point randomization in the proposed molecular platform we were able to find the structure (I) with high forecast kinase inhibitor activity. The greatest value of the likelihood function kinase inhibitory activity was found for compounds with substituents F, OH, negative feedback caused substituents at the nitrogen atom in the 2-oxindolic nucleus.